

Keystone First - CHIP

**PRIOR AUTHORIZATION
CRITERIA**

Effective 07/01/2025

Title: Abaloparatide (Tymlos™)/ teriparatide (Forteo®)

Applicable Drugs:

Brand Name	Generic Name
Tymlos™	abaloparatide
Forteo®	teriparatide

Policy:

Primary or hypogonadal osteoporosis in men and Glucocorticoid-induced osteoporosis in men or women

INITIAL CRITERIA: Teriparatide (Forteo®) is medically necessary when ALL of the following are met:

1. The member is 18 years of age or older; and
2. ONE of the following:
 - a. Primary or hypogonadal osteoporosis in men; or
 - b. Glucocorticoid-induced osteoporosis in men or women (daily dose greater than or equal to 5mg prednisone or equivalent for at least 3 months); and
3. ONE of the following:
 - a. Member is high risk for fracture defined by ONE of the following:
 1. History of osteoporotic fractures (low-trauma fracture of the hip, spine, proximal humerus, pelvis, or distal forearm); or
 2. At least two risk factors for a fracture (e.g., endocrine disorders, gastrointestinal disorders, use of medications associated with low bone mass or bone loss such as corticosteroids); or
 3. Member has a T score of at least -2.5 standard deviations below the young adult mean (T-score $\leq$ -2.5); or
 - b. Inadequate response or inability to tolerate ONE of the following osteoporosis therapies:
 1. Bisphosphonates; or
 2. Hormone replacement therapy; or
 3. Selective estrogen receptor modulators (SERMs); or
 4. Calcitonin salmon (Miacalcin); or
 5. Denosumab (Prolia); and
4. For Forteo® only, inadequate response or inability to tolerate Teriparatide® manufactured by Alvogen

Initial Authorization duration: 12 months

REAUTHORIZATION CRITERIA: Teriparatide (Forteo®) is medically necessary when BOTH of the following are met:

1. Documentation of positive clinical response; and
2. ONE of the following:
 - a. Cumulative lifetime therapy does not exceed 2 years; or
 - b. For Forteo® only, member remains at or has returned to having a high risk for fracture despite a total of 24 months of use for parathyroid hormones

Reauthorization duration: 12 months

Postmenopausal osteoporosis

INITIAL CRITERIA: Abaloparatide (Tymlos™) or teriparatide (Forteo®) is medically necessary when ALL of the following are met:

1. The member is 18 years of age or older; and
2. Diagnosis of postmenopausal osteoporosis; and
3. ONE of the following:
 1. Member is high risk for fracture defined by ONE of the following:
 1. Member has a T score of at least -2.5 standard deviation below the young adult mean (T-score $\leq$ -2.5); or
 2. History of osteoporotic fractures (low-trauma fracture of the hip, spine, proximal humerus, pelvis, or distal forearm); or
 3. At least two risk factors for a fracture (e.g., endocrine disorders, gastrointestinal disorders, use of medications associated with low bone mass or bone loss such as corticosteroids); or
 2. Inadequate response or inability to tolerate ONE of the following osteoporosis therapies:
 1. Bisphosphonates; or
 2. Hormone replacement therapy; or
 3. Selective-estrogen receptor modulators (SERMs); or
 4. Calcitonin-salmon (Miacalcin®); or
 5. Denosumab (Prolia®); and
4. For Forteo® only, inadequate response or inability to tolerate Teriparatide® manufactured by Alvogen

Initial Authorization duration: 12 months

REAUTHORIZATION CRITERIA: Abaloparatide (Tymlos™) or teriparatide (Forteo®) is medically necessary when BOTH of the following are met:

1. Documentation of positive clinical response; and
2. ONE of the following:
 - a. Cumulative lifetime therapy does not exceed 2 years; or
 - b. For Forteo® only, member remains at or has returned to having a high risk for fracture despite a total of 24 months of use for parathyroid hormones

Reauthorization duration: 12 months

Increase bone density in men with osteoporosis at high risk for fracture

INITIAL CRITERIA: Abaloparatide (Tymlos®) is medically necessary when ALL of the following are met:

1. Diagnosis of primary or hypogonadal osteoporosis; and
2. The member is 18 years of age or older; and
3. Both of the following:
 - a. Bone mineral density (BMD) T-score of -2.5 or lower in the lumbar spine, femoral neck, total hip, or radius (one-third radius site); and
 - b. One of the following:
 1. History of low-trauma fracture of the hip, spine, proximal humerus, pelvis, or distal forearm; or
 2. Inadequate response or inability to tolerate at least one osteoporosis treatment (e.g., alendronate, zoledronic acid, Prolia [denosumab])

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Abaloparatide (Tymlos®) is medically necessary when BOTH of the following are met:

1. Documentation of positive clinical response; and
2. Cumulative lifetime therapy does not exceed 2 years

Reauthorization duration: 12 months

* Coverage duration of Teriparatide and Tymlos™ is limited to 730-day supply max per lifetime. All other treatment durations are considered Experimental/Investigational.

**Osteoporosis defined as T score of the individual's bone mineral density (BMD) is at least -2.5 standard deviations below the young adult mean OR history of osteoporotic fracture (i.e. hip, spine, etc.)

P&T Approval Date: Sep-12-2024

Title: Actinic Keratosis agents and Zyclara®

Applicable Drugs:

Brand Name	Generic Name
Picato®	ingenol mebutate
Solaraze® Klisyri™	diclofenac 3% Tirbanibulin
Zyclara™	Imiquimod

Policy:

INITIAL CRITERIA Ingenol mebutate (Picato®), diclofenac 3% (Solaraze®) gel, imiquimod (Zyclara®) 3.75%, 2.5%, or tirbanibulin (Klisyri®) is medically necessary when BOTH of the following are met:

1. Diagnosis of actinic keratosis; and
2. Member is 18 years of age or older; and
3. ONE of the following:
 - a. For imiquimod (Zyclara®) 3.75%, 2.5% only, inadequate response or inability to tolerate imiquimod 5%; or
 - b. For tirbanibulin (Klisyri®) only, inadequate response or inability to tolerate BOTH of the following generics:
 1. Fluorouracil; and
 2. Imiquimod

Initial authorization duration:

- 30 days for tirbanibulin (Klisyri®), ingenol mebutate (Picato®) imiquimod (Zyclara®) 3.75%, 2.5%.
- 3 months for diclofenac 3% (Solaraze®)

REAUTHORIZATION CRITERIA Ingenol mebutate (Picato®), diclofenac 3% (Solaraze®) gel, imiquimod (Zyclara®) 3.75%, 2.5%, or tirbanibulin (Klisyri®) is medically necessary when there is documentation of a diagnosis of actinic keratosis at a different site.

Reauthorization duration:

- 30 days for tirbanibulin (Klisyri®), ingenol mebutate (Picato®) imiquimod (Zyclara®) 3.75%, 2.5%.
- 3 months for diclofenac 3% (Solaraze®)

Genital warts

INITIAL CRITERIA Imiquimod (Zyclara®) 3.75% is medically necessary when BOTH of the following are met:

1. Diagnosis of genital warts; and
2. Member is 12 years of age or older; and
3. Inadequate response or inability to tolerate imiquimod 5%

Initial authorization duration: 30 days

REAUTHORIZATION CRITERIA Imiquimod (Zyclara®) 3.75% is medically necessary when there is documentation of positive clinical response to therapy.

Reauthorization duration: 30 days

1. No concurrent use with rozanolixizumab-noli (Rystiggo), eculizumab (Soliris), ravulizumab-cwvz (Ultomiris) or efgartigimod alfa-fcab (Vyvgart, Vyvgart Hytrulo)

Reauthorization duration: 12 months

P&T Approval Date: Sep-12-2024

Title: Acute Seizure Activity Agents

Applicable Drugs:

Brand name	Generic name
Nayzilam®	Midazolam
Valtoco®	Diazepam
Libervant™	Diazepam

Policy:

INITIAL CRITERIA: Midazolam (Nayzilam®), Diazepam (Libervant™) buccal film or Diazepam (Valtoco®) nasal spray is approved when ALL of the following are met:

1. Diagnosis of intermittent, stereotypic episodes of frequent seizure activity (i.e., seizure clusters, acute repetitive seizures) that are distinct from a patient's usual seizure pattern; and
2. ONE of the following:
 1. For midazolam (Nayzilam®) only, member is 12 years of age or older; or
 2. For diazepam (Libervant™) only, member is 2 to 5 years of age; or
 3. For diazepam (Valtoco®) only, member is 6 years of age or older; and
3. Prescribed by or in consultation with a neurologist/epilepsy specialist

Initial Authorization duration: 2 years

REAUTHORIZATION CRITERIA: Midazolam (Nayzilam®) nasal spray, Diazepam (Libervant™) buccal film or diazepam (Valtoco®) nasal spray is reapproved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

P&T Approval Date: March 20, 2025

Title: Adjunctive treatment for Parkinson's Disease

Applicable Drugs:

Brand Name	Generic Name
Inbrija™	Levodopa inhalation
Nourianz™	Istradefylline
Apokyn®	Apomorphine
Kynmobi™	Apomorphine

Policy:

Parkinson's Disease

INITIAL CRITERIA: Levodopa inhalation (Inbrija™), or istradefylline (Nourianz™) is approved when ALL of the following are met:

1. Diagnosis of Parkinson's disease and member is experiencing intermittent off episodes; and
2. Member is 18 years of age or older; and
3. Concurrent use of carbidopa/levodopa containing product at maximally tolerated dose; and
4. Prescribed by or in consultation with a neurologist; and
5. Member had inadequate response or inability to tolerate TWO of the following:
 - a. MAO-B Inhibitor (e.g., rasagiline, selegiline); or
 - b. Dopamine Agonist (e.g., pramipexole, ropinirole); or
 - c. COMT inhibitor (e.g., entacapone)

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA: Levodopa inhalation (Inbrija®), or istradefylline (Nourianz™) is re-approved when ALL of the following are met:

1. Documentation of positive clinical response to therapy; and
2. Concurrent use of carbidopa/levodopa containing product

Advanced Parkinson's Disease

INITIAL CRITERIA: Apomorphine (Apokyn®, Kynmobi™) is approved when ALL of the following are met:

1. Diagnosis of advanced Parkinson's disease and member is experiencing intermittent "off" episodes; and
2. Member is 18 years of age or older; and

3. One of the following:
 - a. Member is receiving medication in combination with other medications for the treatment of Parkinson's disease at maximally tolerated dose (e.g., carbidopa/levodopa, pramipexole, ropinirole, etc...); or
 - b. Member has a contraindication or intolerance to other medications for the treatment of Parkinson's disease; and
1. Member is not using the medication with any 5-HT3 antagonist (e.g., ondansetron, granisetron, dolasetron, palonosetron, alosetron); and
2. For Apomorphine (Apokyn®) inadequate response or inability to tolerate apomorphine (Kynmobi™); and
3. Prescribed by or in consultation with a neurologist

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA: Apomorphine (Apokyn®, Kynmobi™) is re-approved with documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

P&T Approval Date: Mar-14-2024

Title: Allergen Specific SL Immunotherapy

Applicable Drugs:

Brand Name	Generic Name
Grastek®	grass pollen allergen extract-timothy grass
Oralair®	grass pollen allergen extract-5 grass
Ragwitek®	short ragweed pollen allergen extract
Odactra™	house dust mite allergen extract

Policy:

INITIAL CRITERIA: Odactra™, Oralair®, Grastek® or Ragwitek® is approved when ALL of the following are met:

1. FDA approved indication; and
2. Patient has a positive skin test or in vitro test for ONE of the listed pollen-specific IgE antibodies:
 1. Timothy Grass or cross-reactive grass pollens (GRASTEK® only); or
 2. Any of the five grass species including sweet vernal, orchard perennial rye, timothy or Kentucky blue grass mixed pollens (ORALAIR® only); or
 3. Short ragweed pollen (RAGWITEK® only); or
 4. Dermatophagoides farina or Dermatophagoides pteronyssinus house dust mites (ORDACTRA™ only); and
3. Prescribed by or in consultation with allergist or immunologist and
4. ONE of the following:
 1. For Grastek, member is between 5 to 65 years of age; or
 2. For Odactra, member is between 12 to 65 years of age; or
 3. For Oralair, member is between 5 to 65 years of age; or
 4. For Ragwitek, member is between 5 to 65 years of age; and
5. Patient does not have any of the following:
 1. Severe, unstable or uncontrolled asthma; or
 2. History of eosinophilic esophagitis; and
6. Patient has had an inadequate response or inability to tolerate BOTH of the following:
 1. Intranasal corticosteroid; and
 2. Antihistamine

Initial Authorization duration: 1 year

REAUTHORIZATION CRITERIA: Odactra™, Oralair®, Grastek® or Ragwitek® is re-approved when ALL of the following are met:

1. Use in the age group supported by FDA labeling; and
2. Prescribed by or in consultation with allergist or immunologist; and
3. Patient has experienced improvement in the symptoms of their allergic rhinitis OR a decrease in the number of medications needed to control allergy symptoms

Reauthorization duration: 1 year

P&T Approval Date: March 20, 2025

Title: Alpelisib (Vijoice®)

Applicable Drugs:

Brand Name	Generic Name
Vijoice®	Alpelisib

Policy:

INITIAL CRITERIA Alpelisib (Vijoice) is medically necessary when ALL of the following are met:

1. Diagnosis of PIK3CA-Related Overgrowth Spectrum (PROS); and
2. Documentation of mutation in the PIK3CA gene; and
3. Member is 2 years of age or older; and
4. Documentation of severe clinical manifestations (e.g., Congenital Lipomatous Overgrowth, Vascular malformations, Epidermal nevi, Scoliosis/skeletal and spinal [CLOVES], Facial Infiltrating Lipomatosis [FIL], Klippel-Trenaunay Syndrome [KTS], Megalencephaly-Capillary Malformation Polymicrogyria [MCAP]); and
5. Prescribed by or in consultation with a provider who specialized in the treatment of PROS

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA Alpelisib (Vijoice®) is medically necessary when ALL of the following are met:

1. Documentation of positive clinical response to therapy (e.g., radiological response defined as a $\geq 20\%$ reduction from baseline in the sum of target lesion volume); and
2. Prescribed by or in consultation with a provider who specializes in the treatment of PROS

Reauthorization duration: 12 months

P&T Approval Date: Sep-12-2024

Title: Amifampridine (Firdapse®)

Applicable Drugs:

Brand Name	Generic Name
Firdapse®	amifampridine phosphate

Policy:

INITIAL CRITERIA: Amifampridine (Firdapse®) is approved when ALL of the following are met:

1. Member has a diagnosis of Lambert-Eaton myasthenic syndrome; and
2. Member is 6 years of age or older and
3. Neurological symptoms persist after treatment of malignancy when malignancy is present; and
4. Documentation of symptomatic LEMS that interfere with daily functions (e.g., difficulty climbing stairs, walking up steep hills); and
5. Prescribed by or in consultation with a neurologist; and
6. Member does not have history of seizures

Initial authorization duration: 3 months

CONTINUATION CRITERIA: Amifampridine (Firdapse®) is re-approved when there is documentation of positive clinical response to therapy (e.g., improvement in dynamometry, Timed 25-Foot Walk Test, Timed Up and Go Test)

Reauthorization duration: 2 years

P&T Approval Date: March 20, 2025

Title: Amikacin liposome inhalation suspension (Arikayce)

Applicable Drugs:

Brand Name	Generic Name
Arikayce®	Amikacin liposome inhalation suspension

Policy:

INITIAL CRITERIA: Arikayce® (amikacin liposome inhalation suspension) is approved when ALL of the following are met:

1. Diagnosis of refractory Mycobacterium avium complex (MAC) lung disease; and
2. Member has not achieved negative sputum cultures after a minimum of 6 consecutive months of multidrug background regimen therapy; and
3. Documentation that the medication will be used as part of a combination antibacterial regimen; and
4. Member is 18 years of age or older; and
5. Prescribed by or in consultation with a pulmonologist or infectious diseases specialist

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Arikayce® (amikacin liposome inhalation suspension) is re-approved when both of the following are met:

1. Documentation of positive clinical response to therapy; and
2. Documentation that the medication will be used as part of a combination antibacterial regimen

Reauthorization duration: 12 months

P&T Approval Date: Jul-01-2024

Title: Androgens

Applicable Drugs:

Brand Name	Generic Name
Androgel®	Testosterone
Androderm®	Testosterone
Fortesta®	Testosterone
Natesto®	Testosterone
Striant®	Testosterone
Testim®	Testosterone
Vogelxo®	Testosterone
Aveed®, Jatenzo®, Tlando®, Kyzatrex®, Undecatrex	Testosterone undecanoate
Testred®, Android®, Methitest®	Methyltestosterone
Xyosted™	Testosterone enanthate
Azmiro	Testosterone cypionate

Policy:

Primary or secondary hypogonadism

INITIAL CRITERIA: Androgel®, Androderm®, Fortesta®, Natesto®, Testim®, Vogelxo®, Xyosted™, testosterone undecanoate (Jatenzo®, Tlando®, Kyzatrex®, Aveed®), or methyltestosterone (Methitest®) is approved when ALL of the following are met:

1. Diagnosis of primary or secondary hypogonadism; and
2. Member is 18 years of age or older; and
3. ONE of the following:
 1. Negative history of prostate and breast cancer; or
 2. History of prostate cancer status post prostatectomy and documentation that the risk versus benefit has been assessed; and
4. For Androgel®, Androderm®, Fortesta®, Natesto®, Testim®, Vogelxo®, Xyosted™, testosterone undecanoate (Jatenzo®, Tlando®, Kyzatrex®), methyltestosterone (Methitest®) only, inadequate response or inability to tolerate generic transdermal testosterone; and

5. For Aveed® only, inadequate response or inability to tolerate generic testosterone injection in oil formulation; and
6. New users only, low (morning) testosterone level

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA Androgel®, Androderm®, Fortesta®, Natesto®, Testim®, Vogelxo®, Xyosted™, testosterone undecanoate (Jatenzo®, Tlando®, Kyzatrex®, Aveed®), methyltestosterone (Methitest®) is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

Gender dysphoria

INITIAL CRITERIA Androgel®, Androderm®, Fortesta®, Natesto®, Testim®, Vogelxo®, Xyosted™, testosterone undecanoate (Jatenzo®, Tlando®, Kyzatrex®, Aveed®), or methyltestosterone (Methitest®) is approved for use as hormone therapy in children, adolescents, and adults with gender dysphoria when there is documentation of persistent, well-documented gender dysphoria diagnosed in accordance with criteria established in the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5)

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA Androgel®, Androderm®, Fortesta®, Natesto®, Testim®, Vogelxo®, Xyosted™, testosterone undecanoate (Jatenzo®, Tlando®, Kyzatrex®, Aveed®), methyltestosterone (Methitest®) is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

P&T Approval Date: March 20, 2025

Title: Applicable Age Edits

Applicable Drugs:

Drug Name	Age Edit: Prior Authorization Required (years)
Acne Medications	
Tretinoin, topical (e.g., Atralin, Avita, Retin-A, Retin-A micro, Altreno, etc.)	Age 26 and over
Adapalene (Differin)	Age 26 and over
Adapalene/ Benzoyl Peroxide (Epiduo)	Age 26 and over
Tretinoin/ clindamycin (Ziana)	Age 26 and over
Triafarotene (Aklief)	Age 26 and over
Tazarotene (Fabior, Arazlo, Tazorac)	Age 26 and over
Tretinoin-benzoyl peroxide (Twynéo)	Age 26 and over
Acute migraine Agents	
Eletriptan (Relpax)	Under age 18
Sumatriptan (Imitrex, Onzetra, Xsail, Zembrace Symtouch)	Under age 18
Naratriptan (Amerge)	Under age 18
Rizatriptan (Maxalt/ Maxalt MLT)	Under age 6
Zolmitriptan (Zomig/Zomig ZMT)	Under age 12
Almotriptan	Under age 12
Frovatriptan (Frova)	Under age 18
Miscellaneous	
Auvi-Q 0.1mg	Age 4 and over

Policy:

The drugs in the following table are medically necessary in the age ranges listed when there is documentation of all of the following:

1. FDA or compendia approved indication; and
2. Not used for an indication that is otherwise excluded (i.e., cosmetic)

***Note: Age edits apply to brand and generic products. Some brand name products have prior authorization in addition to age edit.

Authorization Duration: 2 years

P&T Approval Date: March 20, 2025

Title: Aprocitentan (Tryvio™)

Applicable Drugs:

Brand Name	Generic Name
Tryvio™	Aprocitentan

Policy:

INITIAL CRITERIA: Aprocitentan (Tryvio™) is medically necessary when ALL of the following are met:

1. Diagnosis of treatment resistant hypertension; and
2. Member has not achieved target blood pressure (e.g., systolic blood pressure [SBP] less than 130 mmHg) after treatment with all of the following antihypertensive medications from different classes for an adequate duration (minimum 4 weeks each) at a maximally tolerated dose:
 1. One of the following:
 1. Angiotensin converting enzyme (ACE) inhibitor (e.g., captopril, enalapril); or
 2. Angiotensin II receptor blocker (ARB) (e.g., candesartan, valsartan); and
 2. Diuretic (e.g., hydrochlorothiazide, chlorthalidone); and
 3. Calcium channel blocker (e.g., amlodipine, nifedipine); and
 4. Mineralocorticoid receptor antagonist (MRA) [e.g., eplerenone, spironolactone]; and
3. Provider attests other causes of hypertension have been ruled out (e.g., secondary causes [primary hyperaldosteronism], white coat effect, medication nonadherence); and
4. Used as an adjunct to lifestyle modification (e.g., dietary or caloric restriction, exercise, behavioral support, community-based program); and
5. Requested drug will be used in combination with at least 3 antihypertensive medications from different classes; and
6. Prescribed by or in consultation with a specialist experienced in the treatment of resistant hypertension (e.g., cardiologist, nephrologist)

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA: Aprocitentan (Tryvio™) is medically necessary when ALL of the following are met:

1. Member demonstrates positive clinical response to therapy (e.g., systolic blood pressure [SBP] less than 130 mmHg); and
2. Member continues to use Tryvio in combination with at least 3 antihypertensive medications from different classes and is adherent to therapy; and

3. Requested drug will continue to be used as an adjunct to lifestyle modification (e.g., dietary or caloric restriction, exercise, behavioral support, community-based program)

Reauthorization duration: 2 years

P&T Approval Date: Dec-12-2024

Title: Niemann-Pick Disease Type C Agents policy

Applicable Drugs:

Brand Name	Generic Name
Miplyffa™	arimoclomol
Aqneursa	levacetylleucine

Policy:

INITIAL CRITERIA: arimoclomol (Miplyffa™) is medically necessary when ALL of the following are met:

1. Diagnosis of Niemann-Pick disease type C (NPC); and
2. Diagnosis is confirmed by one of the following:
 - a. Genetically confirmed (deoxyribonucleic acid [DNA] sequence analysis) by mutations in both alleles of NPC1 or NPC2; or
 - b. Mutation in only one allele of NPC1 or NPC2 plus either positive filipin staining or elevated cholestane triol/oxysterols (>2 x upper limit of normal); and
3. Member has at least one neurological symptom of the disease (e.g., hearing loss, vertical supranuclear gaze palsy, ataxia, dementia, dystonia, seizures, dysarthria, or dysphagia); and
4. Member is 2 years of age or older; and
5. Will be used in combination with miglustat; and
6. Will not be used in combination with Aqneursa (levacetylleucine); and
7. Prescribed by or in consultation with a specialist knowledgeable in the treatment of Niemann-Pick disease type C

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: arimoclomol (Miplyffa™) is medically necessary when ALL of the following are met:

1. Member demonstrates positive clinical response to therapy (e.g., slowing of disease progression, improvement in neurological symptoms of the disease); and
2. Will be used in combination with miglustat; and
3. Will not be used in combination with Aqneursa (levacetylleucine)

Reauthorization duration: 1 year

INITIAL CRITERIA: levacetylleucine (Aqneursa™) is medically necessary when ALL of the following are met:

1. Diagnosis of Niemann-Pick disease type C (NPC); and
2. Diagnosis is confirmed by one of the following:

1. Genetically confirmed (deoxyribonucleic acid [DNA] sequence analysis) by mutations in both alleles of NPC1 or NPC2; or
2. Mutation in only one allele of NPC1 or NPC2 plus either positive filipin staining or elevated cholestane triol/oxysterols ($>2 \times$ upper limit of normal); and
3. Member has at least one neurological symptom of the disease (e.g., hearing loss, vertical supranuclear gaze palsy, ataxia, dementia, dystonia, seizures, dysarthria, or dysphagia); and
4. Member weighs greater than or equal to 15kg; and
5. Requested drug will not be used in combination with Miplyffa (arimoclomol); and
6. Prescribed by or in consultation with a specialist knowledgeable in the treatment of Niemann-Pick disease type C

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: levacetylleucine (Aqneursa™) is medically necessary when ALL of the following are met:

1. Member demonstrates positive clinical response to therapy (e.g., slowing of disease progression, improvement in neurological symptoms of the disease); and
2. Requested drug will not be used in combination with Miplyffa (arimoclomol)

Reauthorization duration: 12 months

P&T Approval Date: March 20, 2025

Title: Avacopan (Tavneos)

Applicable Drugs:

Brand Name	Generic Name
Tavneos™	Avacopan

Policy:

INITIAL CRITERIA: Avacopan (Tavneos™) is medically necessary when ALL of the following are met:

1. Diagnosis of one of the following types of severe active anti-neutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis:
 - a. Granulomatosis with polyangiitis (GPA); or
 - b. Microscopic polyangiitis (MPA); and
2. Member is receiving concurrent immunosuppressant therapy with one of the following:
 - a. Cyclophosphamide; or
 - b. Rituximab; and
3. One of the following:
 - a. Member is concurrently on glucocorticoids (e.g., prednisone); or
 - b. Inadequate response or inability to tolerate glucocorticoids (e.g., prednisone); and
4. Member is 18 years of age or older; and
5. Prescribed by or in consultation with one of the following:
 - a. Nephrologist; or
 - b. Pulmonologist; or
 - c. Rheumatologist

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Avacopan (Tavneos™) is medically necessary when ALL of the following are met:

1. Member does not show evidence of progressive disease while on therapy; and
2. Member is receiving concurrent immunosuppressant therapy (e.g., azathioprine, cyclophosphamide, methotrexate, rituximab); and
3. Prescribed by or in consultation with one of the following:
 - a. Nephrologist; or
 - b. Pulmonologist; or
 - c. Rheumatologist

Reauthorization duration: 2 years

P&T Approval Date: Dec-12-2024

Title: Aztreonam (Cayston)

Applicable Drugs:

Brand Name	Generic Name
Cayston®	Aztreonam

Policy:

INITIAL CRITERIA: Aztreonam (Cayston®) is approved when ALL of the following are met:

1. Member is 7 years of age or older; and
2. Diagnosis of cystic fibrosis; and
3. Evidence of Pseudomonas aeruginosa in the lungs confirmed by culture; and
4. Susceptibility results indicating that the Pseudomonas aeruginosa is sensitive to aztreonam; and
5. FEV1 that is 25% to 75% of predicted

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA: Aztreonam (Cayston®) is re-approved when ALL of the following are met:

1. Diagnosis of cystic fibrosis; and
2. Evidence of Pseudomonas aeruginosa in the lungs confirmed by culture; and
3. Documentation of positive clinical response to therapy (e.g. improvement in lung function demonstrated by improved FEV1)

Reauthorization duration: 2 years

P&T Approval Date: Jul-01-2024

Title: Becaplermin gel (Regranex®)

Applicable Drugs:

Brand name	Generic name
Regranex®	Becaplermin

Policy:

INITIAL CRITERIA: Becaplermin (Regranex®) gel is approved when BOTH of the following are met:

1. Member has a lower extremity diabetic neuropathic ulcer; and
2. Treatment will be given in combination with ulcer wound care (e.g., debridement, infection control, and/or pressure relief)

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Becaplermin (Regranex®) gel is re-approved when ONE of the following is met:

1. Documentation of lower extremity diabetic neuropathic ulcer at a different treatment site; or
2. Documentation of continued need for treatment beyond 6 months

Reauthorization duration: 6 months

P&T Approval Date: March 20, 2025

Title: Belimumab (Benlysta®)/Voclosporin (Lupkynis™)

Applicable Drugs:

Brand Name	Generic Name
Benlysta®	belimumab
Lupkynis™	voclosporin

Policy:

Systemic Lupus Erythematosus

INITIAL CRITERIA Belimumab (Benlysta®) is approved when ALL of the following are met:

1. Diagnosis of active systemic lupus erythematosus; and
2. Autoantibody positive (ie, anti-nuclear antibody [ANA] titer greater than or equal to 1:80 or anti-dsDNA level greater than or equal to 30 IU/mL), antibodies to DNA [Anti-dsDNA], Anti-Smith [Anti-Sm]); and
3. Currently receiving at least one standard of care treatment for active systemic lupus erythematosus (eg, antimalarials [eg, hydroxychloroquine], corticosteroids, NSAIDs, or immunosuppressants); and
4. Prescribed by or in consultation with a rheumatologist; and
5. Member is 5 years of age or older

Initial Authorization duration: 6 months

REAUTHORIZATION CRITERIA: Belimumab (Benlysta®) is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

Lupus Nephritis

INITIAL CRITERIA Belimumab (Benlysta®) is approved when ALL of the following are met:

1. Member has active lupus nephritis confirmed by kidney biopsy; and
2. Member is receiving standard therapy for lupus nephritis (e.g. corticosteroids, immunosuppressants, azathioprine); and
3. Prescribed by or in consultation with a rheumatologist or nephrologist; and
1. Member is 5 years of age or older

INITIAL CRITERIA Voclosporin (Lupkynis™) is approved when ALL of the following are met:

1. Diagnosis of active lupus nephritis; and
2. Member is 18 years of age or older; and
3. Used in combination with mycophenolate mofetil and corticosteroids; and
4. Prescribed by or in consultation with nephrologist or rheumatologist

Initial Authorization duration: 6 months

REAUTHORIZATION CRITERIA: Belimumab (Benlysta®) or Voclosporin (Lupkynis™) is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

P&T Approval Date: March 20, 2025

Title: Belumosudil (Rezurock™)

Applicable Drugs:

Brand Name	Generic Name
RezurockTM	Belumosudil

Policy:

INITIAL CRITERIA Belumosudil (Rezurock™) is medically necessary when ALL of the following are met:

1. Diagnosis of chronic graft-versus-host disease; and
2. Member is 12 years of age or older; and
3. Inadequate response or inability to tolerate two or more lines of systemic therapy (e.g., corticosteroids, mycophenolate, etc.); and
4. Prescribed by or in consultation with one of the following:
 - a. Hematologist; or
 - b. Oncologist; or
 - c. Physician experienced in the management of transplant patients

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA Belumosudil (Rezurock™) is medically necessary if member does not show evidence of progressive disease while on therapy

Reauthorization duration: 2 years

P&T Approval Date: Sep-12-2024

Title: Birch Triterpenes (Filsuvez)

Applicable Drugs:

Brand Name	Generic Name
Filsuvez®	Birch triterpenes

Policy:

INITIAL CRITERIA: Birch triterpenes (Filsuvez®) is medically necessary when ALL of the following are met:

1. Diagnosis of one of the following:
 1. Dystrophic epidermolysis bullosa (DEB); or
 2. Junctional epidermolysis bullosa (JEB); and
2. Disease is confirmed by one of the following:
 1. Genetic testing confirms mutation in one of the following genes:
 1. For Dystrophic epidermolysis bullosa (DEB), collagen type VII (COL7A1); or
 2. For Junctional epidermolysis bullosa (JEB), one of the following:
 1. ITGA6; or
 2. ITGB4; or
 3. Collagen type XVII (COL17A1); or
 4. LAMA3; or
 5. LAMB3; or
 6. LAMC2; or
 7. ITGA3; or
 8. LAMA3A; or
 2. Skin biopsy; and
3. Member is 6 months of age or older; and
4. Medication will be used for the treatment of wounds that require healing; and
5. DEB or JEB associated wounds are present for at least 21 days; and
6. Member does not have signs of infection for wound being treated; and
7. Member has no evidence or history of basal or squamous cell carcinoma for wound being treated; and
8. Member does not have history of stem cell transplant or gene therapy (e.g., Vyjuvek) for the treatment of epidermolysis bullosa; and
9. Standard wound care management not adequate in healing wounds (e.g., daily wound dressings, pain management, controlling infections); and
10. Prescribed by or in consultation with a dermatologist with expertise in the treatment of epidermolysis bullosa

Initial authorization duration: 3 months

REAUTHORIZATION CRITERIA: Birch triterpenes (Filsuvez®) is medically necessary when ALL of the following are met:

1. Member demonstrates positive clinical response to therapy as evidenced by wound is healing but not completely closed; and
2. Member does not have signs of infection for wound being treated; and
3. Member has no evidence or history of basal or squamous cell carcinoma for wound being treated; and
4. Prescribed by or in consultation with a dermatologist with expertise in the treatment of epidermolysis bullosa

Reauthorization duration: 6 months

P&T Approval Date: March 20, 2025

Title: Blood Modifier Agents

Applicable Drugs:

Brand Name	Generic Name
Promacta®	Eltrombopag olamine
Tavalisse™	fostamatinib
Doptelet®	avatrombopag
Mulpleta®	lusutrombopag
Alvaiz™	eltrombopag choline

Policy:

Chronic Immune (Idiopathic) Thrombocytopenic Purpura (ITP)

INITIAL CRITERIA: Eltrombopag olamine (Promacta®) or eltrombopag choline (Alvaiz™) is approved when ALL of the following are met:

1. Diagnosis of relapsed/refractory chronic immune (idiopathic) thrombocytopenic purpura (ITP) for greater than 6 months; and
2. ONE of the following:
 1. For eltrombopag olamine (Promacta®) only, member is 1 year of age or older; or
 2. For eltrombopag choline (Alvaiz™) only, member is 6 years of age or older; and
3. Baseline platelet count is less than 30,000/mcL; and
4. Insufficient response to corticosteroids, immunoglobulins, or splenectomy; and
5. Prescribed by or in consultation with a hematologist/oncologist ; and
6. Member's degree of thrombocytopenia and clinical condition increase the risk of bleeding

INITIAL CRITERIA: Fostamatinib (Tavalisse™) is approved when all of the following are met:

1. Diagnosis of relapsed/refractory chronic immune (idiopathic) thrombocytopenic purpura (ITP); and
2. Baseline platelet count is less than 30,000/mcL; and
3. Member's degree of thrombocytopenia and clinical condition increase the risk of bleeding; and
4. Documentation of an inadequate response or inability to tolerate ONE of the following:
 - a. Corticosteroids; or
 - b. Immunoglobulins; or
 - c. Splenectomy; or
 - d. Thrombopoietin receptor agonists (e.g., Nplate®, Promacta®); or
 - e. Rituximab; and
5. Prescribed by or in consultation with a hematologist/oncologist; and

6. Member is 18 years of age or older

Initial authorization duration: 2 years

INITIAL CRITERIA: Avatrombopag (Doptelet®) is approved when ALL of the following are met:

1. Diagnosis of relapsed/refractory chronic immune thrombocytopenia purpura (ITP); and
2. Baseline platelet count is less than 30,000/mL; and
3. Inadequate response or inability to tolerate ONE of the following:
 - a. corticosteroids; or
 - b. immunoglobulins; or
 - c. splenectomy; or
 - d. Rituxan (rituximab); and
4. Member's degree of thrombocytopenia and clinical condition increase the risk of bleeding; and
5. Prescribed by or in consultation with a hematologist/oncologist; and
6. Member is 18 years of age or older

Initial authorization duration: 2 years

CONTINUATION CRITERIA: Eltrombopag olamine (Promacta®), eltrombopag choline (Alvaiz™), Fostamatinib (Tavalisse™), avatrombopag (Doptelet®) is re-approved when ALL of the following are met:

1. Diagnosis of chronic immune (idiopathic) thrombocytopenic purpura; and
2. Documentation of a positive clinical response to Promacta®, Alvaiz™, Tavalisse™, Doptelet® therapy as evidence by an increase in platelet count to a level sufficient to avoid clinically important bleeding; and
3. Prescribed by or in consultation with a hematologist/oncologist

Continuation authorization duration: 2 years.

Aplastic anemia

INITIAL CRITERIA: Eltrombopag olamine (Promacta®) is approved when ALL of the following are met:

1. Diagnosis of severe aplastic anemia; and
2. Member is 2 years of age or older; and
3. One of the following:
 - a. Inadequate response or inability to tolerate immunosuppressive therapy with antithymocyte globulin (ATG) and cyclosporine; or
 - b. Documentation that the requested drug will be used in combination with antithymocyte globulin (ATG) and cyclosporin and
4. Member has thrombocytopenia defined as platelet count less than 30,000/mL; and

5. Prescribed by or in consultation with a hematologist/oncologist

Initial authorization duration: 2 years

INITIAL CRITERIA: Eltrombopag choline (Alvaiz™) is approved when ALL of the following are met:

1. Diagnosis of refractory severe aplastic anemia; and
2. Member is 18 years of age or older; and
3. Inadequate response or inability to tolerate immunosuppressive therapy with antithymocyte globulin (ATG) and cyclosporine; and
4. Member has thrombocytopenia defined as platelet count less than 30,000/mcL; and
5. Prescribed by or in consultation with a hematologist/oncologist

Initial authorization duration: 16 weeks

CONTINUATION CRITERIA: Eltrombopag olamine (Promacta®) or eltrombopag choline (Alvaiz™) is re-approved when ALL of the following are met:

1. Diagnosis of severe aplastic anemia; and
2. Documentation of a positive clinical response to therapy as evidenced by an increase in platelet count; and
3. Prescribed by or in consultation with a hematologist/oncologist

Continuation authorization duration: 2 years

Thrombocytopenia associated with hepatitis C

INITIAL CRITERIA: Eltrombopag olamine (Promacta®) or eltrombopag choline (Alvaiz™) is approved when ALL of the following are met:

1. Diagnosis of thrombocytopenia associated with hepatitis C; and
2. Member is 18 years of age or older; and
3. ONE of the following:
 - a. Member has thrombocytopenia defined as platelets less than 90,000/mcL for initiation (pre-treatment) of interferon-based therapy; or
 - b. Member has thrombocytopenia defined as platelets less than 75,000/mcL for maintenance of optimal interferon-based therapy; and
4. Prescribed by or in consultation with one of the following:
 - a. Hematologist/ oncologist
 - b. Gastroenterologist
 - c. Hepatologist
 - d. Infectious disease specialist
 - e. HIV specialist

Initial authorization duration: 48 weeks

CONTINUATION CRITERIA: Eltrombopag olamine (Promacta®) or eltrombopag (Alvaiz®) is re-approved when ALL of the following are met:

1. Diagnosis of thrombocytopenia associated with hepatitis C; and
2. ONE of the following:
 1. For members that started treatment with eltrombopag olamine (Promacta®) or eltrombopag choline (Alvaiz™) prior to initiation of treatment with interferon, BOTH of the following:
 1. Member is currently on antiviral interferon therapy for treatment of chronic hepatitis C, and
 2. Member reached a threshold platelet count that allows initiation of antiviral interferon therapy with eltrombopag olamine (Promacta®) or eltrombopag choline (Alvaiz™) treatment by week 9; or
 2. For members that started treatment with eltrombopag olamine (Promacta®) or eltrombopag choline (Alvaiz™) while on concomitant treatment with interferon, member is currently on antiviral interferon therapy for treatment of chronic hepatitis C; and
3. Prescribed by or in consultation with one of the following:
 1. Hematologist/ oncologist
 2. Gastroenterologist
 3. Hepatologist
 4. Infectious disease specialist
 5. HIV specialist

Continuation authorization duration: 48 weeks

Thrombocytopenia in Chronic Liver Disease Prior to Planned Procedure

Lusutrombopag (Mulpleta®) or Avatrombopag (Doptelet®) is approved when ALL of the following are met:

1. Diagnosis of thrombocytopenia; and
2. Member has chronic liver disease; and
3. Member is scheduled to undergo a procedure; and
4. Baseline platelet count is less than 50,000/mcL; and
5. Member is 18 years of age or older; and
6. For Lusutrombopag (Mulpleta®) only, inadequate response or inability to tolerate avatrombopag (Doptelet®)

Approval duration: 1 month

P&T Approval Date: Sep-12-2024

Title: Budesonide (Eohilia™)

Applicable Drugs:

Brand Name	Generic Name
Eohilia™	Budesonide oral suspension

Policy:

Budesonide (Eohilia™) is approved when ALL of the following are met:

1. Diagnosis of eosinophilic esophagitis (EoE); and
2. Member has symptoms of esophageal dysfunction (e.g., dysphagia, food impaction, heartburn, abdominal pain); and
3. Member has at least 15 intraepithelial eosinophils per high power field (HPF); and
4. Other causes of esophageal eosinophilia have been ruled out; and
5. Member is 11 years of age or older; and
6. Inadequate response or inability to tolerate a minimum 8-week duration of both of the following:
 1. Proton pump inhibitor (e.g., pantoprazole, omeprazole); and
 2. Topical (esophageal) corticosteroid (e.g., budesonide, fluticasone); and
7. Prescribed by or in consultation with one of the following:
 1. Allergist/immunologist; or
 2. Gastroenterologist

Authorization duration: 12 weeks

P&T Approval Date: Jul-01-2024

Title: Budesonide (Tarpeyo™)

Applicable Drugs:

Brand Name	Generic Name
Tarpeyo™	Budesonide

Policy:

Budesonide (Tarpeyo™) is approved when ALL of the following are met:

1. Diagnosis of primary immunoglobulin A nephropathy (IgAN) as confirmed by a kidney biopsy; and
2. Member is 18 years of age or older; and
3. Member is at risk of rapid disease progression (e.g., generally a urine protein-to-creatinine ratio (UPCR) greater than or equal to 1.5 g/g, or by other criteria such as clinical risk scoring using the International IgAN Prediction Tool); and
4. Used to reduce proteinuria; and
5. Estimated glomerular filtration rate (eGFR) greater than or equal to 35 ml/min/1.73 m²; and
6. One of the following:
 1. Member has been on a minimum 90-day trial of maximally tolerated dose and will continue to receive therapy with one of the following:
 1. An angiotensin-converting enzyme (ACE) inhibitor (e.g., benazepril, lisinopril); or
 2. An angiotensin II receptor blocker (ARB) (e.g., losartan, valsartan); or
 2. Member is unable to tolerate BOTH ACE inhibitors and ARBs; and
7. Inadequate response or inability to tolerate another glucocorticoid (e.g., prednisone, methylprednisolone); and
8. Prescribed by or in consultation with a nephrologist

Authorization duration: 9 months

P&T Approval Date: March 20, 2025

Title: Carglumic acid (Carbaglu®)

Applicable Drugs:

Brand Name	Generic Name
Carbaglu®	Carglumic Acid

Policy:

Acute Hyperammonemia due to N-acetylglutamate Synthase (NAGS) Deficiency

APPROVAL CRITERIA: Carglumic Acid (Carbaglu®) is medically necessary when all of the following are met:

1. Diagnosis of acute hyperammonemia due to N-acetylglutamate synthase (NAGS) deficiency; and
2. Medication will be used as adjunctive therapy to other ammonia lowering therapies (e.g., protein restriction, ammonia scavengers, dialysis)
3. Prescribed by or in consultation with a provider who specializes in the treatment of metabolic disorders

Authorization duration: 3 months

Acute Hyperammonemia due to Propionic Acidemia (PA) or Methylmalonic Acidemia (MMA)

APPROVAL CRITERIA: Carglumic Acid (Carbaglu®) is medically necessary when all of the following are met:

1. Diagnosis of acute hyperammonemia due to propionic acidemia (PA) or methylmalonic acidemia (MMA); and
2. Medication will be used as adjunctive therapy to other ammonia lowering therapies (e.g., intravenous glucose, insulin, protein restriction, dialysis); and
3. Patient's plasma ammonia level is greater than or equal to 50 micromol/L; and
4. Medication will be used for a maximum duration of 7 days; and
5. Prescribed by or in consultation with a provider who specializes in the treatment of metabolic disorders

Authorization duration: 3 months

Chronic Hyperammonemia due to N-acetylglutamate Synthase (NAGS) Deficiency

INITIAL CRITERIA: Carglumic Acid (Carbaglu®) is medically necessary when all of the following are met:

1. Diagnosis of chronic hyperammonemia due to N-acetylglutamate synthase (NAGS) deficiency; and
2. NAGS deficiency has been confirmed by genetic/mutational analysis; and

3. Medication will be used as maintenance therapy; and
4. Prescribed by or in consultation with a provider who specializes in the treatment of metabolic disorders

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA: Carglumic acid (Carbaglu®) is medically necessary when there is documentation of positive clinical response to therapy (e.g., plasma ammonia level within the normal range).

Reauthorization duration: 2 years

P&T Approval Date: Sep-12-2024

Title: Cenegermin-bkbj (Oxervate)

Applicable Drugs:

Brand Name	Generic Name
Oxervate™	cenegermin-bkbj

Policy:

INITIAL CRITERIA Cenegermin-bkbj (Oxervate™) is approved when ALL of the following are met:

1. Diagnosis of Stage 2 or 3 neurotrophic keratitis; and
2. Documentation of an inadequate response or inability to tolerate at least one over-the-counter ocular lubricant used at an optimal dose and frequency for at least two weeks (e.g., artificial tears, lubricating gels/ointments, etc.); and
3. Prescribed by or in consultation with an ophthalmologist or optometrist; and
4. Submission of chart documentation indicating treatment of left eye, right eye, or both; and
5. Member will not exceed 8 weeks of Oxervate therapy per affected eye(s)

Initial authorization duration: 3 months

REAUTHORIZATION CRITERIA Cenegermin-bkbj (Oxervate™) is re-approved when ALL of the following are met:

1. Submission of chart documentation indicating treatment of left eye, right eye, or both; and
2. One of the following:
 - a. Member has received less than or equal to 8 weeks of therapy (one course of therapy) per affected eye(s); and
 - b. Documentation of clinical rationale for treatment greater than 8 weeks (e.g., member has a recurrence of neurotropic keratitis in the same eye, or treatment of a different eye); and
3. Documentation of clinical response to prior Oxervate™ therapy; and
4. Member will not exceed a total of 16 weeks of Oxervate™ therapy per affected eye(s); and
5. Prescribed by or in consultation with an ophthalmologist or optometrist

Reauthorization duration: 3 months

Lifetime limit: 16 weeks of therapy per affected eye

P&T Approval Date: Jul-01-2024

Title: Chelation Agents

Applicable Drugs:

Brand Name	Generic Name
Exjade	Deferasirox
Jadenu	Deferasirox
Ferriprox	Deferiprone

Policy:

Chronic iron overload in blood transfusions dependent anemia

INITIAL CRITERIA: Deferasirox (Exjade®/Jadenu®) is medically necessary when ALL of the following are met:

1. Diagnosis of chronic iron overload due to blood transfusions; and
2. Member is 2 years of age or older; and
3. Serum ferritin levels are consistently greater than 1000 mcg/L (as demonstrated with at least two lab values within two months prior to treatment)
4. For Brand Exjade and Brand Jadenu only, inadequate response or inability to tolerate generic deferasirox

Initial authorization duration: 12 months

CONTINUATION CRITERIA: Deferasirox (Exjade®/Jadenu®) is medically necessary there is documentation of a decreased serum ferritin level compared with baseline level for transfusion dependent anemia.

Continuation duration: 2 years

INITIAL CRITERIA: Deferiprone (Ferriprox®) is medically necessary when all of the following are met:

1. Diagnosis of transfusional iron overload due to Sickle Cell disease or other transfusion-dependent anemia; and
2. Member is 3 years of age or older; and
3. Inadequate response or inability to tolerate one of the following chelation therapy:
 - a. Generic deferoxamine; or
 - b. generic deferasirox; and
4. For Brand Ferriprox tablets only, Inadequate response or inability to tolerate generic deferiprone tablets; and
5. Current chelation therapy is inadequate

Initial authorization duration: 12 months

CONTINUATION CRITERIA: Deferiprone (Ferriprox®) is medically necessary when there is documentation of positive clinical response to therapy (e.g., decline in serum ferritin levels from baseline).

Continuation duration: 2 years

Chronic iron overload in non-transfusion-dependent Thalassemia Syndrome

INITIAL CRITERIA: Deferasirox (Exjade®/Jadenu®) is medically necessary when ALL of the following are met:

1. Diagnosis of chronic iron overload in Non-Transfusion-Dependent Thalassemia Syndromes; and
2. Member is 10 years of age or older; and
3. Serum ferritin levels are consistently greater than 300 mcg/L and liver iron concentration (LIC) of at least 5 milligrams of iron per gram of liver dry weight (mg Fe/g dw) (as demonstrated with at least two lab values within 2 months prior to treatment)

Initial authorization duration: 12 months

CONTINUATION CRITERIA: Deferasirox (Exjade®/Jadenu®) is medically necessary when there is documentation of a decreased serum ferritin level compared with the baseline level or reduction in LIC (liver iron concentration) for non-transfusion dependent Thalassemia Syndrome

Continuation duration: 2 years

INITIAL CRITERIA: Deferiprone (Ferriprox®) is medically necessary when ALL of the following are met:

1. Diagnosis of transfusional iron overload due to Thalassemia Syndrome; and
2. Member is 3 years of age or older; and
3. Inadequate response or inability to tolerate one of the following chelation therapy:
 - a. Generic deferoxamine; or
 - b. Generic deferasirox; and
4. For Brand Ferriprox tablets only, Inadequate response or inability to tolerate generic deferiprone tablets; and
5. Current chelation therapy is inadequate

Initial authorization: 12 months

CONTINUATION CRITERIA: Deferiprone (Ferriprox®) is medically necessary when there is documentation of positive clinical response to therapy (e.g., greater than or equal to 20% decline in serum ferritin levels from baseline).

Continuation duration: 2 years

P&T Approval Date: Sep-12-2024

Title: Cholesterol Lowering Agents

Applicable Drugs:

Brand name	Generic name
Juxtapid®	Lomitapide
Praluent®	alirocumab
Repatha®	evolocumab
Nexletol™	Bempedoic acid
Nexlizet™	Bempedoic acid/ezetimibe

Policy:

Hypercholesterolemia

INITIAL CRITERIA: Alirocumab (Praluent®) is medically necessary when ALL of the following are met:

1. Diagnosis of ONE of the following:
 1. Hyperlipidemia; or
 2. Heterozygous familial hypercholesterolemia (HeFH) and member is 10 years of age or older; or
 3. Atherosclerotic cardiovascular disease (ASCVD) as diagnosed by either stress test, angiography, atherosclerotic event (e.g., MI, angina, stroke, claudication, carotid stenosis) or arterial intervention for atherosclerotic diseases (e.g., coronary, peripheral, carotid); and
2. ONE of the following:
 1. While on maximally tolerated statin therapy within the last 120 days:
 1. Member has LDL-C greater than or equal to 70 mg/dL with atherosclerotic cardiovascular disease (ASCVD); or
 2. Member has LDL-C greater than or equal to 100mg/dL without atherosclerotic cardiovascular disease (ASCVD); or
 3. Member requires greater than or equal to 25% LDL-C reduction to achieve goal; or
 2. BOTH of the following:
 1. Member has been receiving PCSK9 therapy as adjunct to maximally tolerated lipid lowering therapy (e.g., statins, ezetimibe); and
 2. LDL-C values drawn within the past 12 months while on maximally tolerated lipid lower therapy is within normal limits; and
3. ONE of the following:
 1. Member has been receiving at least 12 consecutive weeks of highest tolerable dose of statin therapy; or
 2. Member has rhabdomyolysis or symptoms with creatine kinase (CK) exceeding 10 times the upper limit of normal (ULN) on any statin; or
 3. ONE of the following with TWO statins:
 1. Myalgia (no CK elevation); or
 2. Myositis (CK less than 10 times ULN); or
 3. Hepatotoxicity from statin use (increase AST/ALT exceeding 3 times ULN); or
 4. Liver disease documented by Child Pugh A or worse or AST/ALT exceeding 3 times ULN for at least 6 weeks; or
 5. Member has an FDA labeled contraindication to all statins; and
4. Inadequate response or inability to tolerate evolocumab (Repatha®) for members 10 years of age or older

Initial authorization duration: 6 months.

REAUTHORIZATION CRITERIA: Alirocumab (Praluent®) is medically necessary when all of the following are met:

1. Member demonstrates positive clinical response to therapy as evidence by a reduction in LDL-C levels from baseline; and
2. ONE of the following:
 1. Member continues to receive other lipid-lowering therapy (e.g., statins, ezetimibe) at the maximally tolerated dose; or
 2. Member has a documented inability to take other lipid-lowering therapy (e.g., statins, ezetimibe); and
3. Inadequate response or inability tolerate evolocumab (Repatha®) for members 10 years of age or older

Reauthorization duration: 12 months

INITIAL CRITERIA: Evolocumab (Repatha®) is medically necessary when ALL of the following are met:

1. Diagnosis of ONE of the following:
 1. Hyperlipidemia; or
 2. Heterozygous familial hypercholesterolemia (HeFH) and member is 10 years of age or older; or
 3. Atherosclerotic cardiovascular disease (ASCVD) as diagnosed by either stress test, angiography, atherosclerotic event (e.g., MI, angina, stroke, claudication, carotid stenosis) or arterial intervention for atherosclerotic disease (e.g., coronary, peripheral, carotid); and
2. ONE of the following:
 1. While on maximally tolerated statin therapy within the last 120 days:
 1. Member has LDL-C greater than or equal to 70 mg/dL with atherosclerotic cardiovascular disease (ASCVD); or
 2. Member has LDL-C greater than or equal to 100mg/dL without atherosclerotic cardiovascular disease (ASCVD); or
 3. Member requires greater than or equal to 25% LDL-C reduction to achieve goal; or
 2. BOTH of the following:
 1. Member has been receiving PCSK9 therapy as adjunct to maximally tolerated lipid lowering therapy (e.g., statins, ezetimibe); and
 2. LDL-C values drawn within the past 12 months while on maximally tolerated lipid lowering therapy is within normal limits; and
3. ONE of the following:
 1. Member has been receiving at least 12 consecutive weeks of highest tolerable dose of statin therapy; or
 2. Member had rhabdomyolysis or symptoms with creatine kinase (CK) exceeding 10 times the upper limit of normal (ULN) on any statin; or
 3. ONE of the following with TWO statins:
 1. Myalgia (no CK elevation); or
 2. Myositis (CK less than 10 times ULN); or
 3. Hepatotoxicity from statin use (increased AST/ALT exceeding 3 times ULN); OR
 4. Liver disease documented by Child Pugh A or worse OR AST/ALT exceeding 3 times ULN for at least 6 weeks; or
 5. Member has an FDA labeled contraindication to all statins

Initial Authorization duration: 6 months

REAUTHORIZATION CRITERIA: Evolocumab (Repatha®) is medically necessary when all of the following are met:

1. Member demonstrates positive clinical response to therapy as evidenced by a reduction in LDL-C levels from baseline; and
2. One of the following:
 1. Member continues to receive other lipid-lowering therapy (e.g., statins, ezetimibe) at the maximally tolerated dose; or
 2. Member has a documented inability to take other lipid-lowering therapy (e.g., statins, ezetimibe)

Reauthorization duration: 12 months

INITIAL CRITERIA: Bempedoic acid (Nexletol™), bempedoic acid/ezetimibe (Nexlizet™) is medically necessary when ALL of the following are met:

1. ONE of the following:
 1. Heterozygous familial hypercholesterolemia (HeFH); or
 2. Primary hyperlipidemia; and
2. One of the following:
 1. LDL-C greater than or equal to 55mg/dL with atherosclerotic cardiovascular disease (ASCVD) while on maximally tolerate statin therapy within the last 120 days; or
 2. LDL-C greater than or equal to 100mg/dL without atherosclerotic cardiovascular disease (ASCVD) while on maximally tolerate statin therapy within the last 120 days; or
 3. Inability to tolerate statin therapy as documented by ONE of the following:
 1. Member has rhabdomyolysis or symptoms with creatine kinase (CK) exceeding 10 times the upper limit of normal (ULN) on any statin; or
 2. ONE of the following with TWO statins:
 1. Myalgia (no CK elevation); or
 2. Myositis (CK less than 10 times ULN); or
 3. Hepatotoxicity from statin use (increase AST/ALT exceeding 3 times ULN); or
 3. Liver disease documented by Child Pugh A or worse or AST/ALT exceeding 3 times ULN for at least 6 weeks; or
 4. Member has an FDA labeled contraindication to all statins

Initial Authorization duration: 6 months

REAUTHORIZATION CRITERIA: Bempedoic acid (Nexletol™), Bempedoic acid/ezetimibe (Nexlizet™) is medically necessary when member demonstrates positive clinical response to therapy (e.g., reduction in LDL-C levels)

Reauthorization duration: 12 months

Homozygous Familial Hypercholesterolemia (HoFH)

INITIAL CRITERIA: Lomitapide (Juxtapid®) is medically necessary when ALL of the following are met:

1. Diagnosis of Homozygous Familial Hypercholesterolemia (HoFH); and
2. Used as an adjunct to lipid lowering treatments and a low-fat diet with ONE of the following:
 1. Genetic confirmation of 2 mutant alleles at the LDL receptor, Apo B, PCSK9, or LDL receptor adaptor protein 1 (i.e. LDLRAP1 or ARH); or
 2. Untreated LDL-C > 500mg/dL or treated LDL cholesterol ≥ 300mg/dL with either of the following:
 1. Cutaneous or tendinous xanthoma prior to 10 years of age, or
 2. Elevated LDL cholesterol prior to lipid-lowering therapy consistent with HeFH in both parents; and
3. ONE of the following:
 1. Inadequate response to one of the following medications in combination with ezetimibe:
 1. Simvastatin (daily doses ≥ 40mg); or
 2. Atorvastatin (daily doses ≥ 20mg); or
 3. Rosuvastatin (daily doses ≥ 10mg); or
 2. Member has experience ONE of the following:
 1. Rhabdomyolysis or muscle symptoms with creatine kinase (CK) elevations > 10 times upper limit of normal (ULN) on any statin; or
 2. Myalgia (muscle symptoms without CK elevations) or myositis (muscle symptoms with CK elevations < 10 times ULN) with TWO statins; and
4. Inadequate response or inability to tolerate evolocumab (Repatha®); and
5. Not used in combination with a PCSK9 inhibitor; and
6. Prescribed by or in consultation with one of the following:

1. Cardiologist; or
2. Endocrinologist; or
3. Lipid specialist

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Lomitapide (Juxtapid®) is medically necessary when ALL of the following are met:

1. One of the following:
 1. Member continues to receive other lipid-lowering therapy (e.g., statin, ezetimibe); or
 2. Member has an inability to take other lipid-lowering therapy (e.g., statin, ezetimibe); and
2. Reduction in LDL-C of at least 25% from baseline while on therapy; and
3. Prescribed by or in consultation with one of the following:
 1. Cardiologist; or
 2. Endocrinologist; or
 3. Lipid specialist; and
4. Not used in combination with a PCSK9 inhibitor

Reauthorization duration: 12 months

INITIAL CRITERIA: Alirocumab (Praluent®) is medically necessary when ALL of the following are met:

1. Diagnosis of homozygous familial hypercholesterolemia (HoFH) and one of the following:
 1. Genetic confirmation of 2 mutations in the LDL receptor, ApoB, PCSK9, or LDL receptor adaptor protein 1 (i.e., LDLRAP1 or ARH); or
 2. Untreated LDL-C >400mg/dL with either of the following:
 1. Cutaneous or tendinous xanthoma prior to 10 years of age; or
 2. Elevated LDL cholesterol prior to lipid-lowering therapy consistent with HeFH in both parents; and
2. ONE of the following:
 1. Member is receiving other lipid-lowering therapy (e.g., statin, ezetimibe); or
 2. Member has a documented inability to take other lipid-lowering therapy (e.g., statin, ezetimibe); and
3. Member is 10 years of age or older; and
4. Inadequate response or inability to tolerate evolocumab (Repatha®)

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Alirocumab (Praluent®) is medically necessary when all of the following are met:

1. Member demonstrates positive clinical response to therapy as evidenced by a reduction in LDL-C levels from baseline; and
2. One of the following:
 1. Member continues to receive other lipid-lowering therapy (e.g., statins, ezetimibe) at the maximally tolerated dose; or
 2. Member has a documented inability to take other lipid-lowering therapy (e.g., statins, ezetimibe); and
3. Inadequate response or inability to tolerate evolocumab (Repatha®)

Reauthorization duration: 12 months

INITIAL CRITERIA: Evolocumab (Repatha®) is medically necessary when ALL of the following are met:

1. Diagnosis of Homozygous familial hypercholesterolemia (HoFH) and one of the following:
 1. Genetic confirmation of 2 mutations in the LDL receptor, ApoB, PCSK9, or LDL receptor adaptor protein 1 (i.e., LDLRAP1 or ARH); or
 2. Untreated LDL-C >400mg/dL with either of the following:
 1. Cutaneous or tendinous xanthoma prior to 10 years of age; or
 2. Elevated LDL cholesterol prior to lipid-lowering therapy consistent with HeFH in both parents; and

2. ONE of the following:
 1. Member is receiving other lipid-lowering therapy (e.g., statin, ezetimibe); or
 2. Member has a documented inability to take other lipid-lowering therapy (e.g., statin, ezetimibe); and
3. Member is 10 years of age or older

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Evolocumab (Repatha®) is medically necessary when all of the following are met:

1. Member demonstrates positive clinical response to therapy as evidenced by a reduction in LDL-C levels from baseline; and
2. One of the following:
 1. Member continues to receive other lipid-lowering therapy (e.g., statins, ezetimibe) at the maximally tolerated dose; or
 2. Member has a documented inability to take other lipid-lowering therapy (e.g., statins, ezetimibe)

Reauthorization duration: 12 months

REAUTHORIZATION CRITERIA: Evolocumab (Repatha®) is medically necessary when all of the following are met:

1. Member demonstrates positive clinical response to therapy as evidenced by a reduction in LDL-C levels from baseline; and
2. One of the following:
 1. Member continues to receive other lipid-lowering therapy (e.g., statins, ezetimibe) at the maximally tolerated dose; or
 2. Member has a documented inability to take other lipid-lowering therapy (e.g., statins, ezetimibe)

Reauthorization duration: 12 months

Established cardiovascular disease (CVD) or high risk for a CVD event but without established CVD

INITIAL CRITERIA: Bempedoic acid (Nexletol™), bempedoic acid/ezetimibe (Nexlizet™) is medically necessary when ALL of the following are met:

1. ONE of the following:
 1. Member has established cardiovascular disease (CVD) (e.g., coronary artery disease, symptomatic peripheral arterial disease, cerebrovascular atherosclerotic disease); or
 2. Member is at high risk for a CVD event but without established CVD [e.g., diabetes mellitus (type 1 or type 2) in females over 65 years of age or males over 60 years of age]; and
2. One of the following:
 1. LDL-C greater than or equal to 55 mg/dL with atherosclerotic cardiovascular disease (ASCVD) while on maximally tolerate statin therapy within the last 120 days; or
 2. LDL-C greater than or equal to 100 mg/dL without ASCVD while on maximally tolerate statin therapy within the last 120 days; and
 3. Inability to tolerate statin therapy as documented by ONE of the following:
 1. Member has rhabdomyolysis or symptoms with creatine kinase (CK) exceeding 10 times the upper limit of normal (ULN) on any statin; or
 2. ONE of the following with TWO statins:
 1. Myalgia (no CK elevation); or
 2. Myositis (CK less than 10 times ULN); or
 3. Hepatotoxicity from statin use (increase AST/ALT exceeding 3 times ULN); or
 3. Liver disease documented by Child Pugh A or worse or AST/ALT exceeding 3 times ULN for at least 6 weeks; or
 4. Member has an FDA labeled contraindication to all statins

Initial Authorization duration: 6 months

REAUTHORIZATION CRITERIA: Bempedoic acid (Nexletol™), Bempedoic acid/ezetimibe (Nexlizet™) is medically necessary when member demonstrates positive clinical response to therapy (e.g., reduction in LDL-C levels)

Reauthorization duration: 12 months

P&T Approval Date: Jun-05-2025

Title: Cholic acid (Cholbam)

Applicable Drugs:

Brand Name	Generic Name
Cholbam®	cholic acid

Policy:

INITIAL CRITERIA Cholic acid (Cholbam®) is medically necessary when ALL of the following are met:

1. One of the following:
 - a. Treatment of bile acid synthesis disorder due to a single enzyme defect (SED); or
 - b. Adjunctive treatment of peroxisomal disorders (PDs) including Zellweger spectrum disorder in patients who exhibit manifestations of liver disease, steatorrhea, or complications from decreased fat soluble vitamin absorption; and
2. Prescribed by or in consultation with one of the following:
 - a. hepatologist; or
 - b. gastroenterologist; or
 - c. medical geneticist; or
 - d. other specialist that treats inborn errors of metabolism; and
3. No documentation of extrahepatic manifestations of bile acid synthesis disorders due to single enzyme defects (SEDs) or peroxisomal disorders (PDs) including Zellweger spectrum disorder

Initial authorization duration: 3 months

REAUTHORIZATION CRITERIA Cholic acid (Cholbam®) is medically necessary when there is documentation of improved liver function tests (e.g., aspartate aminotransferase [AST], alanine aminotransferase [ALT]) from the start of treatment.

Reauthorization duration: 2 years

P&T Approval Date: Dec-12-2024

Title: Colchicine (Lodoco)

Applicable Drugs:

Brand Name	Generic Name
Lodoco	Colchicine

Policy:

INITIAL CRITERIA: Colchicine (Lodoco) is approved when all of the following are met:

1. Diagnosis of cardiovascular disease (CV); and
2. Used for the secondary prevention of CV disease (e.g., very high-risk patients); and
3. Member is 18 years of age or older; and
4. Member is on guideline therapy management for multiple risk factors (e.g., dyslipidemia, hypertension, hyperglycemia) associated with CV disease

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Colchicine (Lodoco) is re-approved when documentation is provided of positive clinical response to therapy

Reauthorization duration: 6 months

P&T Approval Date: Dec-18-2023

Title: Complement Inhibitors Agents

Applicable Drugs:

Brand Name	Generic Name
Empaveli™	Pegcetacoplan
Fabhalta®	Iptacopan
Voydeya™	Danicopan

Policy:

Paroxysmal Nocturnal Hemoglobinuria

INITIAL CRITERIA Pegcetacoplan (Empaveli™) is medically necessary when ALL of the following are met:

1. Diagnosis of paroxysmal nocturnal hemoglobinuria (PNH); and
2. Member is 18 years of age or older; and
3. Prescribed by or in consultation with a hematologist/oncologist; and
4. Member's Hemoglobin (Hb) level is less than 10.5 g/dL

Initial authorization duration: 12 months

CONTINUATION CRITERIA Pegcetacoplan (Empaveli™) is medically necessary with documentation of positive clinical response to therapy (e.g., improvement in hemoglobin level, hemoglobin stabilization, decrease in the number of red blood cell transfusions)

Continuation authorization duration: 12 months

INITIAL CRITERIA: Iptacopan (Fabhalta®) is medically necessary when ALL of the following are met:

1. Diagnosis of paroxysmal nocturnal hemoglobinuria (PNH); and
2. Member is 18 years of age or older; and
3. Member's Hemoglobin (Hb) level is less than 10 g/dL; and
4. Prescribed by or in consultation with a hematologist/oncologist

Initial authorization duration: 12 months

CONTINUATION CRITERIA: Iptacopan (Fabhalta®) is medically necessary with documentation of positive clinical response to therapy (e.g., improvement in hemoglobin level, hemoglobin stabilization, decrease in the number of red blood cell transfusions)

Continuation authorization duration: 12 months

INITIAL CRITERIA: Danicopan (Voydeya™) is medically necessary when ALL of the following are met:

1. Diagnosis of paroxysmal nocturnal hemoglobinuria (PNH); and
2. Member is 18 years of age and older; and
3. Will be used as add-on therapy to ravulizumab (Ultomiris) or eculizumab (Soliris); and
4. Member's hemoglobin levels less than or equal to 9.5 g/dL; and
5. Absolute reticulocyte count greater than or equal to $120 \times 10^9/L$; and
6. Prescribed by or in consultation with a hematologist/oncologist

Initial authorization duration: 12 months

CONTINUATION CRITERIA: Danicopan (Voydeya™) is medically necessary when ALL of the following are met:

1. Diagnosis of paroxysmal nocturnal hemoglobinuria (PNH); and
2. Documentation of positive clinical response to therapy (e.g., hemoglobin stabilization, decrease in the number of red blood cell transfusions); and
3. Will be used as add-on therapy to ravulizumab (Ultomiris) or eculizumab (Soliris)

Continuation authorization duration: 12 months

Immunoglobulin A nephropathy (IgAN)

INITIAL CRITERIA: Iptacopan (Fabhalta®) is medically necessary when ALL of the following are met:

1. Diagnosis of primary immunoglobulin A nephropathy (IgAN) as confirmed by a kidney biopsy; and
2. Documentation is provided that member is at risk of rapid disease progression [e.g., generally a urine protein-to-creatinine ratio (UPCR) greater than or equal to 1.5 g/g, or by other criteria such as clinical risk scoring using the International IgAN Prediction Tool]; and
3. Medication will be used to reduce proteinuria; and
4. Member has an estimated glomerular filtration rate (eGFR) of greater than or equal to 20 mL/min/1.73 m²; and
5. Member had an inadequate response or inability to tolerate a minimum 90-day trial of a maximally tolerated dose of one of the following:
 1. An angiotensin-converting enzyme (ACE) inhibitor (e.g., benazepril, lisinopril); or
 2. An angiotensin II receptor blocker (ARB) (e.g., losartan, valsartan); and
6. Member is 18 years of age and older; and
7. Prescribed by or in consultation with a nephrologist

Initial authorization duration: 12 months

CONTINUATION CRITERIA: Iptacopan (Fabhalta®) is medically necessary when ALL of the following are met:

1. Documentation of positive clinical response to therapy as demonstrated by a decrease in urine protein-to-creatinine ratio (UPCR) from baseline; and
2. Prescribed by or in consultation with a nephrologist

Continuation authorization duration: 12 months

P&T Approval Date: Dec-12-2024

Title: Compounded products

Applicable Drugs:

Product	Description
Compound claims greater than \$75	Compound where the submitted claim cost is greater than or equal to \$75
Various	Compounding Kit

Policy:

A compounded product, including a commercially available compounding kit, is considered medically necessary when ALL of the following are met:

1. The active prescription ingredient(s) of the compound is FDA approved or supported by accepted compendium as stated in the Off-Label Use policy for the indication and route of administration; and
2. The product as compounded is not commercially available. This may include a current short supply* of the commercially available product or the member has a medical need for a dosage form, strength or formulation other than what can be accomplished with a commercially available product; and
3. Member had an inadequate response or inability to tolerate all commercially available therapeutic alternatives to treat the condition for which the compound has been requested; and
4. The compound does not contain any product(s) that were withdrawn or removed from the market due to safety reasons; and
5. The compound is not used for, nor does it contain, a product that is indicated for an excluded benefit (e.g., cosmetic)

Additionally, authorization may be placed to allow access to the prescription benefit for products that are not considered standard coverage (e.g. drugs administered intravenously) when all the following are met:

1. All of the above criteria are for medically necessary are met for the compounded product; and
2. The product is being used in a compound that will be administered through a route that is considered standard coverage for the prescription benefit (e.g., oral, topical, inhalation, etc.). Bladder installation may be considered if the above criteria are met.

Authorization length for short supply of the commercially available product will be six months. All other authorizations: 2 years

* <http://www.accessdata.fda.gov/scripts/drugshortages/default.cfm>

* <http://www.ashp.org/Drug-Shortages/Current-Shortages>

P&T Approval Date: Jul-01-2024

Title: Continuous Glucose Monitor

Applicable Drugs:

Dexcom® line of products	Medtronic® line of products	Freestyle® line of products
Dexcom® G5 Receivers Dexcom® G6 Receivers Dexcom® G7 Receiver Dexcom® G5 Sensors Dexcom® G6 Sensors Dexcom® G7 Sensor Dexcom® G5 Transmitter Kit Dexcom® G6 Transmitter Kit	Guardian™ Connect Transmitter Guardian™ Sensor Enlite® Sensor Eversense® Sensor/Holder	Freestyle Libre® 14 Day Reader Freestyle Libre® 14 Day Sensor Freestyle Libre® 2 Reader Freestyle Libre® 2 Sensor Freestyle Libre® 3 Sensor

Policy:

INITIAL CRITERIA: Continuous glucose monitor (CGM) products (receivers, transmitters and sensors) are medically necessary when ALL of the following are met:

1. Diagnosis of diabetes; and
2. Member is adherent to current diabetes treatment plan and participates in ongoing diabetes education and support; and
3. One of the following:
 1. Member is treated with insulin; or
 2. Member is non-insulin treated and experiences significant hypoglycemia (e.g., recurrent, unexplained, severe [generally blood glucose levels <50 mg/dL] hypoglycemia or hypoglycemic unawareness); and
4. For Freestyle Libre only, submission of documentation (e.g., chart notes) or paid claim history showing member had a minimum 90-day trial of Dexcom within the last 180 days

Initial authorization duration: 2 years.

REAUTHORIZATION CRITERIA: Continuous glucose monitor (CGM) products (receivers, transmitters and sensors) are medically necessary when ALL of the following are met:

1. Documentation that of a positive clinical response as evidenced by ONE of the following:
 1. Improvement in glycemic control (e.g., lower and/or maintain A1C levels); or
 2. Reduction or improvement in hypoglycemic events; and
2. For Freestyle Libre only, submission of documentation (e.g., chart notes) or paid claim history showing member had a minimum 90-day trial of Dexcom within the last 180 days

Reauthorization duration: 2 years

P&T Approval Date: Sep-12-2024

Title: Contraceptive Formulary Exception

Applicable Drugs:

N/A

Policy:

Non-formulary Exceptions:

A non-formulary contraceptive is medically necessary for \$0 cost-share when BOTH of the following are met:

1. The drug is described as a preventative medication identified by the Women's Preventive Services provision of the Patient Protection and Affordable Care Act (PPACA); and
2. The prescriber has provided documentation indicating the requested product is medically necessary

Authorization duration: 1 year

\$0 Cost-Share Override

An exception to allow \$0 cost-share for contraceptives covered on the formulary is medically necessary when BOTH of the following are met:

1. The drug is described as a preventative medication identified by the Women's Preventive Services provision of the Patient Protection and Affordable Care Act (PPACA); and
2. The prescriber has provided documentation indicating the requested product is medically necessary

Authorization duration: 1 year

*This policy does not apply to the Premium Formulary.

P&T Approval Date: Sep-12-2024

Title: Convenience Packs

Applicable Drugs:

N/A

Policy:

Coverage is subject to the terms, conditions, and limitations of the member's contract.

Convenience packs as described above are not covered under the pharmacy benefit because each product is available independently.

A prescriber may issue a prescription or prescriptions for the individual components of the convenience pack. The individual components will be covered pursuant to the terms of member's benefit.

Examples of convenience packs include, but are not limited to:

- DermacinRx Clorhexacin, which contains the following:
 - Mupirocin 2% ointment – covered as a pharmacy benefit
 - Chlorhexidine gluconate 4% solution, dimethicone 5% cream not covered (not an FDA approved product)
- Diclovix DM PAK 1.5-8% which contains the following:
 - Diclofenac sodium solution 1.5% - covered as a pharmacy benefit
 - Menthol gel 8% therapy pack – not covered (not FDA approved product)

P&T Approval Date: Jul-01-2024

Title: Cosmetic Policy

Applicable Drugs:

N/A

Policy:

Cosmetic drugs, or drugs prescribed for cosmetic purposes, are not covered under the pharmacy benefit. Cosmetic drugs or drugs prescribed for cosmetic purposes are:

- Used for other than the treatment of illness, injuries, congenital birth defect or restoration of physiological function; and
- Used for cleansing, beautifying, promoting attractiveness or altering the appearance of any part of the human body

Examples of drugs prescribed for cosmetic use include, but are not limited to:

Brand Name	Generic Name	FDA Indication
Egrifta SV	Tesamorelin	Reduction of excess abdominal fat in HIV-infected patients with lipodystrophy.
Renova, Refissa (branded product only)	Tretinoin	Adjunctive agent for use in the mitigation (palliation) of fine wrinkles, mottled hyperpigmentation, and tactile roughness of facial skin in patients who do not achieve such palliation using comprehensive skin care and sun avoidance programs alone
Propecia 1mg	Finasteride 1mg	Male pattern alopecia
Multiple (e.g., Blanche cream 4%)	Hydroquinone	Discoloration of skin; Hyperpigmentation of skin
Latisse 0.03% solution	Bimatoprost	Hypotrichosis of the eyelashes
Vaniqa 13.9% cream	Eflornithine	Reduction of unwanted facial hair in women
Multiple (e.g., Rogaine)	Minoxidil topical	Male pattern alopecia; hair regrowth in women

P&T Approval Date: Dec-12-2024

Title: Crinecerfont (Crenessity)

Applicable Drugs:

Brand name	Generic name
Crenessity	Crinecerfont

Policy:

INITIAL CRITERIA: crinecerfont (Crenessity™) is medically necessary when ALL of the following are met:

1. Submission of documentation (e.g., chart notes) confirming the diagnosis of classic 21-hydroxylase deficiency congenital adrenal hyperplasia; and
2. Member is 4 years of age or older; and
3. Member is receiving chronic treatment with glucocorticoid (GC) replacement therapy (e.g., dexamethasone, hydrocortisone, methylprednisolone) for adrenal insufficiency as one of the following:
 1. Both of the following:
 1. Member is 4 to 17 years old; and
 2. Daily GC dose is greater than 12 mg/m²/day in hydrocortisone dose equivalents; or
 2. Both of the following:
 1. Member is 18 years of age or older; and
 2. Daily GC dose is greater than 13 mg/m²/day in hydrocortisone dose equivalents; and
4. Prescribed by or in consultation with an endocrinologist

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: crinecerfont (Crenessity™) is medically necessary when ALL of the following are met:

1. Member demonstrates positive clinical response to therapy (e.g., lowered androgen levels, reduced daily dose of steroids); and
2. Member continues to receive chronic treatment with glucocorticoid (GC) replacement therapy (e.g., dexamethasone, hydrocortisone, methylprednisolone); and
3. Prescribed by or in consultation with an endocrinologist

Reauthorization duration: 12 months

P&T Approval Date: March 20, 2025

Title: Cushing's Disease Agents

Applicable Drugs:

Brand name	Generic name
Signifor®	PasireotideIsturisa
Isturisa®	Osilodrostat
Korlym®	Mifepristone
Recorlev®	Levoketoconazole

Policy:

Cushing's Disease

INITIAL CRITERIA Pasireotide (Signifor®) or osilodrostat (Isturisa®) is medically necessary when ALL of the following are met:

1. Diagnosis of Cushing's disease; and
2. Member has failed surgery or is not a candidate for surgery; and
3. Member is 18 years of age or older; and
4. Prescribed by or in consultation with an endocrinologist; and
5. For osilodrostat (Isturisa®) only, inadequate response or inability to tolerate pasireotide (Signifor® [LAR]); and
6. For osilodrostat (Isturisa®) only, inadequate response or inability to tolerate oral ketoconazole

Initial Authorization duration: 6 months

REAUTHORIZATION CRITERIA Pasireotide (Signifor®) or osilodrostat (Isturisa®) is medically necessary when ALL of the following are met:

1. Documentation of positive clinical response to therapy (i.e., reduction in cortisol levels, improvement in signs or symptoms of the disease); and
2. Prescribed by or in consultation with an endocrinologist

Reauthorization duration: 2 years

INITIAL CRITERIA Levoketoconazole (Recorlev®) is medically necessary when ALL of the following are met:

1. Diagnosis of Cushing's syndrome; and
2. Member is 18 years of age or older; and
3. Member is being treated for endogenous hypercortisolemia (e.g., pituitary adenoma, ectopic tumor, adrenal adenoma); and
4. One of the following:
 - a. Member is not a candidate for surgery; or

- b. Surgery has not been curative; and
5. Inadequate response or inability to tolerate oral ketoconazole; and
6. Prescribed by or in consultation with an endocrinologist

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA Levoketoconazole (Recorlev®) is medically necessary when ALL of the following are met:

1. Documentation of positive clinical response to therapy (i.e., decrease or normalization of urinary free cortisol (UFC) level, improvement in signs or symptoms of the disease); and
2. Prescribed by or in consultation with an endocrinologist

Reauthorization duration: 2 years

Hyperglycemia secondary to Cushing's Syndrome

INITIAL CRITERIA Mifepristone (Korlym®) is medically necessary when ALL of the following are met:

1. Hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing's syndrome who have type 2 diabetes mellitus or glucose intolerance; and
2. Member has failed surgery or is not a candidate for surgery; and
3. Prescribed by or in consultation with an endocrinologist; and
4. Member is not pregnant; and
5. Member is 18 years of age or older

Initial Authorization duration: 6 months

REAUTHORIZATION CRITERIA Mifepristone (Korlym®) is medically necessary when ALL of the following are met:

1. Documentation of positive clinical response to therapy (e.g., improved, or stable glucose tolerance while on therapy); and
2. Prescribed by or in consultation with an endocrinologist

Reauthorization duration: 2 years

P&T Approval Date: Sep-12-2024

Title: Cyanocobalamin inhalation (Nascobal®)

Applicable Drugs:

Brand Name	Generic Name
Nascobal	Cyanocobalamin

Policy:

INITIAL CRITERIA Cyanocobalamin inhalation (Nascobal®) is medically necessary when ALL of the following are met:

1. Diagnosis of ONE of the following:
 - a. Pernicious anemia in members requiring maintenance therapy who are in remission following intramuscular vitamin B12 therapy and who have no nervous system involvement; or
 - b. Dietary deficiency of vitamin B12 due to strict vegetarian diet; or
 - c. Malabsorption of vitamin B12 due to a structural or functional damage to the stomach or ileum; or
 - d. Inadequate secretion of intrinsic factor; or
 - e. Competition for vitamin B12 by intestinal parasites or bacteria (e.g., tapeworm, blind loop syndrome); or
 - f. Inadequate utilization of vitamin B12 (e.g., antimetabolites are employed in treatment of neoplasia); and
2. Member is 18 years of age or older; and
3. Inadequate response or inability to tolerate oral and sublingual cyanocobalamin or member has a documented diagnosis of trypanophobia (i.e., needle-phobia)

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA Cyanocobalamin inhalation (Nascobal®) is medically necessary when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

P&T Approval Date: Sep-12-2024

Title: Cyclosporine (Verkazia®)

Applicable Drugs:

Brand Name	Generic Name
Verkazia®	Cyclosporine ophthalmic emulsion

Policy:

INITIAL CRITERIA Cyclosporine (Verkazia®) is approved when ALL of the following are met:

1. Diagnosis of moderate to severe vernal keratoconjunctivitis confirmed by the presence of clinical signs and symptoms (e.g., itching, photophobia, giant papillae at the upper tarsal conjunctiva or at the limbus, thick mucus discharge, conjunctival hyperaemia); and
2. Member is 4 years of age or older; and
3. Inadequate response or inability to tolerate one of the following:
 - a. Topical ophthalmic "dual-acting" mast cell stabilizer and antihistamine (e.g., olopatadine, azelastine); or
 - b. Topical ophthalmic mast cell stabilizers (e.g., cromolyn); and
4. Inadequate response or inability to tolerate short term use (up to 2 to 3 weeks), of topical ophthalmic corticosteroids (e.g., dexamethasone, prednisolone, fluoromethalone); and
5. Prescribed by or in consultation with one of the following:
 - a. Ophthalmologist or
 - b. Optometrist

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA Cyclosporine (Verkazia®) is re-approved when there is documentation of positive clinical response to therapy as evidenced by an improvement in clinical signs and symptoms (e.g., itching, photophobia, papillary hypertrophy, mucus discharge, conjunctival hyperaemia).

Reauthorization duration: 2 years

P&T Approval Date: Jul-01-2024

Title: Cysteamine-containing products

Applicable Drugs:

Brand Name	Generic Name
Cystagon®	Cysteamine Bitartrate
Cystaran®/Cystadrops®	Cysteamine Hydrochloride
Procysbi®	Cysteamine Bitartrate

Policy:

Cystinosis

INITIAL CRITERIA: Cysteamine hydrochloride (Cystaran®/Cystadrops®) Ophthalmic Solution is medically necessary when ALL of the following are met:

1. Diagnosis of cystinosis; and
2. Member has corneal cystine crystal accumulation; and
3. Prescribed by or in consultation with an ophthalmologist or a specialist with experience in treating cystinosis with corneal cystine crystal accumulation

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA Cysteamine hydrochloride (Cystaran®, Cystadrops®) is medically necessary when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

Nephrotic Cystinosis

INITIAL CRITERIA: Cysteamine bitartrate (Cystagon®) is medically necessary when there is a diagnosis of nephrotic cystinosis.

Initial authorization: 2 years

REAUTHORIZATION CRITERIA Cysteamine bitartrate (Cystagon®) is medically necessary when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

INITIAL CRITERIA: Cysteamine bitartrate (Procysbi®) is medically necessary when ALL of the following are met:

1. Diagnosis of nephrotic cystinosis; and
2. Member is 1 year of age or older; and

3. Inadequate response or titration from cysteamine bitartrate immediate release capsules (Cystagon®)

Initial Authorization duration: 2 years

REAUTHORIZATION CRITERIA: Cysteamine bitartrate (Procysbi®) is medically necessary when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

P&T Approval Date: Dec-12-2024

Title: Cystic Fibrosis Agents (Kalydeco, Orkambi, Trikafta, Symdeko)

Applicable Drugs:

Drug Name	Generic Name
Kalydeco®	Ivacaftor
Orkambi®	Lumacaftor/ivacaftor
Trikafta™	Elexacaftor/tezacaftor/ivacaftor and ivacaftor
Symdeko®	Tezacaftor/ivacaftor

Policy:

INITIAL CRITERIA: Ivacaftor (Kalydeco®) is approved when ALL of the following are met:

1. Diagnosis of cystic fibrosis (CF); and
2. Member is 1 month of age or older; and
3. Prescribed by or in consultation with a pulmonologist or specialist affiliated with a CF care center; and
4. Presence of one mutation in the CFTR gene that is responsive to ivacaftor as noted in the Prescribing Information (if the patient's genotype is unknown, an FDA-cleared test must be used to detect the presence of CFTR mutation followed by verification with bi-directional sequencing when recommended by the mutation test)

INITIAL CRITERIA: Lumacaftor/ivacaftor (Orkambi®) is approved when ALL of the following are met:

1. Diagnosis of cystic fibrosis (CF); and
2. Member is 1 year of age or older; and
3. Prescribed by or in consultation with a pulmonologist or specialist affiliated with a CF care center; and
4. Homozygous for the F508del mutation in the CFTR gene (if the patient's genotype is unknown, an FDA-cleared CR mutation test must be performed to determine the presence of the F508del mutation on both alleles of the CFTR gene)

INITIAL CRITERIA: Elexacaftor/tezacaftor/ivacaftor and ivacaftor (Trikafta™) is approved when ALL of the following are met:

1. Diagnosis of cystic fibrosis (CF); and
2. Member is 2 years of age or older; and
3. One of the following:
 - a. Member has at least one F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene as detected by an FDA-cleared cystic fibrosis mutation test; OR

- b. Member has at least one mutation in the CFTR gene that is responsive based on in vitro data to elxacaftor/tezacaftor/ivacaftor (Trikafta™) as noted in the Prescribing Information; and
1. Prescribed by or in consultation with a pulmonologist or specialist affiliated with a CF care center

INITIAL CRITERIA: Tezacaftor/ivacaftor (Symdeko®) is approved when ALL of the following are met:

1. Diagnosis of cystic fibrosis (CF); and
2. Member is 6 years of age or older; and
3. Prescribed by or in consultation with a pulmonologist or specialist affiliated with a CF care center; and
4. Documentation of one of the following:
 - a. Member is homozygous for the F508del mutation; or
 - b. Member has at least one tezacaftor/ivacaftor responsive mutation in the CFTR gene as noted in the Prescribing Information (If the patient's genotype is unknown, an FDA-cleared test must be used to detect the presence of CFTR mutation followed by verification with bi-directional sequencing when recommended by the mutation test).

Initial Authorization duration: 2 years

REAUTHORIZATION CRITERIA: Ivacaftor (Kalydeco®), Lumacaftor/ivacaftor (Orkambi®), Elxacaftor/tezacaftor/ivacaftor and ivacaftor (Trikafta™), or Tezacaftor/ivacaftor (Symdeko®) is re-approved when there is positive clinical response to therapy (e.g., improvement in lung function or decreased number of pulmonary exacerbations).

Reauthorization duration: 2 years

P&T Approval Date: March 20, 2025

Title: Dalfampridine (Ampyra®)

Applicable Drugs:

Brand Name	Generic Name
Ampyra	Dalfampridine

Policy:

INITIAL CRITERIA: Dalfampridine (Ampyra®) is medically necessary when ALL the following are met:

1. Diagnosis of multiple sclerosis; and
2. Member is 18 years of age or older; and
3. Member has difficulty walking; and
4. Prescribed by or in consultation with a neurologist; and
5. One of the following:
 1. Member has an expanded disability status scale (EDSS) score less than or equal to 7; or
 2. Member is not restricted to using a wheelchair (if EDSS is not measured); and
6. For brand Ampyra® only, inadequate response or inability to tolerate generic dalfampridine

Initial authorization duration: 6 months

CONTINUATION CRITERIA: Dalfampridine (Ampyra®) is medically necessary when ALL of the following are met:

1. Documentation of a 20% improvement in walking speed; and
2. Prescribed by or in consultation with a neurologist; and
3. For brand Ampyra® only, inadequate response or inability to tolerate generic dalfampridine

Continuation authorization duration: 2 years

P&T Approval Date: March 20, 2025

Title: Dextromethorphan hydrobromide and quinidine sulfate (Nuedexta)

Applicable Drugs:

Brand Name	Generic Name
Nuedexta®	dextromethorphan hydrobromide and Quinidine sulfate

Policy:

INITIAL CRITERIA: Dextromethorphan hydrobromide and quinidine sulfate (Nuedexta®) is medically necessary when ALL of the following are met:

1. Diagnosis of pseudobulbar affect; and
2. Prescribed by or in consultation with a neurologist or psychiatrist; and
3. Member is 18 years of age or older; and
4. There is an absence of cardiac rhythm disorder documented by a cardiac test (e.g., electrocardiogram); and
5. Member has one of the following conditions:
 - a. Amyotrophic lateral sclerosis
 - b. Multiple sclerosis
 - c. Alzheimer's disease
 - d. Parkinson's disease
 - e. Stroke
 - f. Traumatic brain injury

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Dextromethorphan hydrobromide and quinidine sulfate (Nuedexta®) is medically necessary when both of the following are met:

1. Documentation of clinical benefit from ongoing therapy (e.g., decrease in laughing/crying episodes); and
2. Prescribed by or in consultation with a neurologist or psychiatrist

Reauthorization duration: 2 years

P&T Approval Date: Dec-12-2024

Title: Dichlorphenamide (Keveyis®, Ormalvi®)

Applicable Drugs:

Brand Name	Generic Name
Keveyis®, Ormalvi®	Dichlorphenamide

Policy:

INITIAL CRITERIA: Dichlorphenamide (Keveyis®, Ormalvi®) is approved when of ALL of the following are met:

1. Treatment of primary hyperkalemic periodic paralysis, primary hypokalemic paralysis, and related variants; and
2. Prescribed by or in consultation with a neurologist; and
3. No documentation of ANY of the following:
 - a. Concomitant use of high dose aspirin; or
 - b. Severe pulmonary disease; or
 - c. Hepatic insufficiency; and
4. Member is 18 years of age or older; and
5. One of the following:
 - a. Member has positive genetic panel for periodic paralysis; or
 - b. One of the following tests demonstrated positive results for periodic paralysis:
 1. EMG/nerve conduction studies, or
 2. Long exercise test, or
 3. Muscle biopsy, or
 4. Muscle MRI

Initial authorization duration: 3 months

CONTINUATION CRITERIA: Dichlorphenamide (Keveyis®, Ormalvi®) is reapproved when there is documentation of positive clinical response to therapy as evidenced by a decrease in weekly attack frequency from baseline .

Continuation authorization duration: 2 years

P&T Approval Date: Jul-01-2024

Title: Diclofenac Products

Applicable Drugs:

Brand Name	Generic Name
Flector®/Licart® Patch	Diclofenac epolamine 1.3% patch
Pennsaid® Solution	Diclofenac sodium 1.5%, 2% solution

Policy:

INITIAL CRITERIA: diclofenac epolamine (Flector®/Licart®) patch, diclofenac sodium 2% solution or Pennsaid® is approved when BOTH of the following are met:

1. Diagnosis of pain; and
2. ONE of the following:
 1. BOTH of the following:
 1. Inadequate response or inability to tolerate TWO of the following:
 1. Meloxicam
 2. Celecoxib
 3. Other oral NSAID; and
 2. Inadequate response or inability to tolerate ONE of the following:
 1. Generic topical diclofenac gel 1%
 2. Generic topical diclofenac solution 1.5%; or
 3. BOTH of the following:
 1. Member is 65 years of age or older; and
 2. Inadequate response or inability to tolerate ONE of the following:
 1. Generic topical diclofenac gel 1%
 2. Generic topical diclofenac solution 1.5%

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: diclofenac epolamine (Flector®/Licart®) patch, diclofenac sodium 2% solution or Pennsaid® is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

P&T Approval Date: March 20, 2025

Title: Doxycycline, Minocycline ER/IR (Oracea, Emrosi)

Applicable Drugs:

Brand Name	Generic Name
Oracea	doxycycline IR/ER
Emrosi	minocycline hydrochloride

Policy:

INITIAL CRITERIA: Doxycycline IR/ER (Oracea), minocycline IR/ER (Emrosi™) is medically necessary when ALL of the following are met:

1. Diagnosis of inflammatory lesions (papules and pustules) rosacea; and
2. Member is 18 years of age or older; and
3. Inadequate response or inability to tolerate both generic doxycycline IR 20mg tablets and minocycline

Initial authorization duration: 9 months

REAUTHORIZATION CRITERIA: Doxycycline IR/ER (Oracea), minocycline IR/ER (Emrosi™) is medically necessary when BOTH of the following are met:

1. Documentation of positive clinical response to therapy; and
2. Documentation of continued need for treatment beyond 9 months

Reauthorization duration: 2 years

P&T Approval Date: March 20, 2025

Title: Doxylamine/pyridoxine (Diclegis, Bonjesta)

Applicable Drugs:

Brand name	Generic name
Diclegis	doxylamine/ pyridoxine
Bonjesta	doxylamine/ pyridoxine

Policy:

Doxylamine/pyridoxine (Diclegis®, Bonjesta®) is medically necessary when ALL of the following are met:

1. Diagnosis of nausea and vomiting of pregnancy; and
2. Inadequate response to conservative management (e.g., change in dietary habits, ginger, acupressure, etc.); and
3. Inadequate response or inability to tolerate generic doxylamine and generic pyridoxine (Vitamin B6) taken together.

Authorization duration: 9 months

P&T Approval Date: Dec-12-2024

Title: Droxidopa (Northera®)

Applicable Drugs:

Generic	Brand
Droxidopa	Northera®

Policy:

INITIAL CRITERIA: Droxidopa (Northera®) is approved when ALL of the following are met:

1. Diagnosis of symptomatic neurogenic orthostatic hypotension; and
2. Prescribed by, or in consultation with, ONE of the following:
 - a. Cardiologist; or
 - b. Neurologist; or
 - c. Nephrologist; and
3. Member is 18 years of age or older; and
4. Attempt has been made to manage neurogenic orthostatic hypotension through at least one non-pharmacologic intervention (e.g. use of compression stockings/abdominal binder, increasing salt/fluid intake, participation in regular exercise, discontinue or reduce hypotensive or antihypertensive medications); and
5. Inadequate response or inability to tolerate midodrine or fludrocortisone; and
6. For the Brand Northera only, inadequate response or inability to tolerate generic droxidopa

Initial authorization duration: 1 month

REAUTHORIZATION CRITERIA: Droxidopa (Northera®) is re-approved when ALL of the following are met:

1. Diagnosis of symptomatic neurogenic orthostatic hypotension; and
2. For the Brand Northera only, inadequate response or inability to tolerate generic droxidopa; and
3. Prescribed by, or in consultation with, ONE of the following:
 1. Cardiologist; or
 2. Neurologist; or
 3. Nephrologist; and
4. Documentation of positive clinical response to therapy (e.g. improvement in symptoms such as orthostatic dizziness, lightheadedness, etc.)

Reauthorization duration: 12 months

P&T Approval Date: Jul-01-2024

Title: Drugs Exceeding Claim Dollar Limit Threshold

Applicable Drugs:

Drug claims where total drug cost exceeds \$10,000

Policy:

Claims that exceed \$10,000 are approved when the use, including indication, dose, frequency, quantity, and duration, for the requested drug is approved by the FDA or considered medically accepted per Off-Label Use policy.

Authorization duration: 2 years, or for the duration of applicable medical necessity approval (for submitted cost plus \$3000)

P&T Approval Date: Jul-01-2024

Title: Duchenne Muscular Dystrophy (DMD) Agents

Applicable Drugs:

Brand Name	Generic Name
Emflaza®	Deflazacort
Agamree®	Vamorolone
Duvyzat™	givinostat

Policy:

INITIAL CRITERIA: Deflazacort (Emflaza®) is medically necessary when ALL of the following are met:

1. Diagnosis of Duchenne muscular dystrophy (DMD) confirmed by ONE of the following:
2. Mutation of the dystrophin gene as confirmed by genetic testing; or
3. Absence of the dystrophin protein confirmed by muscle biopsy; and
4. Member is 2 years of age or older; and
5. Prescribed by or in consultation with a neurologist who has experience treating children; and
6. Member has had an inadequate response or inability to tolerate prednisone or prednisolone given at a dose of 0.75 mg/kg/day or 10 mg/kg/weekend; and
7. Dose will not exceed 0.9 milligrams per kilogram of body weight once daily; and
8. For brand Emflaza® only, inadequate response or inability to tolerate generic deflazacort

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Deflazacort (Emflaza®) is medically necessary when ALL of the following are met:

1. Member has experienced a benefit from therapy (e.g., improvement or preservation of muscle strength); and
2. Dose will not exceed 0.9 milligrams per kilogram of body weight once daily; and
3. For brand Emflaza® only, inadequate response or inability to tolerate generic deflazacort

Reauthorization duration: 12 months

INITIAL CRITERIA: Vamorolone (Agamree®) is medically necessary when ALL of the following are met:

1. Diagnosis of Duchenne muscular dystrophy (DMD); and
2. Member is 2 years of age or older; and
3. Member has received genetic testing for a mutation of the dystrophin gene; and
4. One of the following:
 - a. Member has a confirmed mutation of the dystrophin gene; or
 - b. Muscle biopsy confirmed an absence of dystrophin gene; and
5. Member had inadequate response or inability to tolerate prednisone given at a dose of 0.75 mg/kg/day or 10 mg/kg/weekend; and
6. Prescribed by or in consultation with a neurologist who has experience treating children with DMD; and
7. One of the following:
 - a. For members less than or equal to 50 kg, dose will not exceed 6 mg/kg of body weight once daily; or
 - b. For members greater than 50 kg, dose will not exceed 300 mg/day

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Vamorolone (Agamree®) is medically necessary when ALL of the following are met:

1. Member has experienced a benefit from therapy (e.g., improvement or preservation of muscle strength); and
2. One of the following:
 - a. For members less than or equal to 50 kg, dose will not exceed 6 mg/kg of body weight once daily; or
 - b. For members greater than 50 kg, dose will not exceed 300 mg/day

Reauthorization duration: 12 months

INITIAL CRITERIA: Givinostat (Duvyzat™) is medically necessary when ALL of the following are met:

1. Diagnosis of Duchenne Muscular Dystrophy (DMD); and
2. Member is 6 years of age or older; and
3. Member has received genetic testing for a mutation of the dystrophin gene; and
4. One of the following:
 - a. Member has confirmed mutation of the dystrophin gene; or
 - b. Muscle biopsy confirmed an absence of dystrophin gene; and
5. Member is ambulatory without needing an assistive device (e.g., without side-by-side assist, cane, walker, wheelchair, etc.) prior to initiating givinostat (Duvyzat™); and
6. Requested drug will be used concomitantly with a corticosteroid regimen; and
7. Prescribed by or in consultation with a neurologist who has experience treating children with Duchenne Muscular Dystrophy (DMD)

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Givinostat (Duvyzat™) is medically necessary when ALL of the following are met:

1. Member has experienced a benefit from therapy (e.g., improvement in preservation of muscle strength); and
2. Member is maintaining ambulatory status without needing an assistive device (e.g., without side-by-side assist, cane, walker, wheelchair, etc.); and
3. Member continues to receive concomitant corticosteroid regimen; and
4. Prescribed by or in consultation with a neurologist who has experience treating children with Duchenne Muscular Dystrophy (DMD)

Reauthorization duration: 12 months

P&T Approval Date: March 20, 2025

Title: Dupilumab (Dupixent)

Applicable Drugs:

Brand Name	Generic Name
Dupixent®	dupilumab

Policy:

Atopic Dermatitis

INITIAL CRITERIA: Dupilumab (Dupixent®) is medically necessary ALL of the following are met:

1. Member is 6 months of age or older; and
2. Diagnosis of moderate-severe atopic dermatitis; and
3. One of the following:
 1. Involvement of at least 10% body surface area (BSA)
 2. SCORing Atopic Dermatitis (SCORAD) index value of at least 25; and
4. Prescribed by or in consultation with a dermatologist, allergist, or immunologist; and
5. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate ONE of the following:
 1. Topical steroids, medium potency or higher; or
 2. Topical tacrolimus; or
 3. Topical pimecrolimus; or
 4. Eucrisa; or
 5. Opzelura; and
6. No concurrent therapy with any other biologic agents; and
7. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Dupilumab (Dupixent®) is medically necessary when ALL of the following are met:

1. Documentation of positive clinical response to therapy (e.g., reduction in body surface area involvement, reduction in pruritus severity); and
2. ONE of the following:
 1. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
 2. Member is continuing on the established dose and frequency previously approved

Reauthorization duration: 12 months

DOSE	
Adults	Initial dose: 600 mg (two 300mg injections) Maintenance: 300 mg given every other week

Pediatric patients 6 months to 5 years of age	5 to less than 15 kg: 200 mg (one 200 mg injection) every 4 weeks 15 to less than 30 kg: 300 mg (one 300 mg injection) every 4 weeks
Pediatric patients 6 years to 17 years of age	15 to less than 30 kg: 600 mg (two 300 mg injections) initially, followed by 300 mg every 4 weeks 30 to less than 60 kg: 400 mg (two 200 mg injections) initially, followed by 200 mg every 2 weeks 60 kg or more: 600 mg (two 300 mg injections) initially, followed by 300 mg every 2 weeks

Moderate to severe asthma

INITIAL CRITERIA: Dupilumab (Dupixent®) is medically necessary when ALL of the following are met:

1. Member is 6 years of age or older; and
2. One of the following:
 1. Submission of documentation (e.g., chart notes) confirming a diagnosis of moderate to severe asthma with an eosinophilic phenotype defined as blood eosinophil levels of at least 150 cells/mcL at baseline or at least 300 cells/mcL within the past 12 months; or
 2. Submission of documentation (e.g., chart notes) confirming a diagnosis of Moderate to severe oral corticosteroid-dependent asthma; and
3. ONE of the following:
 1. Member is 6 to less than 12 years of age and paid claim or submission of documentation (e.g., chart notes) confirming the member is currently being treated or has a contraindication or intolerance to one of the following:
 1. Medium-dose inhaled corticosteroids (e.g., greater than 100-200mcg fluticasone propionate equivalent/day) and ONE additional controller medication (e.g., leukotriene receptor antagonist [LTRA] (e.g., montelukast), long-acting beta-2 agonist [LABA] (e.g., salmeterol), long-acting muscarinic antagonist [LAMA] (e.g., tiotropium)); or
 2. One medium-dose combination ICS/LABA product (e.g., Advair [fluticasone propionate/salmeterol], Bre Ellipta [fluticasone furoate/vilanterol], Symbicort® [budesonide/formoterol]); or
 2. Member is 12 years of age or older and paid claims or submission of documentation (e.g., chart notes) confirming member is currently being treated or has a contraindication or intolerance to one of the following:
 1. High dose inhaled corticosteroid (e.g., greater than or equal to 500mcg fluticasone propionate equivalent/day); and ONE additional controller medication (e.g., leukotriene receptor antagonist [LTRA] (e.g., montelukast), long-acting beta-2 agonist [LABA] (e.g., salmeterol), long-acting muscarinic antagonist [LAMA] (e.g., tiotropium)); or

2. One maximally dosed combination ICS/LABA product (e.g., Advair [fluticasone propionate/salmeterol], Bre Ellipta [fluticasone furoate/vilanterol], Symbicort [budesonide/formoterol]); and
4. One of the following:
 1. Member has had at least two or more asthma exacerbations requiring systemic corticosteroids (e.g., prednisone) within the past 12 months; or
 2. Prior asthma-related hospitalization within the past 12 months; and
5. Prescribed by or in consultation with a pulmonologist or allergy/ immunology specialist; and
6. No concurrent therapy with any other biologic agents; and
7. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 12 months

CONTINUATION CRITERIA: Dupilumab (Dupixent®) is medically necessary when ALL of the following are met:

1. Documentation of a positive clinical response to therapy (e.g., reduction in exacerbations, improvement in FEV1, decreased use of rescue medications); and
2. ONE of the following:
 1. Member is 6 to less than 12 years of age and paid claim or submission of documentation (e.g., chart notes) confirming the member is current being treated or has a contraindication or intolerance to one of the following:
 1. Medium-dose inhaled corticosteroids (e.g., greater than 100-200mcg fluticasone propionate equivalent/day) with or without ONE additional controller medication (e.g., leukotriene receptor antagonist [LTRA] (e.g., montelukast), long-acting beta-2 agonist [LABA] (e.g., salmeterol), long-acting muscarinic antagonist [LAMA] (e.g., tiotropium)); or
 2. One medium-dose combination ICS/LABA product (e.g., Advair [fluticasone propionate/salmeterol], Bre Ellipta [fluticasone furoate/vilanterol], Symbicort® [budesonide/formoterol]); or
 2. Member is 12 years of age or older and paid claims or submission of documentation (e.g., chart notes) confirming member is currently being treated or has a contraindication or intolerance to one of the following
 1. High dose inhaled corticosteroid (ICS) (e.g., greater than or equal to 500mcg fluticasone propionate equivalent/day); with or without ONE additional controller medication (e.g., leukotriene receptor antagonist [LTRA] (e.g., montelukast), long-acting beta-2 agonist [LABA] (e.g., salmeterol), long-acting muscarinic antagonist [LAMA] (e.g., tiotropium)); or
 2. One maximally dosed combination ICS/LABA product (e.g., Advair [fluticasone propionate/salmeterol], Bre Ellipta [fluticasone furoate/vilanterol], Symbicort [budesonide/formoterol]); and
3. Prescribed by or in consultation with a pulmonologist or allergy/immunology specialist; and
4. No concurrent therapy with any other biologic agents; and
5. ONE of the following:
 1. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
 2. Member is continuing on the established dose and frequency previously approved

Continuation authorization duration: 12 months

DOSE	
Adults and pediatric patients 12 years and older	Initial dose: 400 mg (two 200 mg injections) Maintenance: 200 mg every 2 weeks OR Initial dose: 600 mg (two 300 mg injections) Maintenance dose: 300 mg every 2 weeks
Dosage for patients with oral corticosteroid-dependent asthma or with co-morbid moderate-to-severe atopic dermatitis or adults with co-morbid chronic rhinosinusitis with nasal polyposis	Initial dose: 600 mg (two 300 mg injections) Maintenance dose: 300 mg every 2 weeks
Pediatric patients 6 years to 11 years of age	15 to less than 30 kg: 300 mg every 4 weeks ≥ 30 kg: 200 mg every other week

Chronic rhinosinusitis with nasal polyposis (CRSwNP)

INITIAL CRITERIA: Dupilumab (Dupixent®) is medically necessary when ALL of the following are met:

1. Submission of documentation (e.g., chart notes) confirming diagnosis of chronic rhinosinusitis with nasal polyposis (CRSwNP); and
2. Member is 12 years of age or older; and
3. Prescribed by or in consultation with an allergist, immunologist, or Ear Nose Throat specialist; and
4. Paid claims or submission of documentation (e.g., chart notes) confirming an inadequate response or inability to tolerate at least a 2-month treatment with intranasal corticosteroid (e.g., fluticasone); and
5. Used in combination with another agent for CRSwNP; and
6. No concurrent therapy with any other biologic agents; and
7. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial Authorization duration: 12 months

REAUTHORIZATION CRITERIA: Dupilumab (Dupixent®) is medically necessary when ALL of the following are met:

1. Documentation of a positive clinical response to therapy (e.g., reduction in nasal polyps score [NPS; 0-8 scale], improvement in nasal congestion/obstruction score [NC; 0-3 scale]); and
2. Prescribed by allergist, immunologist or Ear Nose Throat specialist; and

3. Used in combination with another agent for CRSwNP; and
4. No concurrent therapy with any other biologic agents and
5. ONE of the following:
 1. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
 2. Member is continuing on the established dose and frequency previously approved

Reauthorization duration: 12 months

DOSE	
Adults and pediatric patients 12 years of age and older	300 mg every other week

Eosinophilic Esophagitis (EoE)

INITIAL CRITERIA: Dupilumab (Dupixent®) is medically necessary when ALL of the following are met:

1. Submission of documentation (e.g., chart notes) confirming diagnosis of eosinophilic esophagitis (EoE); and
2. Member has symptoms of esophageal dysfunction (e.g., dysphagia, food impaction, gastroesophageal reflux disease [GERD]/heartburn symptoms, chest pain, abdominal pain); and
3. Member has at least 15 intraepithelial eosinophils per high power field (HPF); and
4. Other causes of esophageal eosinophilia have been ruled out; and
5. Both of the following:
 1. Member is 1 year of age or older; and
 2. Member weighs at least 15 kg; and
6. Paid claims or submission of documentation (e.g., chart notes) confirming an inadequate response or inability to tolerate at least an 8-week trial of one of the following:
 1. Proton Pump Inhibitors (e.g., pantoprazole, omeprazole); or
 2. Topical (esophageal) corticosteroids (e.g., budesonide, fluticasone); and
7. Prescribed by or in consultation with gastroenterologist or allergist/immunologist; and
8. No concurrent therapy with any other biologic agents; and
9. Dose and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Dupilumab (Dupixent®) is medically necessary when ALL of the following are met:

1. Documentation of a positive clinical response to therapy as evidenced by improvement of at least one of the following from baseline:
 1. Symptoms (e.g., dysphagia, food impaction, heartburn, chest pain); or
 2. Histologic measures (e.g., esophageal intraepithelial eosinophil count); or
 3. Endoscopic measures (e.g., edema, furrows, exudates, rings, strictures); and
2. No concurrent therapy with any other biologic agents; and
3. ONE of the following:

1. Dose and frequency does not exceed maximum FDA recommendation per indication requested; or
2. Member is continuing on the established dose and frequency previously approved

Reauthorization duration: 12 months

DOSE	
15 to less than 30 kg	200 mg every other week
30 to less than 40 kg	300 mg every other week
40 kg or more	300 mg every week

Prurigo Nodularis (PN)

INITIAL CRITERIA: Dupilumab (Dupixent®) is medically necessary when ALL of the following are met:

1. Submission of documentation (e.g., chart notes) confirming a diagnosis of Prurigo Nodularis (PN); and
2. Member is 18 years of age or older; and
3. Member has at least 20 nodular lesions; and
4. Paid claims or submission of documentation (e.g., chart notes) confirming inadequate response or inability to tolerate one previous PN treatment (e.g., topical corticosteroids, topical calcineurin inhibitors, topical capsaicin); and
5. Prescribed by or in consultation with allergist/immunologist or dermatologist; and
6. No concurrent therapy with any other biologic agents; and
7. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Dupilumab (Dupixent®) is medically necessary when ALL of the following are met:

1. Documentation of a positive clinical response to therapy as evidenced by at least ONE of the following:
 1. Reduction in the number of nodular lesions from baseline; or
 2. Improvement in symptoms (e.g., pruritus, inflammation) from baseline; and
2. ONE of the following:
 1. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
 2. Member is continuing on the established dose and frequency previously approved

Reauthorization duration: 12 months

DOSE	
Adults	Initial dose: 600 mg (two 300 mg injections) Maintenance dose: 300 mg given every other week

Chronic obstructive pulmonary disease (COPD)

INITIAL CRITERIA: Dupilumab (Dupixent®) is medically necessary ALL of the following are met:

1. Member is 18 years of age or older; and
2. Submission of documentation (e.g., chart notes) confirming a diagnosis of chronic obstructive pulmonary disease (COPD) and Presence of Type 2 inflammation evidenced by blood eosinophils greater than or equal to 300 cells per microliter at baseline; and
3. Paid claims or submission of documentation (e.g., chart notes) confirming member is currently being treated with ONE of the following or is unable to tolerate these medications:
 1. Triple therapy (i.e., an inhaled corticosteroid (ICS), a long-acting muscarinic antagonist (LAMA) and a long-acting beta agonist (LABA); or
 2. If ICS are contraindicated, a LAMA and a LABA; and
4. Post-bronchodilator forced expiratory volume [FEV1] / forced vital capacity [FVC] ratio less than 0.70 while on an optimized therapy; and
5. Member has had one of the following within the past 12 months:
 1. At least two exacerbations where systemic corticosteroids [intramuscular, intravenous, or oral (e.g., prednisone)] were required at least once; or
 2. COPD-related hospitalization; and
6. Member experiences dyspnea during everyday activities (e.g., needs to stop for breath when walking on level ground); and
7. Prescribed by or in consultation with a pulmonologist; and
8. No concurrent therapy with any other biologic agents; and
9. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Dupilumab (Dupixent®) is medically necessary when ALL of the following are met:

1. Member demonstrates a positive clinical response to therapy (e.g., improved lung function, a reduction in COPD exacerbations); and
2. Member continues to receive one of the following therapies at an optimized dose:
 1. Triple therapy (i.e., an inhaled corticosteroid (ICS), a long-acting muscarinic antagonist (LAMA) and a long-acting beta agonist (LABA); or
 2. If ICS are contraindicated, a LAMA and a LABA; and
3. Prescribed by or in consultation with a pulmonologist; and
4. ONE of the following:
 1. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
 2. Member is continuing on the established dose and frequency previously approved

Reauthorization duration: 12 months

DOSE	
Adults	300 mg given every other week

P&T Approval Date: June- 05-2025

Title: Edaravone (Radicava ORS)

Applicable Drugs:

Brand Name	Generic Name
Radicava ORS®	Edaravone

Policy:

INITIAL CRITERIA: Edaravone (Radicava ORS®) is approved when ALL of the following are met:

1. Diagnosis of "definite" or "probable" amyotrophic lateral sclerosis (ALS) per the revised EL Escorial and Airlie House diagnostic criteria; and
2. Prescribed by or in consultation with a neurologist with expertise in the diagnosis of ALS; and
3. Member has scores greater than or equal to 2 in all items of the ALS Functional Rating Scale-Revised (ALSFRS-R) criteria at the start of treatment; and
4. Member has a percent (%) forced vital capacity (%FVC) greater than or equal to 80% at the start of treatment; and
5. Member is not dependent on invasive ventilation or tracheostomy

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Edaravone (Radicava ORS®) is re-approved when BOTH of the following are met:

1. Documentation of positive clinical response to therapy (e.g., slowing in the decline of functional abilities); and
2. Member is not dependent on invasive ventilation or tracheostomy

Reauthorization duration: 12 months

P&T Approval Date: March 20, 2025

Title: Elagolix sodium (Orilissa™)

Applicable Drugs:

Brand Name	Generic Name
Orilissa™	Elagolix

Policy:

Elagolix (Orilissa™) is medically necessary when all of the following are met:

1. Diagnosis of moderate to severe pain associated with endometriosis; and
2. Member is 18 years of age or older; and
3. ONE of the following:
 - a. Inadequate response or inability to tolerate BOTH of the following:
 1. One non-steroidal anti-inflammatory drug; and
 2. Contraceptives; or
 - b. Member has had surgical ablation to prevent recurrence

Authorization duration: 2 years

Coverage duration is limited to:

1. 24 months/ lifetime for 150mg tablet
2. 6 months/ lifetime for 200mg tablet

All other treatment durations are considered Experimental/ Investigational.

P&T Approval Date: Sep-12-2024

Title: Elagolix/estradiol/norethindrone acetate (Oriahnn)/Relugolix, estradiol and norethindrone (Myfembree)

Applicable Drugs:

Brand Name	Generic Name
Oriahnn	Elagolix, estradiol, norethindrone acetate
Myfembree	Relugolix, estradiol, norethindrone acetate

Policy:

Heavy Menstrual Bleeding Associated with Uterine Leiomyomas

INITIAL CRITERIA: Elagolix/estradiol/norethindrone acetate (Oriahnn®) or Relugolix/estradiol/norethindrone acetate (Myfembree®) is medically necessary when ALL of the following are met:

1. Diagnosis of heavy menstrual bleeding associated with uterine leiomyomas (fibroids); and
2. Member is premenopausal; and
3. One of the following:
 1. Inadequate response after at least 3 months OR inability to tolerate ONE of the following:
 1. Combination (estrogen/progestin) contraceptive; or
 2. Progestins; or
 2. Member has had a previous interventional therapy to reduce bleeding (e.g., uterine-artery embolization and magnetic resonance-guided focused ultrasonography); and
4. Treatment duration has not exceeded a total of 24 months

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Elagolix/estradiol/norethindrone acetate (Oriahnn®) or Relugolix/estradiol/norethindrone acetate (Myfembree®) is medically necessary when BOTH of the following are met:

1. Member has improvement in bleeding associated with uterine leiomyomas (fibroids) (e.g., significant/sustained reduction in menstrual blood loss per cycle, improved quality of life, etc.); and
2. Treatment duration has not exceeded a total of 24 months

Reauthorization duration: 12 months

Pain Associated with Endometriosis

INITIAL CRITERIA: Relugolix/estradiol/norethindrone acetate (Myfembree®) is medically necessary when ALL of the following are met:

1. Diagnosis of moderate to severe pain associated with endometriosis; and

2. Member is premenopausal; and
3. One of the following:
 1. Inadequate response after at least 3 months or inability to tolerate one of the following:
 1. Danazol; and
 2. Combination (estrogen/progestin) contraceptive; and
 3. Progestins; or
 2. Member has had surgical ablation to prevent recurrence; and
4. Treatment duration has not exceeded a total of 24 months

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Relugolix/estradiol/norethindrone acetate (Myfembree®)

is medically necessary when BOTH of the following are met:

1. Member has improvement in pain associated with endometriosis (e.g., improvement in dysmenorrhea and non-menstrual pelvic pain); and
2. Treatment duration has not exceeded a total of 24 months

Reauthorization duration: 12 months

Coverage duration is limited to 24 months/lifetime

All other treatment durations are considered experimental/investigational.

P&T Approval Date: Dec-12-2024

Title: Ensifentrine (Ohtuvayre™)

Applicable Drugs:

Brand Name	Generic Name
Ohtuvayre™	Ensifentrine

Policy:

INITIAL CRITERIA: Ensifentrine (Ohtuvayre™) is medically necessary when ALL of the following are met:

1. Diagnosis of maintenance treatment of chronic obstructive pulmonary disease (COPD); and
2. Member is 18 years of age and older; and
3. Post-bronchodilator forced expiratory volume [FEV1] / forced vital capacity [FVC] ratio less than 0.70; and
4. Member is symptomatic despite being on at least two therapies indicated for the treatment of COPD and will continue to be treated with the therapies (e.g. long-acting muscarinic antagonists [e.g., tiotropium], long-acting beta agonist [e.g., formoterol]), unless there is a contraindication or intolerance; and
5. Member experiences dyspnea during everyday activities (e.g., short of breath when walking up a slight hill)

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Ensifentrine (Ohtuvayre™) is medically necessary when ALL of the following are met:

1. Documentation of a positive clinical response to therapy; and
2. Member continues to be treated with at least two therapies indicated for the treatment of COPD (e.g. long-acting muscarinic antagonists [e.g., tiotropium], long-acting beta agonist [e.g., formoterol]), unless there is a contraindication or intolerance

Reauthorization duration: 12 months

P&T Approval Date: March 20, 2025

Title: Epinephrine Products

Applicable Drugs:

Brand Name	Generic Name
Auvi-Q, EpiPen, EpiPen Jr, Neffy	Epinephrine

Policy:

Auvi Q®, EpiPen®, EpiPen Jr.®, Neffy® is approved when ALL of the following are met:

1. ONE of the following:
 1. Documentation of a demonstrated inability to use one chemically equivalent generic agent; or
 2. The member has a genuine allergic reaction to an inactive ingredient in generic agent(s) (allergic reaction(s) must be clearly documented in the patient's medical record); and
2. For Auvi Q® and Neffy® only, documentation that the member or the member's caregivers would be unable to utilize the alternative epinephrine auto-injector devices (e.g., epinephrine) due to significant visual, physical, or functional impairment

Approval duration: 2 years

P&T Approval Date: March 20, 2025

Title: Excluded medications with no significant advantage over covered alternatives

Applicable Drugs:

N/A

Policy:

Coverage is subject to the terms, conditions, and limitations of the member's contract.

The medications listed below do not meet medical necessity, as defined in the member's benefits book, and will be excluded from coverage (not covered) under the prescription drug benefit.

Drug	Components	Rationale
Ibuprofen/famotidine (Duexis®)	Ibuprofen 800mg/ famotidine 26.6mg tablet	Combination of ibuprofen and famotidine; no advantage over the individual components
Metformin modified, extended release (Glumetza®)	Metformin modified, extended release 500mg, 1000mg tablet	Extended-release formulation of metformin; other extended release products are available
Naproxen/esomeprazole (Vimovo®)	Naproxen 500mg/ esomeprazole 20mg tablet Naproxen 375mg/ esomeprazole 20mg tablet	Combination of naproxen and esomeprazole; no advantage over the individual components; esomeprazole 20mg is available over the counter
Omeprazole/aspirin (Yosprala®)	Omeprazole 40mg/ aspirin 81mg tablet Omeprazole 40mg/ aspirin 325mg tablet	Combination of aspirin and omeprazole; no advantage over the individual components
Omeprazole/sodium bicarbonate capsules 40mg/1100mg (Zegerid capsules® 40mg/1100mg)	Omeprazole 40mg/ sodium bicarbonate 1100mg	Combination of omeprazole and sodium bicarbonate offers no advantage over the individual components,

		omeprazole alone, or other proton pump inhibitors
Vanos®	Fluocinonide 0.1% Cream	High Potency Alternatives Available: Clobetasol Propionate, Augmented Betamethasone, Halobetasol
Prenatal Vitamins, Azesco®, Ziphex®, Pregenna®/PNV® Tab, Zalvit®, DermacinRx Tab Pretrate®	Prenatal Vitamins and Minerals With Folic Acid And Iron (Various Dose Combinations)	Multiple Generic, Prescription Strength Prenatal Vitamins Are Available
Chlorzoxazone 250 Mg	Chlorzoxazone 250 Mg	Chlorzoxazone 500mg Tablet Is Functionally Scored to Be Broken In Half
Vanadom®	Carisoprodol 350 Mg	Alternatives Available: Carisoprodol 350mg, Tizanidine, Cyclobenzaprine, Baclofen, Methocarbamol, Chlorzoxazone 500mg
Diclofenac potassium (Lofena) 25mg tablet	Diclofenac potassium 25mg tablet	Alternatives available: diclofenac potassium 50mg, diclofenac sodium delayed release, ibuprofen, naproxen sodium, meloxicam, celecoxib, indomethacin
Methocarbamol 1000mg tab, Tanlor®	Methocarbamol 1000mg tab	Methocarbamol 500mg tablets available. Alternatives available: carisoprodol 350mg, tizanidine, cyclobenzaprine, methocarbamol 500 and 750mg, chlorzoxazone 500mg

P&T Approval Date: Dec-12-2024

Title: Fabry Disease Agents

Applicable Drugs:

Brand Name	Generic Name
Galafold	migalastat

Policy:

INITIAL CRITERIA: Galafold™ (migalastat) is medically necessary when all of the following are met:

1. Diagnosis of Fabry disease; and
2. Member is 16 years of age or older; and
3. Member has an amenable galactosidase alpha gene (GLA) variant (per FDA labeling information) based on in vitro assay data; and
4. Galafold will not be used in combination with other drug(s) indicated for the treatment of Fabry disease (e.g., Fabrazyme)

Initial Authorization duration: 6 months

REAUTHORIZATION CRITERIA: Galafold™ (migalastat) is medically necessary when both of the following are met:

1. Documentation of positive clinical response to therapy [e.g., reduction in plasma or urinary sediment lyso-GL-3, GL-3 compared to baseline, reduction in number of GL-3 inclusions per kidney interstitial capillary (KIC) in renal biopsy samples compared to baseline, or improvement and/or stabilization in symptoms (e.g., renal function, neuropathic pain)], and
2. Galafold will not be used in combination with other drug(s) indicated for the treatment of Fabry disease (e.g., Fabrazyme)

Reauthorization duration: 2 years

P&T Approval Date: Dec-12-2024

Title: FDA Approved Medications Deemed Experimental Investigational

Applicable Drugs:

Brand Name	Generic Name

*Oncology agents are exempt from the review because they are subjected to medical necessity review per criteria established for oncology agents. Line extensions of existing medications using the same brand name and has the same indication are exempt from the review.

Policy:

Prescription drugs or biologics* that are approved by the FDA under the accelerated approval process are subjected to review to determine if the surrogate or intermediate clinical endpoint used in the trial is an acceptable measure of the drug or biologic's efficacy in the condition for which it is approved, and thus medically necessary. If an FDA approved drug or biologic does not demonstrate efficacy for the disease it is approved to treat, then the drug or biologic is determined to be experimental/investigational, despite FDA approval and is therefore not a covered benefit. Medical necessity is defined in the member's benefits book. Medications that do not meet the definition of medical necessity are excluded from coverage under the prescription drug benefit.

A prescription drug or biologic* is considered medically necessary when the following are met:

1. The prescription drug or biologic* must have final approval from the FDA with the following statement in the label *This indication is approved under accelerated approval based on [surrogate marker used in the clinical trial(s)]. Continued approval for this indication may be contingent upon verification of clinical benefit in the confirmatory trial(s).*; and
2. The scientific evidence must permit conclusions concerning the effect of the prescription drug or biologic on health outcomes; and
3. The prescription drug or biologic must improve the net health outcome; and
4. The prescription drug or biologic must be as beneficial as any established alternatives; and
5. The improvement must be attainable outside the investigational settings.

The medications listed below do not meet medical necessity, as defined in the member's benefits book, and will be excluded from coverage (not covered) under the prescription drug benefit.

P&T Approval Date: Dec-12-2024

Title: Fecal Microbiota Agents

Applicable Drugs:

Brand Name	Generic Name
Vowst™	fecal microbiota spores, live-brpk

Policy:

Fecal microbiota spores, live-brpk (Vowst™) is medically necessary when ALL of the following are met:

1. Diagnosis of recurrent clostridioides difficile infection (CDI) as defined by both of the following:
 - a. Presence of diarrhea defined as a passage of 3 or more loose bowel movements within a 24-hour period for 2 consecutive days; and
 - b. A positive stool test for C. difficile toxin or toxigenic C. difficile; and
2. Member is 18 years of age or older; and
3. Member has a history of two or more recurrent episodes of CDI within 12 months; and
4. ALL of the following:
 - a. Member has completed at least 10 consecutive days of one of the following antibiotic therapies 2-4 days prior to initiating Vowst:
 1. Oral vancomycin; or
 2. Difucid (fidaxomicin); and
 - b. Member has completed the recommended bowel prep (e.g. 296mL of magnesium citrate) the day before and at least 8 hours prior to initiating Vowst; and
 - c. Previous episode of CDI is under control (e.g., less than 3 unformed/loose [i.e., Bristol Stool Scale type 6-7] stools/day for 2 consecutive days); and
5. Prescribed by or in consultation with one of the following:
 - a. Gastroenterologist; or
 - b. Infectious disease specialist

Authorization duration: 14 days

P&T Approval Date: Dec-12-2024

Title: Fezolinetant (Veozah)

Applicable Drugs:

Brand Name	Generic Name
Veozah™	Fezolinetant

Policy:

INITIAL CRITERIA: Fezolinetant (Veozah™) is medically necessary when all of the following are met:

1. Diagnosis moderate to severe vasomotor symptoms due to menopause; and
2. Inadequate response or inability to tolerate a minimum 30-day supply of both of the following:
 - a. Menopausal hormone therapy (e.g., generic estradiol vaginal cream, generic estradiol vaginal tablet); and
 - b. Non-hormonal therapy (e.g., paroxetine mesylate, venlafaxine hcl, clonidine, etc.)

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Fezolinetant (Veozah™) is medically necessary with documentation of positive clinical response to therapy (e.g., decrease in frequency and severity of vasomotor symptoms from baseline, etc.)

Reauthorization duration: 12 months

P&T Approval Date: Dec-12-2024

Title: Finerenone (Kerendia)

Applicable Drugs:

Brand Name	Generic Name
Kerendia®	finerenone

Policy:

INITIAL CRITERIA Finerenone (Kerendia®) is approved when ALL of the following are met:

1. Diagnosis of chronic kidney disease (CKD) associated with type 2 diabetes (T2D); and
2. Urine albumin-to-creatinine ratio (UACR) greater than or equal to 30 mg/g; and
3. Estimated glomerular filtration rate (eGFR) greater than or equal to 25 mL/min/1.73 m²; and
4. Serum potassium level less than or equal to 5.0 mEq/L prior to initiating treatment; and
5. Member is 18 years of age or older; and
6. One of the following:
 1. Minimum 30-day supply trial of a maximally tolerated dose and will continue therapy with ONE of the following:
 1. Generic angiotensin-converting enzyme (ACE) inhibitor (e.g., benazepril, lisinopril); or
 2. Generic angiotensin II receptor blocker (ARB) (e.g., losartan, valsartan); or
 3. Sodium-glucose cotransporter-2 (SGLT2) inhibitor (e.g., Jardiance, Farxiga); or
 2. Member has contraindication or intolerance to ACE inhibitors, ARBs or SGLT2; and

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA Finerenone (Kerendia®) is re-approved with documentation of positive clinical response to therapy (e.g., reduced incidence of a sustained decline in eGFR, kidney failure, or renal death)

Reauthorization duration: 2 years

P&T Approval Date: Jul-01-2024

Title: Formulary Exception Policy

Applicable Drugs:

N/A

Policy:

Tier Exceptions:

A non-preferred drug will be covered at the preferred tier for brand medications as listed below when there is documentation of inadequate response or inability to tolerate at least three preferred or generic tier alternatives in the same pharmacological class*. Reasonably equivalent therapeutic class alternatives will be considered when there are limited pharmacological class alternatives available.

1. Brand medication to preferred brand tier or
2. Generic medication to generic tier

Non-formulary Exceptions:

A non-formulary drug is medically necessary when ONE of the following are met:

1. \$0 cost-share will apply when BOTH of the following are met:
 - a. The drug is described as either a preventative medication identified by the US Preventive Services Task Force (USPSTF) or Women's Preventive Services provision of the Patient Protection and Affordable Care Act (PPACA); and if applicable; and
 - b. For branded products, ALL of the following:
 1. Inadequate response or inability to tolerate the generic equivalent, if available; and
 2. Inadequate response or inability to tolerate a formulary alternative; and
 3. The prescriber has provided documentation indicating the requested product is medically necessary; or
2. Appropriate level of cost share will apply when BOTH of the following are met:
 - a. FDA approved, or compendia supported use; and
 - b. ONE of the following:
 1. If biosimilar of the requested reference product or generic equivalent of the requested brand is available, both of the following:
 1. There is documentation of inadequate response or inability to tolerate biosimilar of the requested reference product or generic equivalent of the requested brand; and
 2. There is documentation of inadequate response or inability to tolerate at least two formulary alternatives in the same pharmacological class*. Reasonably equivalent therapeutic class alternatives will be considered when there are limited pharmacological class alternatives available. Safety edits (age and quantity limits) will apply to non-formulary requests; or

2. If biosimilar of the requested reference product or generic equivalent of the requested brand is NOT available: there is documentation of inadequate response or inability to tolerate at least three formulary alternatives in the same pharmacological class*. Reasonably equivalent therapeutic class alternatives will be considered when there are limited pharmacological class alternatives available. Safety edits (age and quantity limits) will apply to non-formulary requests

CHIP (IN Focus ID 10093453)

A brand medication may be covered at the generic benefit level when there is documentation of an inadequate response or inability to tolerate at least three ~~generic~~ formulary alternatives in the same pharmacological class*. Reasonably equivalent therapeutic class alternatives will be considered when there are limited pharmacological class alternatives available.

Compounded Products:

A non-preferred compounded product may be covered at the preferred (formulary) tier when there is an inadequate response or inability to tolerate/use all other formulary alternatives.

Note: Compounded products are specially made products to meet the needs of an individual member and are not considered generics and thus not eligible for an exception to the generic tier.

\$0 Cost-Share Override

An exception to allow no-cost share is medically necessary when:

1. The drug is described as either a preventative medication identified by the US Preventive Services Task Force (USPSTF) or Women's Preventive Services provision of the Patient Protection and Affordable Care Act (PPACA); and if applicable
2. For branded products, ALL of the following:
 1. Inadequate response or inability to tolerate the generic equivalent, if available
 2. Inadequate response or inability to tolerate a formulary alternative
 3. The prescriber has provided documentation indicating the requested product is medically necessary

**If there are fewer than three alternatives, all alternatives in the pharmacological class must be considered.*

Premium Formulary: This policy does not apply to the premium formulary.

Authorization duration: 1 years

P&T Approval Date: Sep-12-2024

Title: Fosdenopterin (Nulibry™)

Applicable Drugs:

Brand Name	Generic Name
Nulibry®	Fosdenopterin

Policy:

INITIAL CRITERIA Fosdenopterin (Nulibry™) is medically necessary when ALL of the following are met:

1. One of the following:
 - a. Presumed diagnosis of molybdenum cofactor (MoCD) Type A deficiency; or
 - b. Diagnosis of molybdenum cofactor (MoCD) Type A deficiency confirmed by genetic test; and
2. Prescribed by or in consultation with a physician who specializes in the treatment of inherited metabolic disorders

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA Fosdenopterin (Nulibry™) is medically necessary when ALL of the following are met:

1. Diagnosis of molybdenum cofactor (MoCD) Type A deficiency as confirmed by genetic test [if not previously confirmed]; and
2. Prescribed by or in consultation with a physician who specializes in the treatment of inherited metabolic disorders; and
3. Document of positive clinical response to therapy (e.g., reduction in urine concentrations of S-sulfocysteine (SSC))

Reauthorization duration: 2 years

P&T Approval Date: Sep-12-2024

Title: Fostemsavir (Rukobia), Enfuvirtide (Fuzeon)

Applicable Drugs:

Brand Name	Generic Name
Rukobia®	Fostemsavir
Fuzeon®	Enfuvirtide

Policy:

INITIAL CRITERIA: Fostemsavir (Rukobia®) is approved when ALL of the following are met:

1. Diagnosis of HIV-1; and
2. Member is 18 years of age or older; and
3. Will be used in combination with other antiretroviral(s); and
4. Member is treatment-experienced with multi-drug resistant HIV-1 infection; and
5. Member is failing their current antiretroviral regimen due to resistance, intolerance, or safety concerns.

Initial Authorization duration: 12 months

CONTINUATION CRITERIA: Fostemsavir (Rukobia®) is re-approved when there is documentation of positive clinical response to therapy (e.g., decrease in viral load from baseline; HIV-1 RNA <200 copies/mL was achieved; increase in CD4+ cell count over time)

Continuation authorization duration: 2 years

INITIAL CRITERIA: Enfuvirtide (Fuzeon®) is approved when ALL of the following are met:

1. Diagnosis of HIV-1; and
2. Member weighs at least 11kg; and
3. Will be used in combination with other antiretroviral(s); and
4. Member is treatment experienced; and
5. Member is experiencing HIV-1 replication despite ongoing antiretroviral therapy

Initial authorization duration: 12 months

CONTINUATION CRITERIA: Enfuvirtide (Fuzeon®) is re-approved when there is documentation of positive clinical response to therapy (e.g., decrease in viral load from baseline; HIV-1 RNA <200 copies/mL was achieved; increase in CD4+ cell count over time)

Continuation authorization duration: 2 years

P&T Approval Date: Jul-01-2024

Title: Gabapentin (Gralise/Horizant)/pregabalin (Lyrica CR)

Applicable Drugs:

Brand Name	Generic Name
Gralise®	gabapentin
Horizant®	Gabapentin enacarbil
Lyrica CR®	pregabalin controlled-release

Policy:

Post-herpetic neuralgia

INITIAL CRITERIA: Gabapentin (Gralise®), gabapentin (Horizant®) or pregabalin (Lyrica CR®) is approved when all of the following are met:

1. Diagnosis of post-herpetic neuralgia, and
2. Member is 18 years of age or older; and
3. Inadequate response or inability to tolerate ONE of the following:
 1. Gabapentin; or
 2. Pregabalin

Initial Authorization duration: 2 years

REAUTHORIZATION CRITERIA: Gabapentin (Gralise®), or gabapentin enacarbil (Horizant®), or Pregabalin (Lyrica CR®) is re-approved when there is positive clinical response to therapy.

Reauthorization duration: 2 years

Restless legs syndrome

INITIAL CRITERIA: Gabapentin enacarbil (Horizant®) is approved ALL of the following are met:

1. Diagnosis of moderate-to-severe primary restless legs syndrome; and
2. Inadequate response or inability to tolerate BOTH of the following:
 1. Pramipexole; and
 2. Ropinirole; and
3. Member is 18 years of age or older

Initial Authorization duration: 2 years

REAUTHORIZATION CRITERIA Gabapentin enacarbil (Horizant®) is re-approved when there is positive clinical response to therapy.

Reauthorization duration: 2 years

Diabetic peripheral neuropathy

INITIAL CRITERIA: Pregabalin (Lyrica CR®) is approved when ALL of the following are met:

1. Diagnosis of neuropathic pain associated with diabetic peripheral neuropathy; and
2. Inadequate response or inability to tolerate ONE of the following:
 1. Gabapentin; or
 2. Pregabalin; and
3. Member is 18 years of age or older

Initial Authorization duration: 2 years

REAUTHORIZATION CRITERIA Pregabalin (Lyrica CR®) is re-approved when there is positive clinical response to therapy.

Reauthorization duration: 2 years

P&T Approval Date: March 20, 2025

Title: Ganaxolone (Ztalmy®)

Applicable Drugs:

Brand Name	Generic Name
Ztalmy®	Ganaxolone

Policy:

INITIAL CRITERIA Ganaxolone (Ztalmy®) is approved when ALL of the following are met:

1. Diagnosis of cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder (CDD); and
2. Documentation of mutation in the CDKL5 gene; and
3. Member is experiencing motor seizures (e.g., bilateral tonic, generalized tonic-clonic, bilateral clonic, atonic, focal, or bilateral tonic-clonic); and
4. One of the following:
 1. Inadequate response or inability to tolerate two formulary anticonvulsants (e.g., valproic acid, levetiracetam, lamotrigine); or
 2. Continuation of therapy with requested medication; and
5. Member is 2 years of age or older; and
6. Prescribed by or in consultation with a neurologist

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA Ganaxolone (Ztalmy®) is re-approved when BOTH of the following are met:

1. Documentation of positive clinical response to therapy (e.g., reduction in frequency of major motor seizures compared to baseline); and
2. Prescribed by or in consultation with a neurologist

Reauthorization duration: 2 years

P&T Approval Date: March 20, 2025

Title: Gaucher Disease Agents

Applicable Drugs:

Brand Name	Generic Name
Zavesca®, Yargesa	miglustat
Cerdelga®	eliglustat

Policy:

Type 1 Gaucher Disease

INITIAL CRITERIA: Miglustat (Zavesca®, Yargesa) is medically necessary when ALL of the following are met:

1. Member is 18 years of age or older; and
2. Diagnosis of mild to moderate type 1 Gaucher disease; and
3. Prescribed as monotherapy for members in whom enzyme replacement therapy is not a therapeutic option (e.g., allergy, hypersensitivity, or poor venous access).

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Miglustat (Zavesca®, Yargesa) is medically necessary when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

INITIAL CRITERIA: Eliglustat (Cerdelga®) is medically necessary when ALL of the following are met:

1. Member is 18 years of age or older; and
2. Diagnosis of Type 1 Gaucher disease; and
3. Member is CYP2D6 extensive metabolizer (EM), intermediate metabolizer (IM), or poor metabolizer (PM) as detected by an FDA-cleared test for determining CYP2D6 genotype [not indicated for Ultra Rapid Metabolizers (URM) as they may not achieve adequate concentration of eliglustat to achieve a therapeutic effect]

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Eliglustat (Cerdelga®) is medically necessary when there is documentation of positive clinical response to therapy (i.e. hemoglobin level decrease by greater than 1.5g/dL from baseline, platelet count decrease by greater than 25% from baseline, spleen volume increased by greater than 25% from baseline, liver volume increased by greater than 20% from baseline).

Reauthorization duration: 2 years

P&T Approval Date: Dec-12-2024

Title: Glucagon-like peptide (GLP-1) Receptor Agonist For Type 2 Diabetes Mellitus

Applicable Drugs:

Brand Name	Generic Name
Byetta®	Exenatide
Bydureon®/Bydureon BCise®	Exenatide extended release
Mounjaro™	Tirzepatide
Ozempic®; Rybelsus®	Semaglutide
Trulicity®	Dulaglutide
Victoza®	liraglutide

Policy:

INITIAL CRITERIA: Exenatide (Byetta®), exenatide ER (Bydureon®/Bydureon BCise®), tirzepatide (Mounjaro™), semaglutide (Ozempic®), semaglutide (Rybelsus®), dulaglutide (Trulicity®), liraglutide is medically necessary when ONE of the following are met:

1. Submission of medical records (e.g., chart notes) confirming diagnosis of type 2 diabetes mellitus; or
2. Submission of medical records (e.g., chart notes) confirming diagnosis of type 2 diabetes mellitus as evidenced by one of the following laboratory values:
 1. A1c greater than or equal to 6.5%; or
 2. Fasting plasma glucose (FPG) greater than or equal to 126mg/dL; or
 3. 2-hour plasma glucose (PG) greater than or equal to 200mg/dL during OGTT (oral glucose tolerance test); or
 4. Random plasma glucose greater than or equal to 200mg/dL

Initial authorization duration: 1 year

INITIAL CRITERIA Brand Victoza® is medically necessary when ALL of the following are met:

1. ONE of the following:
 1. Submission of medical records (e.g., chart notes) confirming diagnosis of type 2 diabetes mellitus; or
 2. Submission of medical records (e.g., chart notes) confirming diagnosis of type 2 diabetes mellitus as evidence by one of the following laboratory values:
 1. A1c greater than or equal to 6.5%; or
 2. Fasting plasma glucose (FPG) greater than or equal to 126mg/dL; or
 3. 2-hour plasma glucose (PG) greater than or equal to 200mg/dL during OGTT (oral glucose tolerance test); or
 4. Random plasma glucose greater than or equal to 200mg/dL; and
2. Submission of documentation (e.g., chart note) confirming inadequate response or inability to tolerate a minimum 90-day supply of TWO of the following:
 1. Bydureon/Bydureon BCise

2. Byetta
3. Ozempic
4. Trulicity
5. Rybelsus
6. Mounjaro

Initial authorization duration: 1 year

REAUTHORIZATION CRITERIA Exenatide (Byetta), exenatide ER (Bydureon/Bydureon BCise), tirzepatide (Mounjaro), semaglutide (Ozempic), semaglutide (Rybelsus), dulaglutide (Trulicity), liraglutide (Victoza); is medically necessary when ALL of the following are met:

1. Documentation of positive clinical response to therapy (e.g., reduction in A1c); and
2. For Brand Victoza only, submission of documentation (e.g., chart note) confirming inadequate response or inability to tolerate a minimum 90-day supply of TWO of the following:
 1. Bydureon/Bydureon BCise
 2. Byetta
 3. Ozempic
 4. Trulicity
 5. Rybelsus
 6. Mounjaro

Reauthorization duration: 1 year

P&T Approval Date: Sep-12-2024

Title: Glycopyrrolate (Dartisla ODT)

Applicable Drugs:

Brand Name	Generic Name
Dartisla ODT™	glycopyrrolate

Policy:

INITIAL CRITERIA Glycopyrrolate (Dartisla ODT™) is medically necessary when ALL of the following are met:

1. Diagnosis of peptic ulcer as confirmed by endoscopy; and
2. One of the following:
 1. Member is on concomitant therapy with a proton-pump inhibitor (PPI) (e.g., lansoprazole, omeprazole); or
 2. Member has inadequate response or inability to tolerate PPI and is receiving concomitant treatment with an H2-receptor antagonist (e.g., famotidine, nizatidine); and
3. One of the following:
 1. Inadequate response or inability to tolerate generic glycopyrrolate tablets; or
 2. Member is unable to swallow tablets; and
4. Prescribed by or in consultation with a gastroenterologist; and
5. Member is 18 years of age or older

Initial authorization duration: 3 months

REAUTHORIZATION CRITERIA Glycopyrrolate (Dartisla ODT™) is medically necessary when ALL of the following are met:

1. One of the following:
 1. Member's peptic ulcer has not healed as confirmed by endoscopy; or
 2. Member has a new peptic ulcer as confirmed by endoscopy; and
2. One of the following:
 1. Member is on concomitant therapy with a proton-pump inhibitor (PPI) (e.g., lansoprazole, omeprazole); or
 2. Member has inadequate response or inability to tolerate PPI and is receiving concomitant treatment with an H2-receptor antagonist (e.g., famotidine, nizatidine); and
3. Member experienced a reduction in peptic ulcer symptoms while on Dartisla ODT™ therapy; and
4. Prescribed by or in consultation with a gastroenterologist; and
5. Other correctable factors (e.g., medication noncompliance, NSAID use, H. pylori infection, etc.) have been addressed

Reauthorization duration: 3 months

P&T Approval Date: Dec-12-2024

Title: Growth Hormones

Applicable Drugs:

Brand Name	Generic Name
Genotropin®	Somatropin
Humatrope®	Somatropin
Norditropin®	Somatropin
Nutropin®/Nutropin® AQ	Somatropin
Omnitrope®	Somatropin
Saizen®	Somatropin
Serostim®	Somatropin
Zomacton®	Somatropin
Zorbtive®	Somatropin
Skytrofa®	Lonapegsomatropin-tcgd
Sogroya®	Somapacitan-beco
Ngenla®	Somatrogon-ghla

Policy:

A. *Children with idiopathic short stature*

INITIAL CRITERIA Somatropin (Omnitrope®, Humatrope®, Genotropin®, Nutropin®[AQ], Norditropin®, or Zomacton®) is medically necessary when all of the following are met:

1. Prescribed by an endocrinologist; and
2. Height less than or equal to 2.25 standard deviations from the mean (1.2 percentile); and
3. Documentation of growth velocity; and
4. Epiphyses are not closed; and
5. For Humatrope®, Genotropin®, Zomacton® only, inadequate response or inability to tolerate ONE of the following:
 - a. Nutropin®/Nutropin AQ®; or
 - b. Norditropin®; or
 - c. Omnitrope®

Initial authorization duration: 1 year

CONTINUATION CRITERIA Somatropin (Omnitrope®, Humatrope®, Genotropin®, Nutropin®[AQ], Norditropin®, or Zomacton®) is medically necessary when all of the following are met:

1. Growth velocity increased by at least 50 percent from baseline; and
2. For Humatrope®, Genotropin®, Zomacton® only, inadequate response or inability to tolerate ONE of the following:
 - a. Nutropin®/Nutropin AQ®; or
 - b. Norditropin®; or
 - c. Omnitrope®; and
3. Yearly evaluation by an endocrinologist

Continuation authorization duration: 1 year

B. Turner Syndrome

INITIAL CRITERIA Somatropin (Humatrope®, Genotropin®, Norditropin®, Nutropin®[AQ], Omnitrope® or Zomacton®) is medically necessary when all of the following are met:

1. Diagnosis of Turner syndrome (Gonadal Dysgenesis); and
2. Prescribed by an endocrinologist; and
3. Height is below the 5th percentile on growth charts for age and gender; and
4. For Humatrope®, Genotropin®, Zomacton® only, inadequate response or inability to tolerate ONE of the following:
 - a. Norditropin®; or
 - b. Nutropin®/Nutropin AQ®; or
 - c. Omnitrope®

Initial authorization duration: 1 year

CONTINUATION CRITERIA Somatropin (Humatrope®, Genotropin®, Norditropin®, Nutropin®[AQ], Omnitrope® or Zomacton®) is medically necessary when all of the following are met:

1. Growth velocity greater than or equal to 2.5 cm/year; and
2. For Humatrope®, Genotropin®, Zomacton® only, inadequate response or inability to tolerate ONE of the following:
 - a. Nutropin®/Nutropin AQ®; or
 - b. Norditropin®; or
 - c. Omnitrope®; and
3. Yearly evaluation by an endocrinologist

Continuation authorization duration: 1 year

C. Growth Hormone deficiency in children

INITIAL CRITERIA: Somatropin (Omnitrope®, Norditropin®, Genotropin®, Humatrope®, Saizen®,

Nutropin® [AQ], Zomacton® somapacitan-beco (Sogroya®), somatrogon-ghla (Ngenla®) or lonapegsomatropin-tcgd (Skytrofa™) is medically necessary when all of the following are met:

1. Prescribed by an endocrinologist; and
2. Growth velocity less than or equal to 5 cm/year after 2 years of age; and
3. Bone age determination documented; and
4. Either ONE of the following responses from provocative testing:
 - a. Abnormal response on insulin-induced hypoglycemia test (less than 5 ng/ml); or
 - b. Abnormal response of less than 10 ng/ml to any other two provocative tests (performed sequentially, not simultaneously), such as but not limited to levodopa and clonidine; and
5. For Genotropin®, Humatrope®, Saizen®, Zomacton®, somapacitan-beco (Sogroya®) only, inadequate response or inability to tolerate ONE of the following:
 - a. Norditropin®; or
 - b. Nutropin®/Nutropin AQ®; or
 - c. Omnitrope®; and
6. For somapacitan-beco (Sogroya®) only, inadequate response or inability to tolerate BOTH of the following:
 - a. somatrogon-ghla (Ngenla®); and
 - b. lonapegsomatropin-tcgd (Skytrofa™)

Initial authorization duration: 1 year

CONTINUATION CRITERIA: Somatropin (Omnitrope®, Norditropin®, Genotropin®, Humatrope®, Saizen®, Nutropin®[AQ], Zomacton®), somapacitan-beco (Sogroya®), somatrogon-ghla (Ngenla®) or lonapegsomatropin-tcgd (Skytrofa™) is medically necessary when all of the following are met:

1. Growth velocity greater than or equal to 2.5cm/year; and
2. For Genotropin®, Humatrope®, Saizen®, Zomacton®, somapacitan-beco (Sogroya®) only, inadequate response or inability to tolerate ONE of the following:
 - a. Nutropin®/Nutropin AQ®; or
 - b. Norditropin®; or
 - c. Omnitrope®; and
3. For somapacitan-beco (Sogroya®) only, inadequate response or inability to tolerate BOTH of the following:
 - a. somatrogon-ghla (Ngenla®); and
 - b. lonapegsomatropin-tcgd (Skytrofa™); and
4. Yearly evaluation by an endocrinologist

Continuation authorization duration: 1 year

***D. Growth hormone deficiency in adults with adult-onset hypothalamic or pituitary disease
OR Replacement of endogenous growth hormone (GH) deficiency***

INITIAL CRITERIA: Somatropin (Omnitrope[®], Norditropin[®], Genotropin[®], Humatrope[®], Saizen[®], Nutropin[®][AQ], Zomacton[®]), somapacitan-beco (Sogroya[®]) is medically necessary when all of the following are met:

1. Prescribed by an endocrinologist; and
2. Clinical history of adult-onset hypothalamic or pituitary disease of organic origin or known causes (e.g., damage from surgery, cranial irradiation, head trauma, or subarachnoid hemorrhage); and
3. Deficiency in any two of the following:
 - a. Follicle-stimulating hormone (FSH) and luteinizing hormone (LH) (demonstrated by a low early morning serum testosterone concentration or a low serum estradiol concentration while FSH and LH concentrations are not elevated); or
 - b. Thyroid-stimulating hormone (TSH) (demonstrated by a low serum T4 concentration and TSH concentration that is not elevated); or
 - c. Adrenocorticotrophic hormone (ACTH) (demonstrated by a low early morning serum cortisol and an ACTH that is not elevated); and
4. GH response of less than 5 ng/ml to insulin-induced hypoglycemia; and
5. For Genotropin[®], Humatrope[®], Saizen[®], Zomacton[®], Sogroya[®] only, inadequate response or inability to tolerate ONE of the following:
 - a. Norditropin[®]; or
 - b. Nutropin[®]/Nutropin AQ[®]; or
 - c. Omnitrope[®]

Initial authorization duration: 1 year

CONTINUATION CRITERIA: Somatropin (Omnitrope[®], Norditropin[®], Genotropin[®], Humatrope[®], Saizen[®], Nutropin[®][AQ], Zomacton[®]), somapacitan-beco (Sogroya[®]) is medically necessary when all of the following are met:

1. For Genotropin[®], Humatrope[®], Saizen[®], Zomacton[®], Sogroya[®] only, inadequate response or inability to tolerate ONE of the following:
 - a. Nutropin[®]/Nutropin AQ[®]; or
 - b. Norditropin[®]; or
 - c. Omnitrope[®]; and
2. Yearly evaluation by an endocrinologist

Continuation authorization duration: 1 year

E. Growth Hormone deficiency in adults with childhood onset hypothalamic or pituitary disease

INITIAL CRITERIA Somatropin (Omnitrope®, Norditropin®, Genotropin®, Humatrope®, Saizen®, Nutropin® [AQ] is medically necessary when all of the following are met:

1. Prescribed by an endocrinologist; and
2. One of the following:
 - a. Clinical history of organic or idiopathic panhypopituitarism as a child; and
 - b. History of idiopathic, isolated GH deficiency in childhood requiring documentation of GH response of less than 5 ng/ml to Insulin-induced hypoglycemia
3. For Genotropin®, Humatrope®, Saizen®, inadequate response or inability to tolerate ONE of the following:
 - a. Norditropin®; or
 - b. Nutropin®/Nutropin® AQ; or
 - c. Omnitrope®

Initial authorization duration: 1 year

CONTINUATION CRITERIA Somatropin (Omnitrope®, Norditropin®, Genotropin®, Humatrope®, Saizen®, Nutropin® [AQ] is medically necessary when all of the following are met:

1. For Genotropin®, Humatrope®, Saizen® only, inadequate response or inability to tolerate ONE of the following:
 - a. Nutropin®/Nutropin® AQ; or
 - b. Norditropin®; or
 - c. Omnitrope®; and
2. Yearly evaluation by an endocrinologist

Continuation authorization duration: 1 year

F. Dwarfism-Noonan syndrome

INITIAL CRITERIA Somatropin (Norditropin®) is medically necessary when ALL of the following are met:

1. Diagnosis of Noonan syndrome; and
2. Prescribed by an endocrinologist

Initial authorization duration: 1 year

CONTINUATION CRITERIA Somatropin (Norditropin®) is medically necessary when there is yearly evaluation by an endocrinologist

Continuation authorization duration: 1 year

G. Dwarfism short stature homeobox containing gene (SHOX) deficiency

INITIAL CRITERIA Somatropin (Humatrope® or Zomacton®) is medically necessary when ALL of the following are met:

1. Diagnosis of short stature or growth failure in children with short stature homeobox containing gene (SHOX) deficiency; and
2. Epiphyses are not closed; and
3. Prescribed by an endocrinologist

Initial authorization duration: 1 year

CONTINUATION CRITERIA Somatropin (Humatrope® or Zomacton®) is medically necessary when there is yearly evaluation by an endocrinologist

Continuation authorization duration: 1 year

H. Small for gestational age

INITIAL CRITERIA Somatropin (Humatrope®, Genotropin®, Norditropin®, Omnitrope®, or Zomacton®) is medically necessary when all of the following are met:

1. Failure to reach the third percentile for length/height by 2 years of age (Genotropin®, Omnitrope®) or 2 to 4 years of age (Norditropin®, Humatrope®); and
2. Prescribed by an endocrinologist; and
3. One of the following:
 - a. Birth length and/or weight less than the third percentile for gestational age
 - b. Birth weight less than 2500 grams and gestational age greater than 37 weeks
4. For Humatrope®, Genotropin®, and Zomacton® only, inadequate response or inability to tolerate ONE of the following:
 - a. Norditropin®; or
 - b. Omnitrope®

Initial authorization duration: 1 year

CONTINUATION CRITERIA Somatropin (Humatrope®, Genotropin®, Norditropin®, Omnitrope®, or Zomacton®) is medically necessary when all of the following are met:

1. Growth velocity greater than or equal to 2.5cm/year; and
2. For Humatrope®, Genotropin®, and Zomacton® only, inadequate response or inability to tolerate ONE of the following:
 - a. Norditropin®; or
 - b. Omnitrope: and
3. Yearly evaluation by an endocrinologist

Continuation authorization duration: 1 year

I. Hypopituitarism in childhood

INITIAL CRITERIA Somatropin (Omnitrope®, Norditropin®, Genotropin®, Humatrope®, Saizen®, Nutropin® [AQ]) is medically necessary when all of the following are met:

1. Clinical evidence of a pituitary lesion or midline central nervous system defect; and

2. Prescribed by an endocrinologist; and
3. Growth velocity less than or equal to 5 cm/year after 2 years of age; and
4. Documentation of one of the following:
 - a. Provocative testing, such as but not limited to the following:
 1. Levadopa
 2. Clonidine
 3. Insulin-induced hypoglycemia
 - b. Deficiencies in two or more other hypothalamic-pituitary axes; and
5. For Genotropin®, Humatrope®, Saizen® only, inadequate response or inability to tolerate ONE of the following:
 - a. Norditropin®; or
 - b. Nutropin®/Nutropin AQ®; or
 - c. Omnitrope®

Initial authorization duration: 1 year

CONTINUATION CRITERIA Somatropin (Omnitrope®, Norditropin®, Genotropin®, Humatrope®, Saizen®, Nutropin® [AQ]) is medically necessary when all of the following are met:

1. For Genotropin®, Humatrope®, Saizen® only, inadequate response or inability to tolerate ONE of the following:
 - a. Nutropin®/Nutropin AQ®; or
 - b. Norditropin®; or
 - c. Omnitrope®; and
2. Yearly evaluation by an endocrinologist

Continuation authorization duration: 1 year

J. Prader-Willi syndrome

INITIAL CRITERIA Somatropin (Omnitrope®, Genotropin®, or Norditropin®) is medically necessary when all of the following are met:

1. Diagnosis of Prader-Willi syndrome; and
2. Prescribed by an endocrinologist; and
3. For Genotropin® only, inadequate response or inability to tolerate ONE of the following:
 - a. Norditropin®; or
 - b. Omnitrope®

Initial authorization duration: 1 year

CONTINUATION CRITERIA Somatropin (Omnitrope®, Genotropin®, or Norditropin®) is medically necessary when BOTH of the following are met:

1. Yearly evaluation by an endocrinologist; and

2. For Genotropin® only, inadequate response or inability to tolerate ONE of the following:
 - a. Norditropin®; or
 - b. Omnitrope®

Continuation authorization duration: 1 year

K. Chronic Kidney Disease (CKD)

INITIAL CRITERIA Somatropin (Nutropin® [AQ]) is medically necessary when all of the following are met:

1. Diagnosis of growth failure associated with CKD; and
2. Height below the third percentile on standardized growth charts; and
3. Member is not a renal transplant recipient; and
4. Prescribed by an endocrinologist or nephrologist

Initial authorization duration: 1 year

CONTINUATION CRITERIA Somatropin (Nutropin® [AQ]) is medically necessary when all of the following are met:

1. No documentation of a renal transplant; and
2. Yearly evaluation by an endocrinologist or nephrologist; and
3. Growth velocity greater than or equal to 2.5 cm/year

Continuation authorization duration: 1 year

L. Short bowel syndrome

INITIAL CRITERIA Somatropin (Zorbtive®) is medically necessary when all of the following are met:

1. Diagnosis of short bowel syndrome; and
2. Member is currently receiving specialized nutritional support (e.g., intravenous parenteral nutrition, fluid, and micronutrient supplements); and
3. Member has not previously received 4 weeks of treatment with Zorbtive

Authorization duration: 6 weeks

M. AIDS wasting syndrome

INITIAL CRITERIA Somatropin (Serostim®) is medically necessary when all of the following are met:

1. Diagnosis of wasting (cachexia) associated with HIV; and
2. Concomitant antiretroviral therapy that has been optimized to decrease the viral load; and
3. Current weight less than 90 percent of ideal body weight; and

4. Nutritional evaluation since onset of wasting first occurred

Initial authorization duration: 12 weeks

CONTINUATION CRITERIA Somatropin (Serostim®) is medically necessary when there is documentation of positive response to therapy (i.e., greater than or equal to 2% increase in body weight and/or body cell mass)

Continuation authorization duration: 36 weeks (for 48 weeks of total treatment)

P&T Approval Date: Sep-12-2024

Title: Heart failure agents

Applicable Drugs:

Brand Name	Generic Name
Corlanor®	ivabradine
Verquvo™	vericiguat

Policy:

Chronic heart failure

INITIAL CRITERIA: Corlanor® (ivabradine) is approved when ALL of the following are met:

1. Diagnosis of stable, symptomatic chronic heart failure; and
2. Member has New York Heart Association (NYHA) Class II, III, or IV symptoms; and
3. Member is 18 years of age or older; and
4. Left ventricular ejection fraction (LVEF) $\leq 35\%$; and
5. Sinus rhythm with resting heart rate ≥ 70 beats per minute; and
6. Member is clinically stable for at least 4 weeks on an optimized and stable clinical regimen which includes ALL of the following:
 - a. Maximally tolerated doses of beta blockers (i.e., bisoprolol, carvedilol, metoprolol succinate ER) or inability to tolerate these beta blockers; and
 - b. ACE inhibitors, ARBs or angiotensin receptor-neprilysin inhibitor (ARNI) (e.g., Entresto) inability to tolerate ACE inhibitor or ARB or ARNI; and
 - c. Sodium-glucose cotransporter-2 (SGLT-2) (e.g., Jardiance, Farxiga); and
 - d. Mineralcorticoid receptor antagonist (MRA) (e.g., spironolactone, eplerenone); and
7. Prescribed by or in consultation with a cardiologist

INITIAL CRITERIA: Vericiguat (Verquvo™) is approved when ALL of the following are met:

1. Diagnosis of chronic heart failure; and
2. Member is age 18 or older; and
3. Member has an ejection fraction of less than 45 percent; and
4. Member has New York Heart Association (NYHA) Class II, III or IV symptoms; and
5. One of the following:
 1. Member was hospitalized for heart failure within the last 6 months; or
 2. Member used outpatient intravenous diuretics (e.g., bumetanide, furosemide) for heart failure within the last 3 months; and
6. Inadequate response or inability to tolerate ALL of the following at a maximally tolerated dose:
 1. One of the following:

1. Angiotensin converting enzyme (ACE) inhibitor (e.g., captopril, enalapril); or
2. Angiotensin II receptor blocker (ARB) (e.g., candesartan, valsartan); or
3. Angiotensin receptor-neprilysin inhibitor (ARNI) [e.g., Entresto (sacubitril and valsartan)]; and
2. Beta blocker (i.e., bisoprolol, carvedilol, metoprolol succinate ER; and
3. Sodium-glucose cotransporter-2 (SGLT-2) inhibitors (e.g., Jardiance, Farxiga); and
4. Mineralcorticoid receptor antagonist (MRA) (e.g., spironolactone, eplerenone); and
7. Prescribed by or in consultation with a cardiologist

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA: Vericiguat (Verquvo™) or ivabradine (Corlanor®) is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

Inappropriate sinus tachycardia

INITIAL CRITERIA: Ivabradine (Corlanor®) is approved when ALL of the following are met:

1. Diagnosis of inappropriate sinus tachycardia confirmed by both of the following:
 1. Sinus heart rate greater than 100 beats per minute at rest; and
 2. Mean 24-hour heart rate greater than 90 beats per minute; and
2. Member is 18 years of age or older; and
3. Documentation that other causes of sinus tachycardia have been ruled out (e.g., hyperthyroidism, anemia, illicit stimulant drug use, caffeine, etc.); and
4. Inadequate response or inability to tolerate one beta-blocker; and-
5. Prescribed by or in consultation with a cardiologist

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA: Ivabradine (Corlanor®) is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

Heart failure due to dilated cardiomyopathy

INITIAL CRITERIA: Ivabradine (Corlanor®) is approved when ALL of the following are met:

1. Diagnosis of stable, symptomatic heart failure due to dilated cardiomyopathy; and
2. Member has New York Heart Association (NYHA) Class II, III, or IV symptoms; and
3. Member is 6 months of age to 18 years of age; and
4. Member is in sinus rhythm; and
5. Member has elevated heart rate; and
6. Prescribed by or in consultation with a cardiologist; and

7. Inadequate response or inability to tolerate to one of the following:
 1. Beta blocker (e.g., bisoprolol, metoprolol succinate extended release)
 2. Angiotensin-converting enzyme (ACE) inhibitor (e.g., captopril, enalapril)
 3. Diuretic Agent (e.g., spironolactone, furosemide)

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA: Ivabradine (Corlanor®) is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

P&T Approval Date: Jul-01-2024

Title: Hemophilia agents

Applicable Drugs:

Advate®

Adynovate®

Afstyla®

Alphanate®

Alphanine SD®

Alprolix®

Altuviiiio™

BeneFIX®

Coagadex®

Corifact®

Eloctate®

Esperoct®

Feiba NF®

Hemlibra®

Hemofil M®

Humate-P®

Hympavzi®

Idelvion®

Ixinity®

Jivi®

Koate-DVI®

Kogenate FS®

Kovaltry®

Mononine®

Novoeight®

Novoseven RT®

Nuwiq®

Obizur®

Profilnine SD®

Rebinyn®

Recombinate®

Riastap®

Rixubis®

Sevenfact®

Tretten®

Vonvendi®

Wilate®

Xyntha®

Policy:

Advate®, Adynovate®, Afstyl®, Alphanate®, Alphanine SD®, Alprolix®, Altuviiiio™, Benefix®, Coagadex®, Corifact®, Eloctate®, Esperoct®, Feiba NF®, Hemlibra®, Hemofil M®, Humate P®, Idelvion®, Ixinity®, Jivi®, Koate DVI®, Kogenate FS®, Kovaltry®, Novoeight®, Novoseven RT®, Nuwiq®, Obizur®, Profilnine®, Rebinyn®, Recombinate®, Riastap®, Rixubis®, Sevenfact®, Tretten®, Vonvendi®, Wilate®, Xyntha®/Xyntha® Solofuse, Hympavzi™ are approved when there is a diagnosis of an FDA approved indication

Approval duration: 2 years

P&T Approval Date: March 20, 2025

Title: Hepatitis C agents

Applicable Drugs:

Brand Name	Generic Name
Epclusa®	velpatasvir/ sofosbuvir
Harvoni®	ledipasvir/ sofosbuvir
Viekira Pak®	ombitasvir/ paritaprevir/ ritonavir and dasabuvir
Sovaldi®	sofosbuvir
Zepatier®	elbasvir/grazoprevir
Mavyret™	glecaprevir/pibrentasvir
Vosevi®	sofosbuvir/velpatasvir/voxilaprevir

Policy:

TREATMENT NAIVE

A. Genotype 1

Mavyret™ is approved when ALL of the following are met:

1. Age 3 years or older; and
2. Diagnosis of chronic HCV genotype 1; and
3. Absence of decompensated cirrhosis (i.e., compensated cirrhosis or no cirrhosis); and
4. Not used in combination with another HCV direct acting antiviral agent; and
5. Approved length of therapy: 56 days (8 weeks)

Velpatasvir/ sofosbuvir (Epclusa®) is approved when ALL of the following are met:

1. Age 3 years or older; and
2. Diagnosis of chronic HCV genotype 1; and
3. Absence of decompensated cirrhosis (i.e., compensated cirrhosis or no cirrhosis); and
4. Approved length of therapy: 84 days (12 weeks)*; and
5. Inadequate response or inability to tolerate brand Epclusa® (applies to velpatasvir/sofosbuvir only), details of intolerability must be provided

Ledipasvir/ sofosbuvir (Harvoni®) is approved when ALL of the following are met:

1. Age 3 years or older; and
2. Diagnosis of chronic HCV genotype 1; and

3. Absence of decompensated cirrhosis (i.e., compensated cirrhosis or no cirrhosis); and
4. Approved length of therapy: 84 days (12 weeks)*; and
5. Inadequate response or inability to tolerate brand Harvoni® (applies to ledipasvir/sofosbuvir only), details of intolerability must be provided

Zepatier® is approved when ALL of the following are met:

1. Age 12 years or older or weighing at least 30kg; and
2. Diagnosis of HCV genotype 1; and
3. Results of testing for baseline high fold-change NS5A resistance-associated variant are provided (for genotype 1a); and
4. Absence of decompensated cirrhosis (i.e., compensated cirrhosis or no cirrhosis); and
5. Documentation of a dispensed prescription for and inability to tolerate glecaprevir/pibrentasvir (Mavyret™), brand Harvoni® or brand Epclusa®, details of intolerability must be provided; and
6. Used concurrently with ribavirin for genotype 1a when baseline high fold-change NS5A resistance-associated variant are detected; and
7. Approved length of therapy:
 - a. Genotype 1a without baseline high fold-change NS5A resistance-associated variant or genotype 1b: 84 days (12 weeks)*
 - b. Genotype 1a with baseline high fold-change NS5A resistance-associated variant: 112 days (16 weeks)*

Viekira Pak® is approved when ALL of the following are met:

1. Age 18 years or older; and
2. Diagnosis of chronic HCV genotype 1; and
3. ONE of the following:
 - a. Genotype 1a without cirrhosis; or
 - b. Genotype 1b with absence of decompensated cirrhosis (i.e., compensated cirrhosis or no cirrhosis); and
4. Documentation of a dispensed prescription for and inability to tolerate glecaprevir/pibrentasvir (Mavyret™), brand Harvoni® or brand Epclusa®, details of intolerability must be provided; and
5. Used concurrently with ribavirin for genotype 1a; and
6. Approved length of therapy: 84 days (12 weeks) *

B. Genotype 2

Mavyret™ is approved when all of the following are met:

1. Age 3 years or older; and
2. Diagnosis of chronic HCV genotype 2; and

3. Absence of decompensated cirrhosis (i.e., compensated cirrhosis or no cirrhosis); and
4. Not used in combination with another HCV direct acting antiviral agent; and
5. Approved length of therapy: 56 days (8 weeks)*

Velpatasvir/ sofosbuvir (Epclusa®) is approved when ALL of the following are met:

1. Age 3 years or older; and
2. Diagnosis of chronic HCV genotype 2; and
3. Absence of decompensated cirrhosis (i.e., compensated cirrhosis or no cirrhosis); and
4. Inadequate response or inability to tolerate brand Epclusa® (applies to velpatasvir/sofosbuvir only), details of intolerability must be provided.; and
5. Approved length of therapy: 84 days (12 weeks)*

C. Genotype 3

Mavyret™ is approved when ALL of the following are met:

1. Age 3 years or older; and
2. Diagnosis of chronic HCV genotype 3; and
3. Absence of decompensated cirrhosis (i.e., compensated cirrhosis or no cirrhosis); and
4. Not used in combination with another HCV direct acting antiviral agent; and
5. Approved length of therapy: 56 days (8 weeks)*

Velpatasvir/ sofosbuvir (Epclusa®) is approved when ALL of the following are met:

1. Age 3 years or older; and
2. Diagnosis of chronic HCV genotype 3; and
3. Absence of decompensated cirrhosis (i.e. compensated cirrhosis or no cirrhosis); and
4. Inadequate response or inability to tolerate brand Epclusa® (applies to velpatasvir/sofosbuvir only), details of intolerability must be provided.; and
5. Concurrent use of ribavirin if compensated cirrhosis and Y93H substitution present; and
6. Approved length of therapy: 84 days (12 weeks)

Vosevi® is approved when ALL of the following are met:

1. Age 18 years or older; and
2. Diagnosis of chronic HCV genotype 3; and
3. Compensated cirrhosis; and
4. Presence of Y93H; and
5. Approved length of therapy: 84 days (12 weeks)*

D. Genotype 4

Mavyret™ is approved when ALL of the following are met:

1. Age 3 years or older; and
2. Diagnosis of chronic HCV genotype 4; and
3. Absence of decompensated cirrhosis (i.e., compensated cirrhosis or no cirrhosis); and
4. Not used in combination with another HCV direct acting antiviral agent; and
5. Approved length of therapy: 56 days (8 weeks)

Velpatasvir/ sofosbuvir (Epclusa®) is approved when ALL of the following are met:

1. Age 3 years or older; and
2. Diagnosis of chronic HCV genotype 4; and
3. Absence of decompensated cirrhosis (i.e., compensated cirrhosis or no cirrhosis); and
4. Inadequate response or inability to tolerate brand Epclusa® (applies to velpatasvir/sofosbuvir only), details of intolerability must be provided; and
5. Approved length of therapy: 84 days (12 weeks)*

Ledipasvir/ sofosbuvir (Harvoni®) is approved when ALL of the following are met:

1. Age 3 years or older; and
2. Diagnosis of chronic HCV genotype 4; and
3. Absence of decompensated cirrhosis (i.e., compensated cirrhosis or no cirrhosis); and
4. Inadequate response or inability to tolerate brand Harvoni® (applies to ledipasvir/sofosbuvir only), details of intolerability must be provided; and
5. Approved length of therapy: 84 days (12 weeks)*

Zepatier® is approved when ALL of the following are met:

1. Age 12 years or older or weighing at least 30kg; and
2. Diagnosis of chronic HCV genotype 4; and
3. Absence of decompensated cirrhosis (i.e., compensated cirrhosis or no cirrhosis); and
4. Documentation of a dispensed prescription for and inability to tolerate glecaprevir/ pibrentasvir (Mavyret™), brand Harvoni® or brand Epclusa®, details of intolerability must be provided; and
5. Approved length of therapy: 84 days (12 weeks)*

E. Genotype 5 or 6

Mavyret™ is approved when ALL of the following are met:

1. Age 3 years or older; and
2. Diagnosis of chronic HCV genotype 5 or 6; and
3. Absence of decompensated cirrhosis (i.e., compensated cirrhosis or no cirrhosis); and

4. Not used in combination with another HCV direct acting antiviral agent; and
5. Approved length of therapy: 56 days (8 weeks)

Velpatasvir/ sofosbuvir (Epclusa®) is approved when ALL of the following are met:

1. Age 3 years or older; and
2. Diagnosis of chronic HCV genotype 5 or 6; and
3. Absence of decompensated cirrhosis (i.e., compensated cirrhosis or no cirrhosis); and
4. Inadequate response or inability to tolerate brand Epclusa® (applies to velpatasvir/sofosbuvir only), details of intolerability must be provided; and
5. Approved length of therapy: 84 days (12 weeks)*

Ledipasvir/ sofosbuvir (Harvoni®) is approved when ALL the following are met:

1. Age 3 years or older; and
2. Diagnosis of chronic HCV genotype 5 or 6; and
3. Absence of decompensated cirrhosis (i.e., compensated cirrhosis or no cirrhosis); and
4. Inadequate response or inability to tolerate brand Harvoni® (applies to ledipasvir/sofosbuvir only), details of intolerability must be provided; and
5. Approved length of therapy: 84 days (12 weeks)*

RETREATMENT (note: Retreatment for interferon or interferon plus first generation protease inhibitor failures should be treated as treatment naïve)

Sofosbuvir-Based and Elbasvir/Grazoprevir Treatment Failures

A. Genotype 1, 2, 4, 5 and 6

Mavyret™ is approved when ALL of the following are met:

1. Age 3 years or older; and
2. Diagnosis of chronic HCV genotype 1, 2, 4, 5, 6; and
3. Absence of decompensated cirrhosis (i.e., compensated cirrhosis or no cirrhosis); and
4. Member failed Sofosbuvir-Based therapy or Zepatier (Elbasvir/Grazoprevir); and
5. Not used in combination with another HCV direct acting antiviral agent; and
6. Approved length of therapy: 112 days (16 weeks)

Vosevi® is approved when ALL the following are met:

1. Age 18 years or older; and
2. Diagnosis of chronic HCV genotype 1, 2, 4, 5, 6; and
3. Absence of decompensated cirrhosis (i.e., compensated cirrhosis or no cirrhosis); and
4. Member failed Sofosbuvir-Based therapy or Zepatier (Elbasvir/Grazoprevir); and
5. Approved length of therapy: 84 days (12 weeks)*

B. Genotype 3

Vosevi® is approved when ALL the following are met:

1. Age 18 years or older; and
2. Diagnosis of chronic HCV genotype 3 and
3. Absence of decompensated cirrhosis (i.e., compensated cirrhosis or no cirrhosis); and
4. Member failed Sofosbuvir-Based therapy or Zepatier (Elbasvir/Grazoprevir); and
5. Approved length of therapy: 84 days (12 weeks)*

Glecaprevir/Pibrentasvir Treatment Failures

A. Genotype 1, 2, 3, 4, 5, 6

Mavyret™ and Sovaldi® is approved when ALL of the following are met:

1. Age 3 years or older; and
2. Diagnosis of chronic HCV genotype 1, 2, 3, 4, 5, 6; and
3. Absence of decompensated cirrhosis (i.e., compensated cirrhosis or no cirrhosis); and
4. Member failed Mavyret (Glecaprevir/Pibrentasvir); and
5. Concurrent use of ribavirin; and
6. Not used in combination with another HCV direct acting antiviral agent; and
7. Approved length of therapy: 112 days (16 weeks)

Vosevi® is approved when ALL the following are met:

1. Age 18 years or older; and
2. Diagnosis of chronic HCV genotype 1, 2, 3, 4, 5, 6; and
3. Absence of decompensated cirrhosis (i.e., compensated cirrhosis or no cirrhosis) ; and
4. Member failed Mavyret (Glecaprevir/Pibrentasvir); and
5. Approved length of therapy: 84 days (12 weeks)

Multiple DAA Treatment Failures (All Genotypes), Including Vosevi® (Sofosbuvir/Velpatasvir/Voxilaprevir) or Sofosbuvir Plus Mavyret™ (Glecaprevir/Pibrentasvir)

A. Genotypes 1, 2, 4, 5, 6

Mavyret™ and Sovaldi is approved when ALL of the following are met:

1. Age 3 years or older; and
2. Diagnosis of chronic HCV genotype 1, 2, 4, 5, 6; and
3. Absence of decompensated cirrhosis (i.e., compensated cirrhosis or no cirrhosis); and

4. Member failed Mavyret (Glecaprevir/Pibrentasvir) and Sovaldi (sofosbuvir) or Vosevi® (Sofosbuvir/Velpatasvir/Voxilaprevir); and
5. Concurrent use of ribavirin; and
6. Not used in combination with another HCV direct acting antiviral agent; and
7. Approved length of therapy: 112 days (16 weeks)

Vosevi® is approved when ALL the following are met:

1. Age 18 years or older; and
2. Diagnosis of chronic HCV genotype 1, 2, 4, 5, 6; and
3. Absence of decompensated cirrhosis (i.e., compensated cirrhosis or no cirrhosis); and
4. Member failed Mavyret (Glecaprevir/Pibrentasvir) and Sovaldi (sofosbuvir) or Vosevi® (Sofosbuvir/Velpatasvir/Voxilaprevir); and
5. Concurrent use of ribavirin (for members with compensated cirrhosis); and
6. Approved length of therapy: 168 days (24 weeks)

B. Genotype 3

Mavyret™ and Sovaldi is approved when ALL of the following are met:

1. Age 3 years or older; and
2. Diagnosis of chronic HCV genotype 3; and
3. Absence of decompensated cirrhosis (i.e., compensated cirrhosis or no cirrhosis); and
4. Member failed Mavyret (Glecaprevir/Pibrentasvir) and Sovaldi (sofosbuvir) or Vosevi® (Sofosbuvir/Velpatasvir/Voxilaprevir); and
5. Concurrent use of ribavirin; and
6. Not used in combination with another HCV direct acting antiviral agent; and
7. Approved length of therapy:
 - a. NO cirrhosis - 112 days (16 weeks)
 - b. Compensated cirrhosis up to 168 days (24 weeks)

Vosevi® is approved when ALL the following are met:

1. Age 18 years or older; and
2. Diagnosis of chronic HCV genotype 3 and
3. Absence of decompensated cirrhosis (i.e., compensated cirrhosis or no cirrhosis) ; and
4. Member failed Mavyret (Glecaprevir/Pibrentasvir) and Sovaldi (sofosbuvir) or Vosevi® (Sofosbuvir/Velpatasvir/Voxilaprevir); and
5. Concurrent use of ribavirin (for members with compensated cirrhosis); and
6. Approved length of therapy: 168 days (24 weeks)

DECOMPENSATED CIRRHOSIS (moderate to severe hepatic impairment; Child Turcotte Pugh B or C)

A. Treatment Naive

Ledipasvir/ sofosbuvir (Harvoni®) is approved when ALL of the following are met:

1. Age 3 years or older; and
2. Diagnosis of chronic HCV genotype 1, 4, 5, or 6; and
3. Documentation of decompensated cirrhosis (defined as Child Turcotte Pugh class B or C) or hepatocellular carcinoma; and
4. One of the following:
 - a. Concurrent use of ribavirin; or
 - b. Member is unable to tolerate ribavirin; and
5. Prescribed by a hepatitis C expert (i.e., hepatologist, liver transplant surgeon) ; and
6. Inadequate response or inability to tolerate brand Harvoni® (applies to ledipasvir/sofosbuvir only), details or intolerability must be provided; and
7. Approved length of therapy:
 - a. Without ribavirin: 168 days (24 weeks)*; or
 - b. With ribavirin: 84 days (12 weeks)*

Velpatasvir/sofosbuvir (Epclusa®) is approved when ALL of the following are met:

1. Age 3 years or older; and
2. Diagnosis of chronic HCV genotype 1, 2, 3, 4, 5, or 6; and
3. Documentation of decompensated cirrhosis (defined as Child Turcotte Pugh class B or C) or hepatocellular carcinoma; and
4. One of the following:
 - a. Concurrent use of ribavirin; or
 - b. Member is unable to tolerate ribavirin; and
5. Prescribed by a hepatitis C expert (i.e., hepatologist, liver transplant surgeon) ; and
6. Inadequate response or inability to tolerate brand Epclusa® (applies to velpatasvir/sofosbuvir only), details of intolerability must be provided; and
7. Approved length of therapy:
 - a. With ribavirin: 168 days (24 weeks)*; or
 - b. Without ribavirin: 168 days (24 weeks)*

B. Retreatment with Prior Sofosbuvir or NS5A inhibitor-base treatment

Ledipasvir/ sofosbuvir (Harvoni®) is approved when ALL of the following are met:

1. Age 3 years or older; and
2. Diagnosis of chronic HCV genotype 1, 4, 5, or 6; and
3. Documentation of decompensated cirrhosis (defined as Child Turcotte Pugh class B or C) or hepatocellular carcinoma; and
4. Prescribed by a hepatitis C expert (i.e., hepatologist, liver transplant surgeon); and

5. Concurrent use of ribavirin; and
6. Inadequate response or inability to tolerate brand Harvoni® (applies to ledipasvir/sofosbuvir only), details of intolerability must be provided; and
7. Approved length of therapy: 168 days (24 weeks)*

Velpatasvir/sofosbuvir (Epclusa®) is approved when ALL of the following are met:

1. Age 3 years or older; and
2. Diagnosis of chronic HCV genotype 1, 2, 3, 4, 5, or 6; and
3. Documentation of decompensated cirrhosis (defined as Child Turcotte Pugh class B or C) or hepatocellular carcinoma; and
4. Prescribed by a hepatitis C expert (i.e., hepatologist, liver transplant surgeon) ; and
5. Concurrent use of ribavirin; and
6. Inadequate response or inability to tolerate brand Epclusa® (applies to velpatasvir/sofosbuvir only) details of intolerability must be provided; and
7. Approved length of therapy: 168 days (24 weeks)*

RECURRENT HCV POST LIVER TRANSPLANT

Genotype 1

Mavyret™ is approved when there is documentation of ALL of the following:

1. Age 3 years or older; and
2. Diagnosis of HCV genotype 1; and
3. Documentation of liver transplant; and
4. Absence of decompensated cirrhosis (i.e., compensated cirrhosis or no cirrhosis); and
5. Not used in combination with another HCV direct acting antiviral agent; and
6. Approved length of therapy: 84 days (12 weeks)*

Ledipasvir/ sofosbuvir (Harvoni®) is approved when there is documentation of ALL of the following:

1. Age 3 years or older; and
2. Diagnosis of HCV genotype 1; and
3. Documentation of liver transplant; and
4. Used with ribavirin; and
5. Inadequate response or inability to tolerate brand Harvoni® (applies to ledipasvir/sofosbuvir only), details of intolerability must be provided; and
6. Approved length of therapy: 84 days (12 weeks)*

Viekira Pak® is approved when ALL of the following are met:

1. Age 18 years or older; and
2. Diagnosis of HCV genotype 1; and

3. Documentation of liver transplant; and
4. Documentation of normal hepatic function; and
5. Documentation of mild fibrosis; and
6. Used with ribavirin; and
7. Documentation of a dispensed prescription for and inability to tolerate glecaprevir/pibrentasvir (Mavyret™) or brand Harvoni®, details of intolerability must be provided; and
8. Approval length: 24 weeks

B. Genotype 2 or 3

Mavyret™ is approved when ALL of the following are met:

1. Age 3 years or older; and
2. Diagnosis of HCV genotype 2 or 3; and
3. Documentation of liver transplant; and
4. Absence of decompensated cirrhosis (i.e., compensated cirrhosis or no cirrhosis); and
5. Not used in combination with another HCV direct acting antiviral agent; and
6. Approved length of therapy: 84 days (12 weeks)*

Velpatasvir/ sofosbuvir (Epclusa®) is approved when ALL the following are met:

1. Age 3 years or older; and
2. Diagnosis of HCV genotype 2 or 3; and
3. Documentation of liver transplant; and
4. Used with ribavirin; and
5. Presence of cirrhosis; and
6. Inadequate response or inability to tolerate brand Epclusa® (applies to velpatasvir/sofosbuvir only), details of intolerability must be provided; and
7. Approved length of therapy: 84 days (12 weeks)*

C. Genotype 4, 5 or 6

Mavyret™ is approved when there is documentation of ALL of the following:

1. Age 3 years or older; and
2. Diagnosis of HCV genotype 4, 5, or 6; and
3. Documentation of liver transplant; and
4. Absence of decompensated cirrhosis (i.e., compensated cirrhosis or no cirrhosis); and
5. Not used in combination with another HCV direct acting antiviral agent; and
6. Approved length of therapy: 84 days (12 weeks)*

Ledipasvir/ sofosbuvir (Harvoni®) is approved when there is documentation of ALL of the following:

1. Age 3 years or older; and
2. Diagnosis of HCV genotype 4, 5, or 6; and
3. Documentation of liver transplant; and
4. Used with ribavirin; and
5. Inadequate response or inability to tolerate brand Harvoni® (applies to ledipasvir/sofosbuvir only), details of intolerability must be provided; and
6. Approved length of therapy: 84 days (12 weeks)*

KIDNEY TRANSPLANT RECIPIENT

A. Genotype 1 or 4

Mavyret™ is approved when there is documentation of ALL of the following:

1. Age 3 years or older ; and
2. Diagnosis of HCV genotype 1 or 4; and
3. Documentation of kidney transplant; and
4. Absence of decompensated cirrhosis (i.e., compensated cirrhosis or no cirrhosis); and
5. Not used in combination with another HCV direct acting antiviral agent; and
6. Approved length of therapy: 84 days (12 weeks)*

Ledipasvir/ sofosbuvir (Harvoni®) is approved when there is documentation of ALL of the following:

1. Age 3 years or older; and
2. Diagnosis of HCV genotype 1 or 4; and
3. Documentation of kidney transplant; and
4. Absence of decompensated cirrhosis (i.e., compensated cirrhosis or no cirrhosis); and
5. Inadequate response or inability to tolerate brand Harvoni® (applies to ledipasvir/sofosbuvir only), details of intolerability must be provided; and
6. Approved length of therapy: 84 days (12 weeks)*

B. Genotype 2,3,5, or 6

Mavyret™ is approved when there is documentation of ALL of the following:

1. Age 3 years or older; and
2. Diagnosis of HCV genotype 2,3,5, or 6; and
3. Documentation of kidney transplant; and
4. Absence of decompensated cirrhosis (i.e., compensated cirrhosis or no cirrhosis); and
5. Not used in combination with another HCV direct acting antiviral agent; and
6. Approved length of therapy: 84 days (12 weeks)*

*Approved length of therapy: if therapy was initiated prior to coverage with the plan, authorization will only be granted to allow completion of the specified therapy. Authorizations will end 180 days after receipt of request.

Maximum doses per day apply

Drug	Maximum dose per day (tablets)
velpatasvir/ sofosbuvir (Epclusa®)	1
velpatasvir/ sofosbuvir (Epclusa®) pack 200-50mg	2
velpatasvir/ sofosbuvir (Epclusa®) pack 150-37.5mg	1
Mavyret™	3
Mavyret™ pak 50-20mg	5
Ledipasvir/sofosbuvir (Harvoni®)	1
Sovaldi®	1
Viekira Pak®	6
Zepatier®	1
Vosevi®	1

HCV Treatment Regimens that are not recommended and considered not medically necessary

1. Sofosbuvir with ribavirin x 24 weeks (except in genotype 2 post liver transplant)
2. Peg-interferon and ribavirin with or without sofosbuvir, simeprevir, telaprevir, or boceprevir)
3. Monotherapy with peg-interferon, ribavirin, or a direct-acting antiviral
4. Simeprevir, paritaprevir, or elbasvir/grazoprevir based regimens in those decompensated cirrhosis

P&T Approval Date: Jul-01-2024

Title: Hereditary Angioedema Agents

Applicable Drugs:

Brand Name	Generic Name
Firazyr®/Sajazir™	Icatibant
Haegarda®	C1 esterase inhibitor subcutaneous [human]
Cinryze®	C1 esterase inhibitor [human]
Beriner®	C1 esterase inhibitor [human]
Orladeyo™	Berotrastat
Ruconest®	C1 esterase inhibitor [recombinant]
Takhzyro®	Ianadelumab-flyo

Policy:

Prophylaxis against angioedema attacks

INITIAL CRITERIA: C1 esterase inhibitor (human) (Cinryze® or Haegarda®) is approved when ALL of the following are met:

1. Diagnosis of hereditary angioedema (HAE); and
2. One of the following:
 - a. Diagnosis has been confirmed by C1 inhibitor (C1-INH) deficiency or dysfunction (Type I or II HAE) as documented by one of the following:
 - i. C1-INH antigenic level below the lower limit of normal; or
 - ii. C1-INH functional level below the lower limit of normal; or
 - b. Diagnosis has been confirmed by both of the following:
 - i. Member has normal C1-INH level (HAE-n1-C1INH previously referred to as HAE Type 3); and
 - ii. One of the following:
 1. Confirmed presence of a FXII, plasminogen gene mutation, angiopoietin-1 mutation, or kininogen mutation; or
 2. Member has recurrent angioedema attacks that are refractory to high-dose antihistamines (e.g., cetirizine) with a confirmed family history of recurrent angioedema; and
3. Prescribed by or in consultation with an immunologist, allergist, or pulmonologist; and
4. Member is 6 years of age or greater; and
5. For prophylaxis against HAE attacks; and
6. For Cinryze only, inadequate response or inability to tolerate ONE of the following:

- a. Haegarda; or
- b. Takhzyro; or
- c. Orladeyo

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA C1 esterase inhibitors (human) (Cinryze® or Haegarda®) is re-approved with documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

INITIAL CRITERIA: Lanadelumab-flyo (Takhzyro®) injection or berotralstat (Orladeyo®) is approved when all of the following are met:

1. Diagnosis of hereditary angioedema (HAE); and
2. One of the following:
 - a. Diagnosis has been confirmed by C1 inhibitor (C1-INH) deficiency or dysfunction (Type I or II HAE) as documented by one of the following:
 - i. C1-INH antigenic level below the lower limit of normal; or
 - ii. C1-INH functional level below the lower limit of normal; or
 - b. Diagnosis has been confirmed by both of the following:
 - i. Member has normal C1-INH level (HAE-n1-C1INH previously referred to as HAE Type 3); and
 - ii. One of the following:
 1. Confirmed presence of a FXII, plasminogen gene mutation, angiopoietin-1 mutation, or kininogen mutation; or
 2. Member has recurrent angioedema attacks that are refractory to high-dose antihistamines (e.g., cetirizine) with a confirmed family history of recurrent angioedema; and
3. For prophylaxis against HAE attacks; and
4. One of the following:
 - a. For Takhzyro, member is 2 years of age or older; or
 - b. For Orladeyo, member is 12 years of age or older; and
5. Prescribed by or in consultation with an immunologist, allergist, or pulmonologist

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA: Lanadelumab-flyo (Takhzyro®), or berotralstat (Orladeyo®) is re-approved with documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

Treatment of angioedema attacks

INITIAL CRITERIA: C1 esterase inhibitor (human) (Berinert®) is approved when ALL of the following are met:

1. Diagnosis of hereditary angioedema (HAE); and
2. One of the following:
 - a. Diagnosis has been confirmed by C1 inhibitor (C1-INH) deficiency or dysfunction (Type I or II HAE) as documented by one of the following:
 - i. C1-INH antigenic level below the lower limit of normal; or
 - ii. C1-INH functional level below the lower limit of normal; or
 - b. Diagnosis has been confirmed by both of the following:
 - i. Member has normal C1-INH level (HAE-n1-C1INH previously referred to as HAE Type 3); and
 - ii. One of the following:
 1. Confirmed presence of a FXII, plasminogen gene mutation, angiopoietin-1 mutation, or kininogen mutation; or
 2. Member has recurrent angioedema attacks that are refractory to high-dose antihistamines (e.g., cetirizine) with a confirmed family history of recurrent angioedema; and
3. Prescribed by or in consultation with an immunologist, allergist, or pulmonologist; and
4. For the treatment of acute abdominal, facial, or laryngeal HAE attacks; and
5. One of the following:
 - a. Inadequate response or inability to tolerate C1 esterase inhibitor recombinant (Ruconest®); or
 - b. One of the following:
 - i. Member is 12 years of age or younger; or
 - ii. Documentation that member has history of laryngeal attacks

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA: C1 esterase inhibitors (human) (Berinert®) is re-approved with documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

INITIAL CRITERIA: C1 esterase inhibitor recombinant (Ruconest®) is approved when ALL of the following are met:

1. Diagnosis of hereditary angioedema (HAE); and
2. One of the following:
 - a. Diagnosis has been confirmed by C1 inhibitor (C1-INH) deficiency or dysfunction (Type I or II HAE) as documented by one of the following:
 - i. C1-INH antigenic level below the lower limit of normal; or

- ii. C1-INH functional level below the lower limit of normal; or
- b. Diagnosis has been confirmed by both of the following:
 - i. Member has normal C1-INH level (HAE-n1-C1INH previously referred to as HAE Type 3); and
 - ii. One of the following:
 - 1. Confirmed presence of a FXII, plasminogen gene mutation, angiopoietin-1 mutation, or kininogen mutation; or
 - 2. Member has recurrent angioedema attacks that are refractory to high-dose antihistamines (e.g., cetirizine) with a confirmed family history of recurrent angioedema; and
- 3. Prescribed by or in consultation with an immunologist, allergist, or pulmonologist; and
- 4. Member is 13 years of age or older; and
- 5. For the treatment of acute HAE attacks

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA: C1 esterase inhibitor recombinant (Ruconest®) is re-approved with documentation of positive clinical response to therapy

Reauthorization duration: 2 years

INITIAL CRITERIA: Icatibant (Firazyr® /Sajazir™) is approved when ALL of the following are met:

- 1. Member is 18 years of age or older; and
- 2. Diagnosis of hereditary angioedema; and
- 3. One of the following:
 - a. Diagnosis has been confirmed by C1 inhibitor (C1-INH) deficiency or dysfunction (Type I or II HAE) as documented by one of the following:
 - i. C1-INH antigenic level below the lower limit of normal; or
 - ii. C1-INH functional level below the lower limit of normal; or
 - b. Diagnosis has been confirmed by both of the following:
 - i. Member has normal C1-INH level (HAE-n1-C1INH previously referred to as HAE Type 3); and
 - ii. One of the following:
 - 1. Confirmed presence of a FXII, plasminogen gene mutation, angiopoietin-1 mutation, or kininogen mutation; or
 - 2. Member has recurrent angioedema attacks that are refractory to high-dose antihistamines (e.g., cetirizine) with a confirmed family history of recurrent angioedema; and
- 4. For the treatment of acute HAE attacks; and
- 5. Prescribed by or in consultation with an immunologist, allergist, or pulmonologist

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA Icatibant (Firazyr®/Sajazir™) is re-approved with documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

P&T Approval Date: Jul-01-2024

Title: Hereditary Tyrosinemia Agents

Applicable Drugs:

Brand Name	Generic Name
Nityr®, Orfadin®	Nitisinone

Policy:

INITIAL CRITERIA Nitisinone (Nityr®, Orfadin®) is medically necessary when all of the following are met:

1. Diagnosis of hereditary tyrosinemia type 1; and
2. Will be used in combination with dietary restriction of tyrosine and phenylalanine; and
3. Diagnosis confirmed by the presence of succinylacetone in the plasma or urine; and
4. Prescribed by or in consultation with one of the following:
 1. Gastroenterologist
 2. Hepatologist
 3. Other specialist with experience in treating inborn errors of metabolism; and
5. For Nitisinone (Nityr®) only, inadequate response or inability to tolerate Orfadin®

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA Nitisinone (Nityr®, Orfadin®) is medically necessary when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

P&T Approval Date: Sep-12-2024

Title: Hypoactive Sexual Desire Disorder (HSDD) agents

Applicable Drugs:

Brand name	Generic name
Addyi®	Flibanserin
Vyleesi™	Bremelanotide

Policy:

INITIAL CRITERIA Flibanserin (Addyi®) is medically necessary when ALL of the following are met:

1. Diagnosis of one of the following:
 1. Acquired, generalized hypoactive sexual desire disorder (HSDD); or
 2. Female sexual interest/arousal disorder; and
2. Member is premenopausal; and
3. Symptoms of HSDD or female sexual interest/arousal disorder have persisted for at least 6 months; and
4. Member is 18 years of age or older; and
5. HSDD is not attributed to one of the following
 1. A co-existing medical or psychiatric condition
 2. Problems within a relationship
 3. Effects of a medication or other drug substance

Initial authorization duration: 3 months

REAUTHORIZATION CRITERIA Flibanserin (Addyi®) is medically necessary when ALL of the following are met:

1. Positive clinical response to flibanserin (Addyi®) therapy; and
2. Member continues to be premenopausal

Reauthorization duration: 12 months

INITIAL CRITERIA Bremelanotide (Vyleesi™) is medically necessary when ALL of the following are met:

1. Diagnosis of one of the following:
 1. Acquired, generalized hypoactive sexual desire disorder (HSDD); or
 2. Female sexual interest/arousal disorder; and
2. Symptoms of HSDD or female sexual interest/arousal disorder have persisted for at least 6 months; and
3. Member is premenopausal; and
4. HSDD is not attributed to one of the following
 1. A co-existing medical or psychiatric condition
 2. Problems within a relationship
 3. Effects of a medication or other drug substance; and

5. Member does not have either of the following:
 1. Uncontrolled hypertension; or
 2. Known cardiovascular disease; and
6. Member is 18 years of age or older

Initial authorization duration: 3 months

REAUTHORIZATION CRITERIA Bremelanotide (Vyleesi™) is medically necessary when ALL of the following are met:

1. Documentation of positive clinical response to Vyleesi™ therapy; and
2. Member continues to be premenopausal; and
3. Member does not have either of the following:
 1. Uncontrolled hypertension; or
 2. Known cardiovascular disease

Reauthorization duration: 12 months

P&T Approval Date: Dec-12-2024

Title: Hypoxia-Inducible Factor Prolyl Hydroxylase (HIF-PH) Inhibitor

Applicable Drugs:

Brand Name	Generic Name
Jesduvroq™	Daprodustat
Vafseo®	Vadadustat

Policy:

INITIAL CRITERIA: Daprodustat (Jesduvroq), vadadustat (Vafseo®) is medically necessary when ALL of the following are met:

1. Documentation is provided of chronic kidney disease (CKD); and
2. Member is 18 years of age or older; and
3. Member has been on dialysis for at least 4 months for daprodustat (Jesduvroq) and 3 months for vadadustat (Vafseo); and
4. Adequate iron stores confirmed by one of the following:
 - a. Member's ferritin level is greater than 100 mcg/L; or
 - b. Member's transferrin saturation (TSAT) is greater than 20%; and
5. Pretreatment hemoglobin level of less than 11 g/dL; and
6. Inadequate response to a minimum 12-week trial or inability to tolerate one of the following:
 1. Retacrit
 2. Procrit
 3. Aranesp; and
7. Prescribed by or in consultation with one of the following:
 - a. Hematologist
 - b. Nephrologist; and
8. Member is not on concurrent treatment with an erythropoietin stimulating agent [ESA] (e.g., Aranesp, Epogen, Procrit)

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Daprodustat (Jesduvroq), vadadustat (Vafseo®) is medically necessary when ALL of the following are met:

1. Documentation is provided of a positive clinical response to therapy (e.g. increase in hemoglobin); and
2. Hemoglobin level does not exceed 12 g/dL; and
3. Adequate iron stores confirmed by one of the following:
 - a. Member's ferritin level is greater than 100 mcg/L; or
 - b. Member's transferrin saturation (TSAT) is greater than 20%; and

4. Member is not on concurrent treatment with an erythropoietin stimulating agents [ESA] (e.g., Aranesp, Epogen, Procrit)

Reauthorization duration: 2 years

Black Box Warning as shown in the drug Prescribing Information:

WARNING: INCREASED RISK OF DEATH, MYOCARDIAL INFARCTION, STROKE, VENOUS THROMBOEMBOLISM, and THROMBOSIS OF VASCULAR ACCESS.

- JESDUVROQ, VAFSEO increases the risk of thrombotic vascular events, including major adverse cardiovascular events (MACE).
- Targeting a hemoglobin level greater than 11 g/dL is expected to further increase the risk of death and arterial venous thrombotic events, as occurs with erythropoietin stimulating agents (ESAs), which also increase erythropoietin levels.
- No trial has identified a hemoglobin target level, dose of JESDUVROQ, VAFSEO, or dosing strategy that does not increase these risks.
- Use the lowest dose of JESDUVROQ, VAFSEO sufficient to reduce the need for red blood cell transfusions.

P&T Approval Date: Dec-12-2024

Title: Icosapent ethyl (Vascepa)

Applicable Drugs:

Brand name	Generic name
Vascepa®	Icosapent ethyl

Policy:

Severe Hypertriglyceridemia

INITIAL CRITERIA: Icosapent ethyl (Vascepa®) is approved when ALL of the following are met:

1. Diagnosis of severe hypertriglyceridemia defined as pre-treatment triglyceride level greater than or equal to 500 mg/dl; and
2. Member is 18 years of age or older; and
3. Medication will be used adjunct to an appropriate lipid-lowering diet; and
4. Member has an inadequate response or inability to tolerate omega-3-acid ethyl esters (generic Lovaza®); and
5. For Brand Vascepa® only, inadequate response or inability to tolerate generic Icosapent ethyl capsules

Initial authorization duration: 6 Months

REAUTHORIZATION CRITERIA: Icosapent ethyl (Vascepa®) is approved when ALL of the following are met:

1. Documentation of positive clinical response to therapy; and
2. Member continues to use the medication adjunct to an appropriate lipid-lowering diet

Reauthorization duration: 2 years

Hypertriglyceridemia—Reduction of risk of cardiovascular events

INITIAL CRITERIA Icosapent ethyl (Vascepa®) is approved when ALL of the following are met:

1. Diagnosis of hypertriglyceridemia; and
2. Member is 18 years of age or older; and
3. Member has pre-treatment triglyceride level between 150 mg/dL to 499 mg/dL; and
4. ONE of the following:
 - a. Member has established cardiovascular disease; or
 - b. Both of the following:
 1. Diagnosis of diabetes mellitus; and

2. Member has 2 or more additional risk factors for cardiovascular disease (e.g., cigarette smoking, hypertension, creatinine clearance less than 60 ml/min, etc.); and
5. One of the following:
 - a. Member has been receiving 12 consecutive weeks of statin therapy at maximally tolerated dose and will continue to receive statin therapy at maximally tolerated dose; or
 - b. Inability to tolerate statin therapy; and
6. For Brand Vascepa® only, inadequate response or inability to tolerate generic Icosapent ethyl capsules

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA Icosapent ethyl (Vascepa®) is re-approved when BOTH of the following are met:

1. Documentation of positive clinical response to therapy; and
2. One of the following:
 - a. Member continues to receive statin therapy at maximally tolerated dose; or
 - b. Inability to tolerate statin therapy

Reauthorization duration: 2 years

P&T Approval Date: Jul-01-2024

Title: Immune Modulating Therapies**Applicable Drugs:**

Brand Name	Generic Name
Cimzia®	certolizumab
Cosentyx™	secukinumab
Enbrel®	etanercept
Kineret®	anakinra
Simponi®	golimumab
Orencia®	abatacept
Otezla®	apremilast
Xeljanz [XR]®	tofacitinib
Otrexup®, Rasuvo™, Reditrex	methotrexate
Taltz™	ixekizumab
Kevzara®	sarilumab
Siliq™	brodalumab
Tremfya®	guselkumab
Olumiant®	baricitinib
Arcalyst®	rilonacept
Skyrizi SQ	risankizumab-rzaa
Rinvoq, Rinvoq LQ	upadacitinib
Zeposia®	ozanimod
Adbry®	Tralokinumab-idrm
Cibinqo®	Abrocitinib
Sotyktu™	Deucravacitinib
Litfulo®	ritlectinib
Bimzelx	bimekizumab-bkzx
OmvoH	mirikizumab-mrkz
Velsipity	etrasimod
Entyvio SQ	vedolizumab
Zymfentra	Infliximab-dyyb
Nemluvio	Nemolizumab-ilto

Ebglyss

Lebrikizumab-lbkz

Preferred Adalimumab Product(s)^{‡1}	Non-preferred Adalimumab Product(s)
Adalimumab-aacf (by Fresenius Kabi)	Adalimumab (Humira by Abbvie) Adalimumab (Humira by Cordavis)
Adalimumab-adbm (by Boehringer Ingelheim) 10mg/0.2ml and 20mg/0.4ml injections only	Adalimumab-atto (Amjevita™ by Amgen)
	Adalimumab-adbm (Cyltezo® by Boehringer Ingelheim) Adalimumab-adbm (by Boehringer Ingelheim, all strength and formulation except the preferred products listed)
	Adalimumab-adaz (Hyrimoz® by Sandoz) Adalimumab-adaz (by Sandoz) Adalimumab-adaz (Hyrimoz® by Cordavis)
	Adalimumab-aacf (Idacio® by Fresenius)
	Adalimumab-bwwd (Hadlima™ by Asmedsolut or Organon)
	Adalimumab-aqvh (Yusimry™ by Coherus Biosciences)
	Adalimumab-aaty (Yuflyma™ by Celltrion USA) Adalimumab-aaty (by Celltrion)
	Adalimumab-fkjp (Hulio® by Mylan Specialty L.P.) Adalimumab-fkjp (by Mylan Specialty L.P.) Adalimumab-fkjp (by Biocon biologics) Adalimumab-fkjp (Hulio® by Biocon biologics)
	Adalimumab-afzb (Abrilada® by Pfizer U.S.)
	Adalimumab-ryvk (Simlandi® by Teva) Adalimumab-ryvk (by Quallent) Adalimumab-ryvk (by Quallent)

Preferred Ustekinumab Product(s) ²	Non-preferred Ustekinumab Product(s)
Ustekinumab-kfce (Yesintek™ by Biocon Biologics)	Ustekinumab (Stelara® by Janssen Biotech)
	Ustekinumab-stba (Steqeyma® by Celltrion)
	Ustekinumab-aekn (Selarsdi™ by Teva)
	Ustekinumab-ttwe (Pyzchiva® by Sandoz)

Preferred Tocilizumab Product(s) ³	Non-preferred Tocilizumab Product(s)
Tocilizumab-aazg (Tyenne® by Fresenius Kabi) Tocilizumab (Actemra® by Genentech)	None

Policy:

Adalimumab Products Non-preferred

Non-preferred adalimumab product(s)¹ is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming ONE of the following diagnoses:
 1. moderate to severe rheumatoid arthritis
 2. moderate to severe polyarticular juvenile idiopathic arthritis (PJIA)
 3. active psoriatic arthritis
 4. moderate to severe chronic plaque psoriasis
 5. Ankylosing spondylitis
 6. moderate to severe Crohn's disease
 7. moderate to severe ulcerative colitis
 8. moderate to severe hidradenitis suppurative (i.e., Hurley stage II or III)
 9. non-infectious intermediate, posterior, or panuveitis; and
2. Submission of medical records (e.g., chart notes) confirming ONE of the following:
 1. BOTH of the following:
 1. Member has had an inadequate response to ONE preferred adalimumab product¹ for a period sufficient to determine clinical response as outlined in the clinical trial⁴ for the indication requested; and
 2. Details on why the preferred adalimumab product¹ has not been effective is provided; or

2. BOTH of the following:
 1. Member has an inability to tolerate ONE preferred adalimumab product¹; and
 2. Details of intolerability is provided; and
3. No concurrent therapy with any of other biologic DMARD (i.e., tumor necrosis factor antagonists); and
4. ONE of the following:
 1. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
 2. Member is continuing on the established dose and frequency previously approved

Authorization duration: 12 months

INDICATION	DOSE
Rheumatoid Arthritis	40 mg every other week; may increase to 40 mg every week or 80 mg every other week in patients not receiving concomitant methotrexate
Ankylosing Spondylitis	40mg every other week
Polyarticular juvenile idiopathic arthritis	Pediatric patients 2 years or older: 10 kg to <15 kg: 10 mg every other week 15 kg to <30 kg: 20 mg every other week ≥30 kg: 40mg every other week
Psoriatic arthritis	40mg every other week
Plaque psoriasis	Loading dose: 80mg on day 1, 40mg every other week starting 1 week after the initial dose Maintenance dose: 40mg every other week
Crohn's Disease	Adults: Loading dose: 160mg on day 1, 80mg on day 15, 40mg every other week starting on day 29 Maintenance dose: 40mg every 2 weeks Pediatric Patients 6 Years of Age and Older: 17 kg to <40 kg: 80mg on day 1, 40mg on day 15, 20mg every other week starting on day 29 ≥40 kg: 160mg on day 1, 80mg on day 15, 40mg every other week starting on day 29
Ulcerative Colitis	Adults: Loading dose: 160mg on day 1, 80mg on day 15, 40mg every other week starting on day 29 Maintenance dose: 40mg every other week Pediatric Patients 5 Years of Age and Older: 20 kg to <40 kg: 80mg on day 1, 40mg on day 8, 40mg on day 15, 40mg every other week or 20mg every week starting on day 29 ≥40 kg: 160mg on day 1, 80mg on day 8, 80mg on day 15, 80mg every other week or 40mg every week starting on day 29

Pediatric patients 2 years or older:
 10 kg to <15 kg: 10 mg every other week
 15 kg to <30 kg: 20 mg every other week
 ≥30 kg: 40mg every other week

INDICATION	DOSE

Psoriatic arthritis	Adults: 45mg at 0 and 4 weeks, and then 45mg every 12 weeks thereafter. PA with PP or patients weighing >100kg: 90mg at 0 and 4 weeks, and then 90mg every 12 weeks Pediatric (6 to 17 years old): Weight-based dosing is recommended at the initial dose, 4 weeks later, then every 12 weeks thereafter <60kg: 0.75mg/kg ≥60kg: 45mg >100kg with co-existent moderate-to-severe plaque psoriasis: 90mg
Plaque psoriasis	Adult: (Weight ≤100kg): Loading dose: 45mg week 0 and week 4 Maintenance dose: 45mg every 12 weeks (Weight > 100kg): Loading dose: 90mg week 0 and week 4 Maintenance dose: 90mg every 12 weeks Psoriasis Pediatric Patients (6 to 17 years old): Weight-based dosing is recommended at the initial dose, 4 weeks later, then every 12 weeks thereafter <60kg: 0.75mg/kg 60kg to 100kg: 45mg >100kg: 90mg
Crohn's Disease	Maintenance dose: 90 mg every 8 weeks; begin maintenance dosing 8 weeks after the IV induction dose.
Ulcerative Colitis	Maintenance dose: 90 mg every 8 weeks; begin maintenance dosing 8 weeks after the IV induction dose.

Tocilizumab Products Non-preferred

Non-preferred tocilizumab product(s)³ is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming ONE of the following diagnoses:
 1. Moderate to severe rheumatoid arthritis
 2. Moderate to severe polyarticular juvenile idiopathic arthritis
 3. Giant cell arteritis
 4. Active systemic juvenile idiopathic arthritis
 5. Systemic sclerosis-associated interstitial lung disease; and
2. Submission of medical records (e.g., chart notes) confirming ONE of the following:
 1. BOTH of the following:
 1. Member has an inadequate response to ONE preferred tocilizumab product³ for a period sufficient to determine clinical response as outlined in the clinical trial⁴ for the indication requested; and

2. Details on why the preferred tocilizumab product³ has not been effective is provided; or
2. BOTH of the following:
 1. Member has an inability to tolerate ONE preferred tocilizumab product³; and
 2. Details of intolerability is provided; and
3. No concurrent therapy with any of other biologic DMARD (i.e., tumor necrosis factor antagonists); and
4. ONE of the following:
 1. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
 2. Member is continuing on the established dose and frequency previously approved

Authorization duration: 12 months

INDICATION	DOSE
Rheumatoid arthritis	If <100kg: 162mg once every other week; increase to 162 mg once every week based on clinical response. If ≥100kg: 162 mg once every week
Polyarticular juvenile idiopathic arthritis	Pediatric patients 2 years or older: <30kg: 162 mg once every three weeks. ≥30 kg: 162mg once every two weeks
Giant cell arteritis	162 mg given once every week
Systemic juvenile idiopathic arthritis	<30kg: 162mg every two weeks. ≥30kg: 162 every week.
Systemic sclerosis-associated interstitial lung disease	162mg once every week

4. Clinical trial supporting indication approval as described in the drug Prescribing Information, or in accordance with criteria outlined in the Off-Label Use policy.

Rheumatoid Arthritis (RA)

INITIAL CRITERIA Preferred adalimumab product¹ is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderate to severe rheumatoid arthritis (RA); and
2. Member is 18 years of age or older; and
3. Prescribed by or in consultation with a rheumatologist; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had inadequate response of inability to tolerate ONE of the following disease-modifying anti-rheumatic drugs (DMARDS) at maximally tolerated doses: methotrexate, hydroxychloroquine, leflunomide, azathioprine, sulfasalazine; and
5. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA Certolizumab (Cimzia®), golimumab (Simponi®), etanercept (Enbrel®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderate to severe rheumatoid arthritis (RA); and
2. Member is 18 years of age or older; and
3. Prescribed by or in consultation with a rheumatologist; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had inadequate response of inability to tolerate ONE of the following disease-modifying anti-rheumatic drugs (DMARDS) at maximally tolerated doses: methotrexate, hydroxychloroquine, leflunomide, azathioprine, sulfasalazine; and
5. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA Tofacitinib (Xeljanz [XR]® tablets/extended-release tablets) or upadacitinib (Rinvoq™) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderate to severe rheumatoid arthritis (RA); and
2. Member is 18 years of age or older; and
3. Prescribed by or in consultation with a rheumatologist; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had inadequate response of inability to tolerate ONE of the following disease-modifying anti-rheumatic drugs (DMARDS) at maximally tolerated doses: methotrexate, hydroxychloroquine, leflunomide, azathioprine, sulfasalazine; and
5. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
6. Member has had an inadequate response or intolerance to one or more TNF inhibitors (e.g., adalimumab, certolizumab pegol, etanercept, golimumab); and
7. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA Anakinra (Kineret®), sarilumab (Kevzara®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderate to severe rheumatoid arthritis (RA); and
2. Member is 18 years of age or older; and
3. Prescribed by or in consultation with a rheumatologist; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had inadequate response of inability to tolerate ONE of the following disease-modifying anti-rheumatic drugs (DMARDS) at maximally tolerated doses: methotrexate, hydroxychloroquine, leflunomide, azathioprine, sulfasalazine; and
5. ONE of the following:
 1. Both of the following:
 1. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate TWO of the following:
 1. One preferred adalimumab product¹
 2. certolizumab (Cimzia®)
 3. golimumab (Simponi®)

4. etanercept (Enbrel®)
5. tofacitinib (Xeljanz [XR]® tablets/extended-release tablets)
6. upadacitinib (Rinvoq®); and
2. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate BOTH of the following: abatacept (Orencia® SQ) and preferred tocilizumab product³; or
2. Paid claims or submission of medical records (e.g., chart notes) confirming a continuation of therapy with the requested product, defined as no more than a 45-day gap in therapy; and
6. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
7. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA Baricitinib (Olumiant®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderate to severe rheumatoid arthritis (RA); and
2. Member is 18 years of age or older; and
3. Prescribed by or in consultation with a rheumatologist; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had inadequate response or inability to tolerate ONE of the following disease-modifying anti-rheumatic drugs (DMARDs) at maximally tolerated doses: methotrexate, hydroxychloroquine, leflunomide, azathioprine, sulfasalazine; and
5. ONE of the following:
 1. Both of the following:
 1. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate TWO of the following:
 1. One preferred adalimumab product¹
 2. certolizumab (Cimzia®)
 3. golimumab (Simponi®)
 4. etanercept (Enbrel®)
 5. tofacitinib (Xeljanz [XR]® tablets/extended-release tablets)
 6. upadacitinib (Rinvoq™); and
 2. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate BOTH of the following: abatacept (Orencia® SQ) and preferred tocilizumab product; or
 2. Paid claims or submission of medical records (e.g., chart notes) confirming a continuation of therapy with the requested product, defined as no more than a 45-day gap in therapy; and
6. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
7. Member has had an inadequate response or intolerance to one or more TNF inhibitors (e.g., adalimumab, certolizumab pegol, etanercept, golimumab); and
8. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA Abatacept (Orencia® SQ) or preferred tocilizumab product³ is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderate to severe rheumatoid arthritis (RA); and
2. Member is 18 years of age or older; and
3. Prescribed by or in consultation with a rheumatologist; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had an inadequate response or inability to tolerate ONE of the following disease-modifying anti-rheumatic drugs (DMARDS) at maximally tolerated doses: methotrexate, hydroxychloroquine, leflunomide, azathioprine, sulfasalazine; and
5. One of the following:
 1. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate TWO of the following:
 1. One preferred adalimumab product¹
 2. certolizumab (Cimzia®)
 3. golimumab (Simponi®)
 4. etanercept (Enbrel®)
 5. tofacitinib (Xeljanz [XR]® tablets/extended-release tablets)
 6. upadacitinib (Rinvoq®); or
 2. Paid claims or submission of medical records (e.g., chart notes) confirming a continuation of therapy with the requested product, defined as no more than a 45-day gap in therapy; and
6. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
7. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Methotrexate injection (i.e., Otrexup™, Rasuvo®, Reditrex™) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of severe, active rheumatoid arthritis (RA); and
2. Prescribed by or in consultation with a rheumatologist; and
3. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had an inadequate response or inability to tolerate oral methotrexate; and
4. For Otrexup™ and Reditrex™ only: paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate Rasuvo®; and
5. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA Preferred adalimumab product¹, certolizumab (Cimzia®), golimumab (Simponi®), tofacitinib (Xeljanz [XR]® tablets/extended-release tablets), upadacitinib (Rinvoq™), anakinra (Kineret®), etanercept (Enbrel®), sarilumab (Kevzara®), baricitinib (Olumiant®), abatacept (Orencia® SQ), preferred tocilizumab product³ or methotrexate injection (i.e., Otrexup™, Rasuvo®, Reditrex™) is medically necessary when BOTH of the following are met:

1. There is documentation of positive clinical response to therapy as evidenced by at least one of the following:
 - a. Reduction in total active (swollen and tender) joint count from baseline; or
 - b. Improvement in symptoms (e.g., pain, stiffness, inflammation) from baseline; and
2. ONE of the following:

- a. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
- b. Member is continuing on the established dose and frequency previously approved

Reauthorization duration: 12 months

DRUG	DOSE
Adalimumab (Humira®) and its biosimilars	40 mg every other week; may increase to 40 mg every week or 80 mg every other week in patients not receiving concomitant methotrexate
Certolizumab (Cimzia®)	Loading dose: 400mg (2 injections) week 0, week 2 and week 4 Maintenance dose: 200mg every 2 weeks/400mg every 4 weeks
Golimumab (Simponi®)	50mg once a month
Tofacitinib (Xeljanz®)	5 mg twice daily
Tofacitinib (Xeljanz XR®)	11 mg once daily
Upadacitinib (Rinvoq®)	15mg once daily
Anakinra (Kineret®)	100 mg daily
Etanercept (Enbrel®)	50mg once weekly
Sarilumab (Kevzara®)	200 mg every two weeks
Baricitinib (Olumiant®)	2mg once daily
Abatacept (Orencia SQ®)	125 mg once weekly.
Tocilizumab (Actemra SQ®) and its biosimilars	If <100kg: 162mg once every other week; increase to 162 mg once every week based on clinical response. If ≥100kg: 162 mg once every week
Methotrexate	Initial, 7.5 mg once weekly; individualize and adjust dose gradually for optimal response; at doses exceeding 20 mg per week the incidence and severity of toxic reactions are increased

Ankylosing Spondylitis (AS)

INITIAL CRITERIA: Preferred adalimumab product¹ is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of ankylosing spondylitis (AS); and
2. Member is 18 years of age or older; and
3. Prescribed by or in consultation with a rheumatologist; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had an inadequate response or inability to tolerate two different NSAIDs at maximally tolerated doses; and
5. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and

6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Certolizumab (Cimzia®), etanercept (Enbrel®), or golimumab (Simponi®), Ixekizumab (Taltz®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of ankylosing spondylitis (AS); and
2. Member is 18 years of age or older; and
3. Prescribed by or in consultation with a rheumatologist; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had an inadequate response or inability to tolerate two different NSAIDS at maximally tolerated doses; and
5. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Secukinumab (Cosentyx®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of active ankylosing spondylitis (AS); and
2. Member is 18 years of age or older; and
3. Prescribed by or in consultation with a rheumatologist; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had inadequate response or inability to tolerate two different NSAIDS at maximally tolerated doses; and
5. One of the following:
 1. Both of the following:
 1. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had an inadequate response or inability to tolerate TWO of the following:
 1. One preferred adalimumab product¹
 2. certolizumab (Cimzia®)
 3. golimumab (Simponi®)
 4. etanercept (Enbrel®)
 5. tofacitinib (Xeljanz [XR]® tablets/extended-release tablets)
 6. upadacitinib (Rinvoq™); and
 2. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate BOTH ixekizumab (Taltz®) and bimekizumab (Bimzelx) or
 2. Paid claims or submission of medical records (e.g., chart notes) confirming a continuation of therapy with the requested product, defined as no more than a 45-day gap in therapy; and
6. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
7. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Bimekizumab (Bimzelx®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of active ankylosing spondylitis (AS); and

2. Member is 18 years of age or older; and
3. Prescribed by or in consultation with a rheumatologist; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had inadequate response or inability to tolerate two different NSAIDs at maximally tolerated doses; and
5. One of the following:
 1. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had an inadequate response or inability to tolerate TWO of the following:
 1. One preferred adalimumab product¹
 2. certolizumab (Cimzia®)
 3. golimumab (Simponi®)
 4. etanercept (Enbrel®)
 5. tofacitinib (Xeljanz [XR]® tablets/extended-release tablets)
 6. upadacitinib (Rinvoq™)
 7. ixekizumab (Taltz®); and
 2. Paid claims or submission of medical records (e.g., chart notes) confirming a continuation of therapy with the requested product, defined as no more than a 45-day gap in therapy; and
6. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
7. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA Tofacitinib (Xeljanz [XR]® tablets/extended-release tablets) or upadacitinib (Rinvoq®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of active ankylosing spondylitis (AS); and
2. Member is 18 years of age or older; and
3. Prescribed by or in consultation with a rheumatologist; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had an inadequate response or inability to tolerate two different NSAIDs at maximally tolerated doses; and
5. Paid claims or submission of medical records (e.g., chart notes) confirming inadequate response or intolerance to one of more TNF inhibitors (e.g., adalimumab, certolizumab pegol, etanercept, golimumab); and
6. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonist); and
7. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Preferred adalimumab product¹, certolizumab (Cimzia®), golimumab (Simponi®), Etanercept (Enbrel®), secukinumab (Cosentyx®), tofacitinib (Xeljanz [XR]® tablets/extended-release tablets), ixekizumab (Taltz®), upadacitinib (Rinvoq®), or bimekizumab (Bimzelx®) is medically necessary when BOTH of the following are met:

1. There is documentation of positive clinical response to therapy as evidence by improvement from baseline by at least one of the following:
 - a. Disease activity (e.g., pain, fatigue, inflammation, stiffness); or

- b. Lab values (erythrocyte sedimentation rate, C-reactive protein level); or
 - c. Axial status (e.g., lumbar spine motion, chest expansion); or
 - d. Total active (swollen or tender) joint count; and
2. ONE of the following:
- a. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
 - b. Member is continuing on the established dose and frequency previously approved

Reauthorization duration: 12 months

DRUG	DOSE
Adalimumab (Humira®) and its biosimilars	40mg every other week
Certolizumab (Cimzia®)	Loading dose: 400mg (2 injections) week 0, week 2 and week 4 Maintenance dose: 200mg every 2 weeks/400mg every 4 weeks
Golimumab (Simponi®)	50 mg once a month
Tofacitinib (Xeljanz®)	5 mg twice daily
Tofacitinib (Xeljanz XR®)	11 mg once daily
Etanercept (Enbrel®)	50mg once weekly
Ixekizumab (Taltz®)	Loading dose: 160 mg (given as two 80mg injections) at week 0, followed by 80 mg every 4 weeks Maintenance dose: 80 mg every 4 weeks
Secukinumab (Cosentyx®)	Loading dose: 150mg at Weeks 0, 1, 2, 3 and 4 Maintenance dose: 150mg every 4 weeks; may consider a dosage of 300 mg every 4 weeks if active disease persists
Upadacitinib (Rinvoq®)	15 mg PO once daily
Bimekizumab (Bimzelx®)	160mg every 4 weeks

Polyarticular Juvenile Idiopathic Arthritis

INITIAL CRITERIA: Preferred adalimumab product¹ is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderate to severe polyarticular juvenile idiopathic arthritis (PJIA); and
2. Member is 2 years of age or older; and
3. Prescribed by or in consultation with a rheumatologist; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had an inadequate response or inability to tolerate ONE of the following DMARDs at maximally tolerated doses: methotrexate, hydroxychloroquine, leflunomide, azathioprine, sulfasalazine; and
5. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and

6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Etanercept (Enbrel®), certolizumab pegol (Cimzia®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderate to severe polyarticular juvenile idiopathic arthritis (PJIA); and
2. Member is 2 years of age or older; and
3. Prescribed by or in consultation with a rheumatologist; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had an inadequate response or inability to tolerate ONE of the following DMARDs at maximally tolerated doses: methotrexate, hydroxychloroquine, leflunomide, azathioprine, sulfasalazine; and
5. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Sarilumab (Kevzara®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of active polyarticular juvenile idiopathic arthritis (PJIA); and
2. Member weighs at least 63 kg; and
3. Prescribed by or in consultation with a rheumatologist; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had an inadequate response or inability to tolerate ONE of the following DMARDs at maximally tolerated doses: methotrexate, hydroxychloroquine, leflunomide, azathioprine, sulfasalazine; and
5. One of the following:
 1. Both of the following:
 1. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate TWO of the following:
 1. One preferred adalimumab product¹
 2. tofacitinib (Xeljanz® tablets and oral solution)
 3. etanercept (Enbrel®)
 4. upadacitinib (Rinvoq/Rinvoq LQ®)
 5. certolizumab pegol (Cimzia®); and
 2. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate BOTH of the following:
 1. Preferred tocilizumab product³; and
 2. Abatacept (Orencia®); or
 2. Paid claims or submission of medical records (e.g., chart notes) confirming continuation of therapy with the requested product, defined as no more than a 45-day gap in therapy; and
6. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
7. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: preferred tocilizumab product³ abatacept (Orencia® SQ) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderate to severe polyarticular juvenile idiopathic arthritis (PJIA); and
2. Member is 2 years of age or older; and
3. Prescribed by or in consultation with a rheumatologist; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had an inadequate response or inability to tolerate ONE of the following DMARDs at maximally tolerated doses: methotrexate, hydroxychloroquine, leflunomide, azathioprine, sulfasalazine; and
5. One of the following:
 - a. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate TWO of the following:
 1. One preferred adalimumab product¹
 2. tofacitinib (Xeljanz® tablets and oral solution)
 3. etanercept (Enbrel®)
 4. Upadacitinib (Rinvoq®/Rinvoq LQ)
 5. Certolizumab pegol (Cimzia®); or
 - b. Paid claims or submission of medical records (e.g., chart notes) confirming continuation of therapy with the requested product, defined as no more than a 45-day gap in therapy; and
6. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
7. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA Tofacitinib (Xeljanz® tablets and oral solution), Upadacitinib (Rinvoq®, Rinvoq LQ®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderate to severe polyarticular juvenile idiopathic arthritis (PJIA); and
2. Member is 2 years of age or older; and
3. Prescribed by or in consultation with a rheumatologist; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had an inadequate response or inability to tolerate ONE of the following DMARDs at maximally tolerated doses: methotrexate, hydroxychloroquine, leflunomide, azathioprine, sulfasalazine; and
5. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
6. Member had an inadequate response or inability to tolerate one or more TNF inhibitors (e.g., adalimumab, etanercept, certolizumab pegol); and
7. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Methotrexate injection (i.e., Otrexup™, Rasuvo®, Reditrex™) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of polyarticular juvenile idiopathic arthritis (PJIA); and
2. Prescribed by or in consultation with a rheumatologist; and
3. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate oral methotrexate; and

4. For Otrexup™ and Reditrex™ only: paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate Rasuvo®; and
5. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA Preferred adalimumab product¹, preferred tocilizumab product³, abatacept (Orencia® SQ), tofacitinib (Xeljanz® tablets and oral solution), Upadacitinib (Rinvoq®, Rinvoq LQ®), etanercept (Enbrel®), Sarilumab (Kevzara®), certolizumab pegol (Cimzia®) or methotrexate injection (i.e., Otrexup™, Rasuvo®, Reditrex™) is medically necessary when BOTH of the following are met:

1. There is documentation of positive clinical response to therapy as evidenced by at least one of the following:
 - a. Reduction in the total active (swollen and tender) joint count from baseline; or
 - b. Improvement in symptoms (e.g., pain, stiffness, inflammation) from baseline; and
2. ONE of the following:
 - a. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
 - b. Member is continuing on the established dose and frequency previously approved

Reauthorization duration: 12 months

DRUG	DOSE
Adalimumab (Humira®) and its biosimilars	Pediatric patients 2 years or older: 10 kg to <15 kg: 10 mg every other week 15 kg to <30 kg: 20 mg every other week ≥30 kg: 40mg every other week
Tocilizumab (Actemra SQ®) and its biosimilars	Pediatric patients 2 years or older: <30kg: 162 mg once every three weeks. ≥30 kg: 162mg once every two weeks
Abatacept (Orencia SQ®)	Pediatric patients 2 years or older: 10 kg to < 25 kg: 50 mg once weekly 25 kg to <50 kg: 87.5 mg once weekly ≥50 kg: 125 mg once weekly
Upadacitinib (Rinvoq, Rinvoq LQ)	Pediatric patients 2 years or older: 10 kg to < 20 kg: 3 mg (3ml Rinvoq LQ) twice daily 20 kg to < 30 kg: 4 mg (4 ml Rinvoq LQ) twice daily ≥30 kg: 6 mg (6 ml Rinvoq LQ) twice daily or 15mg (Rinvoq) once daily
Sarilumab (Kevzara)	Patients who weigh 63 kg or greater: 200mg SQ every 2 weeks

Tofacitinib (Xeljanz®) tablet or oral solution	10kg to < 20kg: 3.2mg oral solution twice daily 20kg to <40kg: 4mg oral solution twice daily 40kg or more: 5mg oral tablet or solution twice daily
Etanercept (Enbrel®)	Pediatric patients 2 years or older: ≥63 kg: 50 mg once weekly <63 kg: 0.8 mg/kg once weekly
Certolizumab (Cimzia®)	10kg (22 lbs) to less than 20kg (44 lbs): 100mg initially and at weeks 2 and 4, followed by 50mg every other week 20kg (44 lbs) to less than 40kg (88 lbs): 200mg initially and at weeks 2 and 4, followed by 100mg every other week Greater than or equal to 40kg (88 lbs): 400mg initially and at weeks 2 and 4, followed by 200mg every other week
Methotrexate	Initial, 10 mg/m(2) once weekly; Individualize and adjust dose gradually for optimal response; optimal duration of therapy is unknown

Psoriatic Arthritis

INITIAL CRITERIA: Preferred adalimumab product¹ is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of active psoriatic arthritis; and
2. Member is 18 years of age or older; and
3. Prescribed by or in consultation with a rheumatologist or dermatologist; and
4. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
5. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Certolizumab (Cimzia®), apremilast (Otezla®), golimumab (Simponi®), guselkumab (Tremfya®), ixekizumab (Taltz®) or risankizumab (Skyrizi® SQ), is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of active psoriatic arthritis; and
2. Member is 18 years of age or older; and
3. Prescribed by or in consultation with a rheumatologist or dermatologist; and
4. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
5. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Etanercept (Enbrel®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of active psoriatic arthritis; and
2. Member is 2 years of age or older; and

3. Prescribed by or in consultation with a rheumatologist or dermatologist; and
4. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
5. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Preferred ustekinumab product² is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of active psoriatic arthritis; and
2. Member is 6 years of age or older; and
3. Prescribed by or in consultation with a rheumatologist or dermatologist; and
4. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
5. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Upadacitinib (Rinvoq®, Rinvoq LQ®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of active psoriatic arthritis; and
2. Member is 2 years of age or older; and
3. Prescribed by or in consultation with a rheumatologist or dermatologist; and
4. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
5. Paid claims or submission of medical records (e.g., chart notes) confirming the member has had an inadequate response or intolerance to one or more TNF inhibitors (e.g., adalimumab, certolizumab pegol, etanercept, golimumab); and
6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Tofacitinib (Xeljanz®/Xeljanz® XR tablets/extended-release tablets) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of active psoriatic arthritis; and
2. Member is 18 years of age or older; and
3. Prescribed by or in consultation with a rheumatologist or dermatologist; and
4. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
5. Paid claims or submission of medical records (e.g., chart notes) confirming the member has had an inadequate response or intolerance to one or more TNF inhibitors (e.g., adalimumab, certolizumab pegol, etanercept, golimumab); and
6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Abatacept (Orencia® SQ) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of active psoriatic arthritis; and
2. Member is 2 years of age or older; and
3. Prescribed by or in consultation with a rheumatologist or dermatologist; and
4. One of the following:

1. Paid claims or submission of medical records (e.g., chart notes) confirming the member has had an inadequate response or inability to tolerate TWO of the following:
 1. One preferred adalimumab product¹
 2. certolizumab (Cimzia®)
 3. One preferred ustekinumab product²
 4. golimumab (Simponi®)
 5. etanercept (Enbrel®)
 6. guselkumab (Tremfya®)
 7. risankizumab (Skyrizi™)
 8. tofacitinib (Xeljanz®/Xeljanz® XR tablets/extended-release tablets)
 9. upadacitinib (Rinvoq/Rinvoq LQ®)
 10. ixekizumab (Taltz®); or
2. Paid claims or submission of medical records (e.g., chart notes) confirming a continuation of therapy with the requested product, defined as no more than a 45-day gap in therapy; and
5. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Secukinumab (Cosentyx®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of active psoriatic arthritis; and
2. Member is 2 years of age or older; and
3. Prescribed by or in consultation with a rheumatologist or dermatologist; and
4. One of the following:
 1. All of the following:
 1. Paid claims or submission of medical records (e.g., chart notes) confirming the member has had an inadequate response or inability to tolerate TWO of the following:
 1. One preferred adalimumab product¹
 2. certolizumab (Cimzia®)
 3. golimumab (Simponi®)
 4. One preferred ustekinumab product²
 5. etanercept (Enbrel®)
 6. guselkumab (Tremfya®)
 7. risankizumab (Skyrizi™)
 8. tofacitinib (Xeljanz®/Xeljanz® XR tablets/extended-release tablets)
 9. upadacitinib (Rinvoq/Rinvoq LQ®); and
 2. Paid claims or submission of medical records (e.g., chart notes) confirming the member has had an inadequate response or inability to tolerate BOTH of the following: ixekizumab (Taltz®) AND abatacept (Orencia® SQ) or bimekizumab (Bimzelx®); or
 2. Paid claims or submission of medical records (e.g., chart notes) confirming a continuation of therapy with the requested product, defined as no more than a 45-day gap in therapy; and

5. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Bimekizumab (Bimzelx®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of active psoriatic arthritis; and
2. Member is 18 years of age or older; and
3. Prescribed by or in consultation with a rheumatologist or dermatologist; and
4. One of the following:
 1. Paid claims or submission of medical records (e.g., chart notes) confirming the member has had an inadequate response or inability to tolerate TWO of the following:
 1. One preferred adalimumab product¹
 2. certolizumab (Cimzia®)
 3. golimumab (Simponi®)
 4. One preferred ustekinumab product²
 5. etanercept (Enbrel®)
 6. guselkumab (Tremfya®)
 7. risankizumab (Skyrizi™)
 8. tofacitinib (Xeljanz®/Xeljanz® XR tablets/extended-release tablets)
 9. upadacitinib (Rinvoq/Rinvoq LQ®)
 10. ixekizumab (Taltz®); and
 2. Paid claims or submission of medical records (e.g., chart notes) confirming a continuation of therapy with the requested product, defined as no more than a 45-day gap in therapy; and
5. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Methotrexate injection (i.e., Otrexup®, Rasuvo®, Reditrex™) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of psoriatic arthritis (PsA); and
2. Prescribed by or in consultation with a rheumatologist or dermatologist; and
3. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate oral methotrexate; and
4. For Otrexup™ and Reditrex™ only: Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate Rasuvo®; and
5. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Preferred adalimumab product^{*1}, certolizumab (Cimzia®), preferred ustekinumab product², apremilast (Otezla®), golimumab (Simponi®), guselkumab (Tremfya®), abatacept (Orencia® SQ), tofacitinib (Xeljanz®/Xeljanz® XR tablets/extended-release tablets), ixekizumab (Taltz®), etanercept (Enbrel®), secukinumab (Cosentyx®), methotrexate injection (i.e., Otrexup®, Rasuvo®,

Reditrex™), upadacitinib (Rinvoq™®, Rinvoq LQ®), risankizumab (Skyrizi® SQ), or bimekizumab (Bimzelx®) is medically necessary when BOTH of the following are met:

1. There is documentation of positive clinical response to therapy as evidenced by at least one of the following:
 - a. Reduction in the total active (swollen and tender) joint count from baseline; or
 - b. Improvement in symptoms (e.g., pain, stiffness, pruritus, inflammation) from baseline; or
 - c. Reduction in the body surface area involvement from baseline; and
2. ONE of the following:
 - a. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
 - b. Member is continuing on the established dose and frequency previously approved

Reauthorization duration: 12 months

DRUG	DOSE
Adalimumab (Humira®) and its biosimilars	40mg every other week
Certolizumab (Cimzia®)	Loading dose: 400mg (2 injections) week 0, week 2 and week 4 Maintenance: 200mg every 2 weeks/400mg every 4 weeks
Ustekinumab (Stelara®)	Adults: 45mg at 0 and 4 weeks, and then 45mg every 12 weeks thereafter. PA with PP or patients weighing >100kg: 90mg at 0 and 4 weeks, and then 90mg every 12 weeks
Apremilast (Otezla®)	Pediatric (6 to 17 years old): Weight-based dosing is recommended at the initial dose, 4 weeks later, then every 12 weeks thereafter <60kg: 0.75mg/kg ≥60kg: 45mg >100kg with co-existent moderate-to-severe plaque psoriasis: 90mg Loading: 5-day titration - Starter pack Day 1 10mg, Day 2 20mg, Day 3 30mg, Day 4 40mg, Day 5 60mg Maintenance dose: 30 mg twice daily
Golimumab (Simponi®)	50 mg once a month
Guselkumab (Tremfya®)	Loading dose: 100mg at Week 0, Week 4 Maintenance dose: 100mg every 8 weeks
Abatacept (Orencia SQ®)	125 mg once weekly
Tofacitinib (Xeljanz®)	5 mg twice daily
Tofacitinib Extended-Release (Xeljanz XR®)	11 mg once daily
Ixekizumab (Taltz®)	Loading dose: 160 mg (given as two 80mg injections) at week 0, followed by 80 mg (for psoriatic arthritis patients with coexistent

Etanercept (Enbrel®)	moderate-to-severe plaque psoriasis, use the dosing regimen for adult plaque psoriasis Maintenance dose: 80 mg every 4 weeks Adults: 50 mg once weekly
	Pediatric: 63kg (138 pounds) or more: 50mg weekly Less than 63 (138 pounds): 0.8mg/kg weekly
Secukinumab (Cosentyx®)	Loading dose: 150mg at Weeks 0, 1, 2, 3 and 4 Maintenance dose: 150mg every 4 weeks; may consider a dosage of 300 mg every 4 weeks if active disease persists
Upadacitinib (Rinvoq®, Rinvoq LQ)	Adults: 15mg once daily
	Pediatric patients 2 years to less than 18 years of age: 10 kg to < 20 kg: 3 mg (3 ml of Rinvoq LQ) twice daily 20 kg to < 30 kg: 4 mg (4 ml of Rinvoq LQ) twice daily ≥ 30 kg: 6 mg (6 ml of Rinvoq LQ) twice daily or 15mg (Rinvoq) once daily.
Risankizumab (Skyrizi® SQ)	Loading dose: 150mg at Week 0, Week 4 Maintenance dose: 150mg every 12 weeks
Bimekizumab (Bimzelx®)	160mg every 4 weeks
Methotrexate	Initial, 7.5 mg once weekly; individualize and adjust dose gradually for optimal response; at doses exceeding 20 mg per week the incidence and severity of toxic reactions are increased

Plaque Psoriasis

INITIAL CRITERIA: Preferred adalimumab product¹ is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderate to severe chronic plaque psoriasis; and
2. Member is 18 years of age or older; and
3. Prescribed by or in consultation with a dermatologist; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had inadequate response of inability to tolerate ONE of the following: topical calcipotriene containing products, topical anthralin, topical steroids, topical immune modulators (Elidel®, Protopic®), topical retinoids; and
5. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Guselkumab (Tremfya®), certolizumab (Cimzia®), deucravacitinib (Sotyktu™) or risankizumab (Skyrizi® SQ) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderate to severe chronic plaque psoriasis; and
2. Member is 18 years of age or older; and
3. Prescribed by or in consultation with a dermatologist; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had inadequate response of inability to tolerate ONE of the following: topical calcipotriene containing products, topical anthralin, topical steroids, topical immune modulators (Elidel®, Protopic®), topical retinoids; and
5. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Apremilast (Otezla®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of plaque psoriasis; and
2. Both of the following:
 - a. Member is 6 years of age or older; and
 - b. Member weighs at least 20 kg; and
3. Prescribed by or in consultation with a dermatologist; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had inadequate response of inability to tolerate ONE of the following: topical calcipotriene containing products, topical anthralin, topical steroids, topical immune modulators (Elidel®, Protopic®), topical retinoids; and
5. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Preferred ustekinumab product² or ixekizumab (Taltz™) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderate to severe chronic plaque psoriasis; and
2. Member is 6 years of age or older; and
3. Prescribed by or in consultation with a dermatologist; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had inadequate response of inability to tolerate ONE of the following: topical calcipotriene containing products, topical anthralin, topical steroids, topical immune modulators (Elidel®, Protopic®), topical retinoids; and
5. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA Secukinumab (Cosentyx™) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderate to severe chronic plaque psoriasis; and
2. Member is 6 years of age or older; and
3. Prescribed by or in consultation with a dermatologist; and

4. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had inadequate response or inability to tolerate ONE of the following: topical calcipotriene containing products, topical anthralin, topical steroids, topical immune modulators (Elidel®, Protopic), topical retinoids; and
5. One of the following:
 1. BOTH of the following:
 1. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate TWO of the following:
 1. certolizumab (Cimzia®)
 2. One preferred adalimumab product¹
 3. One preferred ustekinumab product²
 4. etanercept (Enbrel®)
 5. guselkumab (Tremfya®)
 6. risankizumab (Skyrizi™)
 7. apremilast (Otezla®)
 8. deucravacitinib (Sotyktu®); and
 2. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate BOTH ixekizumab (Taltz®) and bimekizumab (Bimzelx®); or
 2. BOTH of the following:
 1. Paid claims or submission of medical records (e.g., chart notes) confirming a continuation of therapy with the requested product, defined as no more than a 45-day gap in therapy; and
 2. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate BOTH ixekizumab (Taltz®) and bimekizumab (Bimzelx®); and
6. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
7. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA Etanercept (Enbrel®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderate to severe chronic plaque psoriasis; and
2. Member is 4 years of age or older; and
3. Prescribed by or in consultation with a dermatologist; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had inadequate response or inability to tolerate ONE of the following: topical calcipotriene containing products, topical anthralin, topical steroids, topical immune modulators (Elidel®, Protopic), topical retinoids; and
5. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonist); and
6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Methotrexate injection (i.e., Otrexup™, Rasuvo®, Reditrex™) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of severe psoriasis; and

2. Member is age 18 years or older; and
3. Prescribed by or in consultation with a dermatologist; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response to ALL other standard therapy (e.g., oral methotrexate, all topical therapy modalities, phototherapy, etc.); and
5. For Otrexup™ and Reditrex™ only: Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate Rasuvo®; and
6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA Bimekizumab (Bimzelx®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderate to severe chronic plaque psoriasis; and
2. Member is 18 years of age or older; and
3. Prescribed by or in consultation with a dermatologist; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had inadequate response or inability to tolerate ONE of the following: topical calcipotriene containing products, topical anthralin, topical steroids, topical immune modulators (Elidel®, Protopic), topical retinoids; and
5. One of the following:
 1. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate TWO of the following:
 1. certolizumab (Cimzia®),
 2. One preferred adalimumab product¹
 3. One preferred ustekinumab product²
 4. etanercept (Enbrel®)
 5. guselkumab (Tremfya®)
 6. risankizumab (Skyrizi™)
 7. apremilast (Otezla®)
 8. ixekizumab (Taltz®)
 9. deucravacitinib (Sotyktu®); and
 2. Paid claims or submission of medical records (e.g., chart notes) confirming a continuation of therapy with the requested product, defined as no more than a 45-day gap in therapy; and
6. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
7. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA Preferred adalimumab product¹, guselkumab (Tremfya®), certolizumab (Cimzia®), risankizumab (Skyrizi® SQ), apremilast (Otezla®), Preferred ustekinumab product², secukinumab (Cosentyx™), ixekizumab (Taltz™), etanercept (Enbrel®), deucravacitinib (Sotyktu™), bimekizumab (Bimzelx®) or methotrexate injection (i.e., Otrexup™, Rasuvo®, Reditrex™) is medically necessary when ALL of the following are met:

1. There is documentation of positive clinical response to therapy as evidenced by one of the following:
 - a. Reduction in body surface area (BSA) involvement from baseline; or

- b. Improvement in symptoms (e.g., pruritus, inflammation) from baseline; and
- 2. For secukinumab (Cosentyx) only, paid claim or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate BOTH ixekizumab (Taltz) and bimekizumab (Bimzelx®); and
- 3. ONE of the following:
 - a. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
 - b. Member is continuing on the established dose and frequency previously approved

Reauthorization duration: 12 months

INITIAL CRITERIA Brodalumab (Siliq™) is medically necessary when ALL of the following are met:

- 1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderate to severe chronic plaque psoriasis; and
- 2. Member is 18 years of age or older; and
- 3. Prescribed by or in consultation with a dermatologist; and
- 4. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had inadequate response or inability to tolerate ONE of the following: topical calcipotriene containing products, topical anthralin, topical steroids, topical immune modulators (Elidel®, Protopic®), topical retinoids; and
- 5. One of the following:
 - 1. BOTH of the following:
 - 1. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate TWO of the following:
 - 1. One preferred adalimumab product¹
 - 2. One preferred ustekinumab product²
 - 3. certolizumab (Cimzia®)
 - 4. etanercept (Enbrel®)
 - 5. risankizumab (Skyrizi)
 - 6. guselkumab (Tremfya®)
 - 7. apremilast (Otezla®)
 - 8. deucravacitinib (Sotyktu®); and
 - 2. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate BOTH bimekizumab (Bimzelx) and ixekizumab (Taltz®); or
 - 2. BOTH of the following:
 - 1. Paid claims or submission of medical records (e.g., chart notes) confirming continuation of therapy with the requested product, defined as no more than a 45-day gap in therapy; and
 - 2. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate BOTH bimekizumab (Bimzelx) and ixekizumab (Taltz®); and
- 6. Member has been evaluated for depression and suicidal ideations using the Patient Health Questionnaire (PHQ)-9; and
- 7. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonist); and
- 8. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 16 weeks

REAUTHORIZATION CRITERIA Brodalumab (Siliq™) is medically necessary when ALL of the following are met:

1. Member has positive response to therapy with brodalumab (Siliq®) as evidenced by one of the following:
 - a. Reduction of the body surface area (BSA) involvement from baseline; or
 - b. Improvement in symptoms (e.g., pruritus, inflammation) from baseline; and
2. Paid claim or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate bimekizumab (Bimzelx) and ixekizumab (Taltz); and
3. Member has been evaluated for depression and suicidal ideations using the Patient Health Questionnaire (PHQ)-9; and
4. ONE of the following:
 - a. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
 - b. Member is continuing on the established dose and frequency previously approved

Reauthorization duration: 12 months

DRUG	DOSE
Adalimumab (Humira®) and its biosimilars	Loading dose: 80mg on day 1, 40mg every other week starting 1 week after the initial dose Maintenance dose: 40mg every other week
Certolizumab (Cimzia®)	Loading dose: 400mg (2 injections) week 0, week 2 and week 4 Maintenance dose: 200mg every 2 weeks/400mg every 4 weeks
Ustekinumab (Stelara®)	Adult: (Weight ≤100kg): Loading dose: 45mg week 0 and week 4 Maintenance dose: 45mg every 12 weeks (Weight > 100kg): Loading dose: 90mg week 0 and week 4 Maintenance dose: 90mg every 12 weeks Psoriasis Pediatric Patients (6 to 17 years old): Weight-based dosing is recommended at the initial dose, 4 weeks later, then every 12 weeks thereafter <60kg: 0.75mg/kg 60kg to 100kg: 45mg >100kg: 90mg
Apremilast (Otezla®)	Loading: 5-day titration - Starter pack Day 1 10mg, Day 2 20mg, Day 3 30mg, Day 4 40mg, Day 5 60mg 30 mg twice daily
Guselkumab (Tremfya®)	100 mg at weeks 0, 4, and then every 8 weeks thereafter.
Ixekizumab (Taltz®)	Adult: Loading dose: 160 mg (two 80mg injections) subQ at week 0,

	followed by 80 mg at weeks 2, 4, 6, 8, 10, and 12 Maintenance dose: 80 mg every 4 weeks Pediatric: <25kg: 40mg at week 0, followed by 20mg every 4 weeks 25kg to 50kg: 80mg at week 0, followed by 40mg every 4 weeks >50kg: 160mg (two 80mg injections) at week 0, followed by 80mg every 4 weeks
Etanercept (Enbrel®)	loading dose: 50 mg twice weekly for 3 months Maintenance dose: 50mg weekly
Secukinumab (Cosentyx®)	Loading dose: 300mg at Weeks 0, 1, 2, 3 and 4 Maintenance dose: 300mg every 4 weeks; some patients may only need 150 mg
Risankizumab (Skyrizi® SQ)	Loading dose: 150mg at Week 0, Week 4 Maintenance dose: 150mg every 12 weeks
Brodalumab (Siliq®)	Initial: 210 mg at weeks 0, 1, and 2 Maintenance dose: 210 mg once every 2 weeks. (Continuing treatment beyond 16 weeks in patients without an adequate response is not likely to result in greater success).
Deucravacitinib (Sotyktu™)	6 mg orally once daily
Methotrexate	10 to 25 mg once weekly; adjust dose gradually for optimal response, generally not exceeding 30 mg/week
Bimekizumab-bkzx (Bimzelx)	320mg (two 160mg injections) by SQ injection at weeks 0, 4, 8, 12, and 16, then every 8 weeks thereafter. For those weighing greater than or equals to 120kg, consider a dose of 320mg every 4 weeks after week 16.

Crohn's Disease

INITIAL CRITERIA: Preferred adalimumab product¹ is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderate to severe Crohn's disease; and
2. Member is 6 years of age or older; and
3. Prescribed by or in consultation with a gastroenterologist; and
4. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
5. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had inadequate response or inability to tolerate one drug from any of TWO of the following groups:
 - a. Corticosteroids: budesonide (Entocort® EC), prednisone, hydrocortisone, methylprednisolone; or
 - b. Aminosalicylates: sulfasalazine, mesalamine (Asacol®, Rowasa®, Canasa®, Pentasa®); or
 - c. Immunomodulators: azathioprine, 6-mercaptopurine, cyclosporine, tacrolimus (Prograf®), methotrexate; or
 - d. Antibiotics: metronidazole, levofloxacin; and

6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Certolizumab (Cimzia®), Preferred ustekinumab product², guselkumab (Tremfya® SQ), mirikizumab (Omvoh® SQ) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderate to severe Crohn's disease; and
2. Member is 18 years of age or older; and
3. Prescribed by or in consultation with a gastroenterologist; and
4. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
5. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had inadequate response or inability to tolerate one drug from any of TWO of the following groups:
 - a. Corticosteroids: budesonide (Entocort® EC), prednisone, hydrocortisone, methylprednisolone; or
 - b. Aminosalicylates: sulfasalazine, mesalamine (Asacol®, Rowasa®, Canasa®, Pentasa®); or
 - c. Immunomodulators: azathioprine, 6-mercaptopurine, cyclosporine, tacrolimus (Prograf®), methotrexate; or
 - d. Antibiotics: metronidazole, levofloxacin; and
6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Risankizumab (Skyrizi® SQ) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderate to severe Crohn's disease; and
2. Member is 18 years of age or older; and
3. Prescribed by or in consultation with a gastroenterologist; and
4. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
5. Paid claims or submission of medical records (e.g., chart notes) confirming ONE of the following:
 1. Member had inadequate response or inability to tolerate one drug from any of TWO of the following groups:
 1. Corticosteroids: budesonide (Entocort® EC), prednisone, hydrocortisone, methylprednisolone; or
 2. Aminosalicylates: sulfasalazine, mesalamine (Asacol®, Rowasa®, Canasa®, Pentasa®); or
 3. Immunomodulators: azathioprine, 6-mercaptopurine, cyclosporine, tacrolimus (Prograf®), methotrexate; or
 4. Antibiotics: metronidazole, levofloxacin; or
 2. Risankizumab (Skyrizi® SQ) will be used as a maintenance dose following the intravenous induction doses; and
6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Upadacitinib (Rinvoq®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderate to severe Crohn's disease; and
2. Member is 18 years of age or older; and
3. Prescribed by or in consultation with a gastroenterologist; and

4. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
5. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had inadequate response or inability to tolerate one drug from any of TWO of the following groups:
 - a. Corticosteroids: budesonide (Entocort® EC), prednisone, hydrocortisone, methylprednisolone; or
 - b. Aminosalicylates: sulfasalazine, mesalamine (Asacol®, Rowasa®, Canasa®, Pentasa®); or
 - c. Immunomodulators: azathioprine, 6-mercaptopurine, cyclosporine, tacrolimus (Prograf®), methotrexate; or
 - d. Antibiotics: metronidazole, levofloxacin; and
6. Member has had an inadequate response or intolerance to one or more TNF inhibitors (e.g., adalimumab, certolizumab pegol, golimumab); and
7. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Methotrexate injection (i.e., Otrexup™, Rasuvo®, Reditrex™) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderate to severe Crohn's disease; and
2. Member is 18 years of age or older; and
3. Prescribed by or in consultation with a gastroenterologist; and
4. For Otrexup™ and Reditrex™ only: Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate Rasuvo®; and
5. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Infliximab (Zymfentra™) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderately to severely active Crohn's disease; and
2. Member is 18 years of age or older; and
3. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
4. ONE of the following:
 1. BOTH of the following:
 1. Paid claims of submission of medical records (e.g., chart notes) confirming that the member had inadequate response or inability to tolerate one drug from any of TWO of the following groups:
 1. Corticosteroids: budesonide (Entocort® EC), prednisone, hydrocortisone, methylprednisolone; or
 2. Aminosalicylates: sulfasalazine, mesalamine (Asacol®, Rowasa®, Canasa®, Pentasa®); or
 3. Immunomodulators: azathioprine, 6-mercaptopurine, cyclosporine, tacrolimus (Prograf®), methotrexate; or
 4. Antibiotics: metronidazole, levofloxacin; and
 2. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had inadequate response or inability to tolerate TWO of the following:
 1. One preferred adalimumab product¹

2. Certolizumab (Cimzia®)
3. Risankizumab (Skyrizi®)
4. Upadacitinib (Rinvoq®)
5. One preferred ustekinumab product²; or
2. Submission of medical records (e.g., chart notes) confirming that the member has achieved a clinical response following a minimum of 10 weeks of IV infliximab; and
5. Prescribed by or in consultation with a gastroenterologist; and
6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Vedolizumab (Entyvio®) SQ is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderately to severely active Crohn's disease; and
2. Member is 18 years of age or older; and
3. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
4. ONE of the following:
 1. BOTH of the following:
 1. Paid claims of submission of medical records (e.g., chart notes) confirming that the member had inadequate response or inability to tolerate one drug from any of TWO of the following groups:
 1. Corticosteroids: budesonide (Entocort® EC), prednisone, hydrocortisone, methylprednisolone; or
 2. Aminosalicylates: sulfasalazine, mesalamine (Asacol®, Rowasa®, Canasa®, Pentasa®); or
 3. Immunomodulators: azathioprine, 6-mercaptopurine, cyclosporine, tacrolimus (Prograf®), methotrexate; or
 4. Antibiotics: metronidazole, levofloxacin; and
 2. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had inadequate response or inability to tolerate TWO of the following:
 1. One preferred adalimumab product¹
 2. Certolizumab (Cimzia®)
 3. Risankizumab (Skyrizi®)
 4. One preferred ustekinumab product²
 5. Upadacitinib (Rinvoq®); or
 2. Paid claims or submission of medical records (e.g., chart notes) confirming ONE of the following:
 1. Will be used as maintenance dose following two doses of Entyvio IV for induction; or
 2. Member is currently established on Entyvio IV; and
5. Prescribed by or in consultation with a gastroenterologist; and
6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA Preferred adalimumab product¹, certolizumab (Cimzia®), Preferred ustekinumab product², risankizumab (Skyrizi® SQ), infliximab (Zymfentra™), vedolizumab (Entyvio®),

methotrexate injection (i.e., Otrexup™, Rasuvo®, Reditrex™), upadacitinib (Rinvoq®), guselkumab (Tremfya® SQ), mirikizumab (Omvo® SQ) is medically necessary when BOTH of the following are met:

1. There is documentation of positive clinical response to therapy as evidenced by improvement from baseline for at least one of the following:
 - a. Improvement in intestinal inflammation (e.g., mucosal healing, improvement of lab values [platelet counts, erythrocyte counts, erythrocyte sedimentation rate, C-reactive protein level]) from baseline; or
 - b. Reversal of high fecal output state; and
2. ONE of the following:
 - a. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
 - b. Member is continuing on the established dose and frequency previously approved

Reauthorization duration: 12 months

DRUG	DOSE
Adalimumab (Humira®) and its biosimilars	Adults: Loading dose: 160mg on day 1, 80mg on day 15, 40mg every other week starting on day 29 Maintenance dose: 40mg every 2 weeks Pediatric Patients 6 Years of Age and Older: 17 kg to <40 kg: 80mg on day 1, 40mg on day 15, 20mg every other week starting on day 29 ≥40 kg: 160mg on day 1, 80mg on day 15, 40mg every other week starting on day 29
Certolizumab (Cimzia®)	Loading dose: 400mg (2 injections) week 0, week 2 and week 4 Maintenance dose: 200mg every 2 weeks/400mg every 4 weeks
Risankizumab (Skyrizi® SQ)	Maintenance dose: 180mg or 360mg administered subcutaneously at week 12, and every 8 weeks thereafter after the IV induction.
Ustekinumab (Stelara®)	Maintenance dose: 90 mg every 8 weeks; begin maintenance dosing 8 weeks after the IV induction dose.
Infliximab (Zymfentra)	Maintenance dose only: Inject 120 mg subcutaneously once every two weeks starting week 10.
Vedolizumab (Entyvio SQ)	Maintenance dose only: Inject 108 mg subcutaneously once every two weeks starting week 6.
Methotrexate	25mg per week

Ulcerative Colitis

INITIAL CRITERIA: One preferred ustekinumab product² or golimumab (Simponi®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderate to severe ulcerative colitis (UC); and
2. Member is 18 years of age or older; and
3. Prescribed by or in consultation with a gastroenterologist; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had inadequate response or inability to tolerate ONE of the following medications: corticosteroids, azathioprine, 6-mercaptopurine; and
5. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Risankizumab (Skyrizi® SQ), guselkumab (Tremfya® SQ), mirikizumab (Omvo® SQ) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderate to severe ulcerative colitis (UC); and
2. Member is 18 years of age or older; and
3. Prescribed by or in consultation with a gastroenterologist; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming ONE of the following:
 - a. member had inadequate response or inability to tolerate ONE of the following medications: corticosteroids, azathioprine, 6-mercaptopurine; or
 - b. Risankizumab-rzaa (Skyrizi® SQ), guselkumab (Tremfya® SQ), mirikizumab (Omvo® SQ) will be used as a maintenance dose following the intravenous induction doses; and
5. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Preferred adalimumab product¹ is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderate to severe ulcerative colitis (UC); and
2. Member is 5 years of age or older; and
3. Prescribed by or in consultation with a gastroenterologist; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had inadequate response or inability to tolerate ONE of the following medications: corticosteroids, azathioprine, 6-mercaptopurine; and
5. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Ozanimod (Zeposia®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderate to severe ulcerative colitis (UC); and
2. Member is 18 years of age or older; and
3. Prescribed by or in consultation with a gastroenterologist; and

4. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had inadequate response or inability to tolerate ONE of the following medications: corticosteroids, azathioprine, 6-mercaptopurine; and
5. One of the following:
 1. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate TWO of the following:
 1. One preferred adalimumab product¹
 2. One preferred ustekinumab product²
 3. golimumab (Simponi®)
 4. upadacitinib (Rinvoq®)
 5. Risankizumab (Skyrizi®)
 6. tofacitinib (Xeljanz®/Xeljanz® XR)
 7. guselkumab (Tremfya® SQ)
 8. Mirikizumab (Omvoh® SQ); or
 2. Paid claims or submission of medical records (e.g., chart notes) confirming a continuation of therapy with the requested product, defined as no more than a 45-day gap in therapy; and
6. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
7. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Etrasimod (Velsipity™) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderate to severe ulcerative colitis (UC); and
2. Member is 18 years of age or older; and
3. Prescribed by or in consultation with a gastroenterologist; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had inadequate response or inability to tolerate ONE of the following medications: corticosteroids, azathioprine, 6-mercaptopurine; and
5. One of the following:
 1. BOTH of the following:
 1. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate TWO of the following:
 1. One preferred adalimumab product¹
 2. One preferred ustekinumab product²
 3. golimumab (Simponi®)
 4. upadacitinib (Rinvoq®)
 5. Risankizumab (Skyrizi®)
 6. tofacitinib (Xeljanz®/Xeljanz® XR)
 7. guselkumab (Tremfya®)
 8. Mirikizumab (Omvoh® SQ); and
 2. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate ozanimod (Zeposia®); or
 2. BOTH of the following:

1. Paid claims or submission of medical records (e.g., chart notes) confirming a continuation of therapy with the requested product, defined as no more than a 45-day gap in therapy; and
2. Documentation of positive clinical response to therapy as evidenced by ONE of the following:
 1. Improvement in intestinal inflammation (e.g., mucosal healing, improvement of lab values [platelet counts, erythrocyte sedimentation rate, C-reactive protein level]) from baseline; or
 2. Reversal of high fecal output state; and
6. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
7. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Tofacitinib (Xeljanz®/Xeljanz® XR tablets/extended-release tablets), or upadacitinib (Rinvoq®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderate to severe ulcerative colitis (UC); and
2. Member is 18 years of age or older; and
3. Prescribed by or in consultation with a gastroenterologist; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had inadequate response or inability to tolerate ONE of the following medications: corticosteroids, azathioprine, 6-mercaptopurine; and
5. One of the following:
 - a. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate ONE of more TNF inhibitors (e.g., adalimumab, golimumab); or
 - b. Paid claims or submission of medical records (e.g., chart notes) confirming a continuation of therapy with the requested product, defined as no more than a 45-day gap in therapy; and
6. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
7. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Vedolizumab (Entyvio®) SQ is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderate to severe Ulcerative colitis (UC); and
2. Member is 18 years of age or older; and
3. Prescribed by or in consultation with a gastroenterologist; and
4. ONE of the following:
 1. BOTH of the following:
 1. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had inadequate response or inability to tolerate ONE of the following medications: corticosteroids, azathioprine, 6-mercaptopurine; and
 2. Paid claims or submission of medical records (e.g., chart notes) confirming inadequate response or inability to tolerate TWO of the following:
 1. One preferred adalimumab product¹
 2. One preferred ustekinumab product²

3. Golimumab (Simponi®)
 4. Upadacitinib (Rinvoq®)
 5. Risankizumab (Skyrizi®)
 6. Tofacitinib (Xeljanz®/Xeljanz® XR)
 7. Guselkumab (Tremfya® SQ)
 8. Mirikizumab (Omvoh® SQ); or
2. Paid claims or submission of medical records (e.g., chart notes) confirming ONE of the following:
 1. Will be used as a maintenance dose following two doses of Entyvio IV for induction; or
 2. Member is currently established on Entyvio IV; and
 5. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonist); and
 6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Infliximab (Zymfentra™) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderately to severely active ulcerative colitis; and
2. Member is 18 years of age or older; and
3. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
4. ONE of the following:
 1. BOTH of the following:
 1. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had inadequate response or inability to tolerate ONE of the following medications: corticosteroids, azathioprine, 6-mercaptopurine; and
 2. Paid claims or submission of medical records (e.g., chart notes) confirming inadequate response or inability to tolerate TWO of the following:
 1. One preferred adalimumab product¹
 2. One preferred ustekinumab product²
 3. Golimumab (Simponi®)
 4. Upadacitinib (Rinvoq®)
 5. Risankizumab (Skyrizi®)
 6. Tofacitinib (Xeljanz®/Xeljanz® XR)
 7. Guselkumab (Tremfya® SQ)
 8. Mirikizumab (Omvoh® SQ); or
 2. Submission of medical records (e.g., chart notes) confirming that the member has achieved a clinical response to therapy following a minimum of 10 weeks of IV infliximab; and
5. Prescribed by or in consultation with a gastroenterologist; and
6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA Preferred adalimumab product¹, Preferred ustekinumab product², golimumab (Simponi®), tofacitinib (Xeljanz®/Xeljanz® XR tablets/extended-release tablets), upadacitinib (Rinvoq®), ozanimod (Zeposia®), mirikizumab (Omvoh™), etrasimod (Velsipity™), vedolizumab (Entyvio®)

SQ, infliximab (Zymfentra™), Risankizumab (Skyrizi® SQ), guselkumab (Tremfya® SQ) is medically necessary when BOTH of the following are met:

1. There is documentation of positive clinical response to therapy as evidenced by at least one of the following:
 - a. Improvement in intestinal inflammation (e.g., mucosal healing, improvement in lab values [platelet counts, erythrocyte sedimentation rate, C-reactive protein level]) from baseline; or
 - b. Reversal of high fecal output state; and
2. ONE of the following:
 - a. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
 - b. Member is continuing on the established dose and frequency previously approved

Reauthorization duration: 12 months

DRUG	DOSE
Adalimumab (Humira®) and its biosimilars	Adults: Loading dose: 160mg on day 1, 80mg on day 15, 40mg every other week starting on day 29 Maintenance dose: 40mg every other week Pediatric Patients 5 Years of Age and Older: 20 kg to <40 kg: 80mg on day 1, 40mg on day 8, 40mg on day 15, 40mg every other week or 20mg every week starting on day 29 ≥40 kg: 160mg on day 1, 80mg on day 8, 80mg on day 15, 80mg every other week or 40mg every week starting on day 29
Golimumab (Simponi®) Ustekinumab (Stelara®) Tofacitinib (Xeljanz®) Tofacitinib Extended-Release (Xeljanz® XR) Ozanimod (Zeposia®)	Induction: 200 mg at week 0, then 100 mg at week 2 Maintenance dose: 100 mg every 4 weeks. Maintenance dose: 90 mg every 8 weeks; begin maintenance dosing 8 weeks after the IV induction dose. Loading dose: 10mg twice daily for 8 weeks; may continue for up to 16 weeks Maintenance dose: 5mg twice daily Loading dose: 22mg once daily for 8 weeks; may continue for up to 16 weeks Maintenance dose: 11mg once daily Initial dose: 0.23 mg PO once daily on days 1 through 4; then 0.46 mg once daily on days 5 through 7 Maintenance dose: 0.92 mg once daily starting on day 8
Upadacitinib (Rinvoq®)	Initial dose: 45 mg ER PO once daily for 8 weeks Maintenance dose: 15mg ER PO once daily; 30 mg ER once daily may be considered for patients with refractory, severe, or extensive disease. Discontinue if an adequate response is not achieved with 30 mg.

Mirikizumab-mrkz (Omvoq SQ)	Maintenance dose only: Inject 200mg (two consecutive injections of 100mg each) subcutaneously once every four weeks starting week 12
Vedolizumab (Entyvio SQ)	Maintenance dose only: Inject 108 mg subcutaneously once every two weeks starting week 6.
Infliximab (Zymfentra)	Maintenance dose only: Inject 120 mg subcutaneously once every two weeks starting week 10.
Etrasimod (Velsipity)	2mg once daily
Risankizumab (Skyrizi SQ)	Maintenance dose only: Inject 180mg or 360mg subcutaneously once every 8 weeks starting week 12.
Guselkumab (Tremfya® SQ)	Maintenance dose only: 100mg at week 16, and every 8 weeks thereafter, OR 200mg at week 12, and every 4 weeks thereafter Use the lowest effective recommended dosage to maintain therapeutic response.

Cryopyrin-Associated Periodic Syndromes

INITIAL CRITERIA: Anakinra (Kineret®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of Neonatal-Onset Multisystem Inflammatory Disease (NOMID); and
2. Prescribed by or in consultation with a rheumatologist or other appropriate specialist; and
3. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
4. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA Anakinra (Kineret®) is medically necessary when BOTH of the following are met:

1. Documentation of positive clinical response to therapy; and
2. ONE of the following:
 - a. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
 - b. Member is continuing on the established dose and frequency previously approved

Reauthorization duration: 12 months

INITIAL CRITERIA: Rilonacept (Arcalyst®) is medically necessary when there ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of Cryopyrin-Associated Periodic Syndromes including Familial cold Auto-Inflammatory Syndrome (FCAS) and/or Muckle-Wells Syndrome (MWS); and

2. Prescribed by or in consultation with an immunologist, allergist, dermatologist, rheumatologist, neurologist, or other medical specialist; and
3. Member is 12 years of age or older; and
4. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
5. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA rilonacept (Arcalyst®) is medically necessary when BOTH of the following are met:

1. There is documentation of positive clinical response to therapy as evidenced by one of the following:
 - a. Improvement in rash, fever, joint pain, headache, or conjunctivitis; or
 - b. Decreased number of disease flare days; or
 - c. Normalization of inflammatory markers (C-reactive protein [CRP], erythrocyte sedimentation rate [ESR], serum amyloid A [SAA]); or
 - d. Corticosteroid dose reduction; or
 - e. Improvement in MD global score or active joint count; and
2. ONE of the following:
 - a. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
 - b. Member is continuing on the established dose and frequency previously approved

Reauthorization duration: 12 months

DRUG	DOSE
Anakinra (Kineret®)	1 to 2 mg/kg once daily; may increase in 0.5 to 1 mg/kg increments to MAX 8 mg/kg/day; may split into 2 daily doses
Rilonacept (Arcalyst®)	Adults: Loading dose: 320 mg (160 mg at 2 different sites on the same day) maintenance dose: 160 mg SUBQ once weekly
	Pediatric patients 12 years to 17 years: Loading dose: 4.4mg/kg, up to a maximum of 320 mg, delivered as 1 or 2 injections (not to exceed 2 mL/injection) Maintenance dose: 2.2 mg/kg, up to a maximum of 160 mg (2 mL) injection, once weekly

Hidradenitis Suppurativa

INITIAL CRITERIA: Preferred adalimumab product¹ is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderate to severe hidradenitis suppurativa (i.e., Hurley stage II or III); and
2. Prescribed by or in consultation with a dermatologist; and

3. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
4. Member is 12 years of age or older; and
5. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: bimekizumab-bkzx (Bimzelx®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderate to severe hidradenitis suppurativa (i.e., Hurley stage II or III); and
2. Member is 18 years of age or older; and
3. One of the following:
 1. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had an inadequate response or inability to tolerate ONE preferred adalimumab product¹; or
 2. Paid claims or submission of medical records (e.g., chart notes) confirming a continuation of therapy with the requested product, defined as no more than 45 days gap in therapy; and
4. Prescribed by or in consultation with a dermatologist; and
5. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Secukinumab (Cosentyx®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderate to severe hidradenitis suppurativa (i.e., Hurley stage II or III); and
2. Member is 18 years of age or older; and
3. One of the following:
 1. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had an inadequate response or inability to tolerate TWO of the following:
 1. One preferred adalimumab product¹; and
 2. Bimekizumab-bkzx (Bimzelx®); or
 2. Paid claims or submission of medical records (e.g., chart notes) confirming a continuation of therapy with the requested product, defined as no more than a 45-day gap in therapy; and
4. Prescribed by or in consultation with a dermatologist; and
5. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA Preferred adalimumab product¹, bimekizumab-bkzx (Bimzelx®), Secukinumab (Cosentyx®) is medically necessary when BOTH of the following are met

1. There is documentation of positive clinical response to therapy; and
2. ONE of the following:

- a. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
- b. Member is continuing on the established dose and frequency previously approved

Reauthorization duration: 12 months

DRUG	DOSE
Adalimumab (Humira®) and its biosimilars	Adults: Loading dose: 160mg on day 1, 80mg on day 15, 40mg every other week starting on day 29 Maintenance dose: 40mg every other week
	Adolescents 12 years of age and older: 30kg to <60kg: 80mg on day 1, 40mg on day 8, 40mg every other week for subsequent doses >60kg: 160mg on day 1, 80mg on day 15, 40mg every week or 80mg every other week starting on day 29 and subsequent doses
Bimzelx (bimekizumab)	Adults: 160mg every 4 weeks
Cosentyx (secukinumab)	Adults: Loading dose: 300mg at weeks 0, 1, 2, 3, 4 Maintenance: 300mg every 4 weeks thereafter. If inadequate response, consider increasing the dosage to 300mg every 2 weeks.

Uveitis

INITIAL CRITERIA: Preferred adalimumab product¹ is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of non-infectious intermediate, posterior, or panuveitis; and
2. Prescribed by or in consultation with an ophthalmologist or rheumatologist; and
3. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had inadequate response or inability to tolerate ophthalmic and oral corticosteroids; and
4. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
5. Member is 2 years of age or older; and
6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA Preferred adalimumab product¹ is medically necessary when BOTH of the following are met:

1. There is documentation of positive clinical response to therapy; and
2. ONE of the following:
 - a. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
 - b. Member is continuing on the established dose and frequency previously approved

Reauthorization duration: 12 months

DRUG

Adalimumab (Humira®) and its biosimilars

DOSE

Adults:

Loading dose: 80mg on day 1, 40mg every other week starting 1 week after the initial dose
Maintenance dose: 40mg every other week

Pediatric patients 2 years or older:

10 kg to <15 kg: 10 mg every other week
15 kg to <30 kg: 20 mg every other week
≥30 kg: 40mg every other week

Giant Cell Arteritis

INITIAL CRITERIA: upadacitinib (Rinvoq), preferred tocilizumab product³ medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of Giant Cell Arteritis; and
2. Prescribed by or in consultation with a rheumatologist; and
3. Member is 18 years of age or older; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had inadequate response or inability to tolerate a glucocorticoid (i.e., prednisone); and
5. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: upadacitinib (Rinvoq), preferred tocilizumab product³ is medically necessary when BOTH of the following are met:

1. There is documentation of positive clinical response to therapy; and
2. ONE of the following:
 - a. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
 - b. Member is continuing on the established dose and frequency previously approved

Reauthorization duration: 12 months

DRUG	DOSE
Upadacitinib (Rinvoq)	15mg once daily
Tocilizumab (Actemra® SQ) and its biosimilars	162 mg given once every week

Systemic Juvenile Idiopathic Arthritis

INITIAL CRITERIA: preferred tocilizumab product³ is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of active systemic juvenile idiopathic arthritis (SIJA); and
2. Prescribed by or in consultation with a rheumatologist; and
3. Member is 2 years of age or older; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate ONE of the following conventional therapies at maximally tolerated doses:

- a. Non-steroidal anti-inflammatory drug (NSAID) (e.g., ibuprofen); or
 - b. Systemic glucocorticoid (e.g., prednisone)
 - c. DMARDs (e.g., leflunomide, methotrexate); and
5. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Preferred tocilizumab product³ is medically necessary when BOTH of the following are met:

1. There is documentation of positive clinical response to therapy as evidenced by at least one of the following:
 - a. Reduction in the total active (swollen and tender) joint count from baseline; or
 - b. Improvement in clinical features or symptoms (e.g., pain, fever, inflammation, rash, lymphadenopathy, serositis) from baseline; and
2. ONE of the following:
 - a. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
 - b. Member is continuing on the established dose and frequency previously approved

Reauthorization duration: 12 months

DRUG	DOSE
Tocilizumab (Actemra® SQ) and its biosimilar	<30kg: 162mg every two weeks. ≥30kg: 162 every week.

Non-radiographic axial spondyloarthritis (nr-axSpA)

INITIAL CRITERIA: Certolizumab (Cimzia®), Ixekizumab (Taltz®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation; and
2. Member has objective signs of inflammation (e.g., C-reactive protein [CRP] levels above the upper limit of normal and/or sacrolitis on magnetic resonance imaging [MRI], indicative of inflammatory disease, but without definitive radiographic evidence of structural damage on sacroiliac joints); and
3. Member is 18 years of age or older; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming inadequate response or inability to tolerate two different NSAIDs (e.g., diclofenac, meloxicam, naproxen) at maximally tolerated doses; and
5. Prescribed by or in consultation with a rheumatologist; and
6. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
7. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA Upadacitinib (Rinvoq™) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation; and
2. Member has objective signs of inflammation (e.g., C-reactive protein [CRP] levels above the upper limit of normal and/or sacrolitis on magnetic resonance imaging [MRI], indicative of

inflammatory disease, but without definitive radiographic evidence of structural damage on sacroiliac joints); and

3. Member is 18 years of age or older; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming inadequate response or inability to tolerate two different NSAIDs (e.g., diclofenac, meloxicam, naproxen) at maximally tolerated doses; and
5. Prescribed by or in consultation with a rheumatologist; and
6. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
7. Member has had an inadequate response or intolerance to one or more TNF inhibitors (e.g., certolizumab pegol); and
8. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Secukinumab (Cosentyx®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation; and
2. Member has objective signs of inflammation (e.g., C-reactive protein [CRP] levels above the upper limit of normal and/or sacrolitis on magnetic resonance imaging [MRI], indicative of inflammatory disease, but without definitive radiographic evidence of structural damage on sacroiliac joints); and
3. Member is 18 years of age or older; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming inadequate response or inability to tolerate two different NSAIDs (e.g., diclofenac, meloxicam, naproxen) at maximally tolerated doses; and
5. Prescribed by or in consultation with a rheumatologist; and
6. One of the following:
 - a. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate ALL of the following: certolizumab (Cimzia®), Upadacitinib (Rinvoq™), Ixekizumab (Taltz®), and bimekizumab (Bimzelx®); or
 - b. Paid claims or submission of medical records (e.g., chart notes) confirming a continuation of therapy with the requested product, defined as no more than a 45-day gap in therapy; and
7. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
8. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Bimekizumab (Bimzelx®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation; and
2. Member has objective signs of inflammation (e.g., C-reactive protein [CRP] levels above the upper limit of normal and/or sacrolitis on magnetic resonance imaging [MRI], indicative of inflammatory disease, but without definitive radiographic evidence of structural damage on sacroiliac joints); and
3. Member is 18 years of age or older; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming inadequate response or inability to tolerate two different NSAIDs (e.g., diclofenac, meloxicam, naproxen) at maximally tolerated doses; and

5. Prescribed by or in consultation with a rheumatologist; and
6. One of the following:
 1. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate TWO of the following:
 1. certolizumab (Cimzia®),
 2. Upadacitinib (Rinvoq™),
 3. Ixekizumab (Taltz®); or
 2. Paid claims or submission of medical records (e.g., chart notes) confirming a continuation of therapy with the requested product, defined as no more than 45-day gap in therapy; and
7. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
8. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA Certolizumab (Cimzia®), upadacitinib (Rinvoq™), ixekizumab (Taltz®), secukinumab (Cosentyx®) or Bimekizumab (Bimzelx®) is medically necessary when BOTH of the following are met:

1. There is documentation of positive clinical response to therapy as evidenced by improvement from baseline for at least one of the following:
 1. Disease activity (e.g., pain, fatigue, inflammation, stiffness); or
 2. Lab values (erythrocyte sedimentation rate, C-reactive protein level); or
 3. Function; or
 4. Axial status (e.g., lumbar spine motion, chest expansion); or
 5. Total active (swollen and tender) joint count; and
2. ONE of the following:
 1. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
 2. Member is continuing on the established dose and frequency previously approved

Reauthorization duration: 12 months

DRUG	DOSE
Certolizumab (Cimzia®)	Loading dose: 400mg (2 injections) week 0, week 2 and week 4 Maintenance dose: 200mg every 2 weeks/400mg every 4 weeks
Ixekizumab (Taltz®)	80 mg every 4 weeks
Secukinumab (Cosentyx®)	Loading dose: 150mg at Weeks 0, 1, 2, 3 and 4 Maintenance dose: 150mg every 4 weeks
Upadacitinib (Rinvoq®)	15 mg once daily
Bimekizumab (Bimzelx®)	160 mg every 4 weeks

Ulcer of the mouth associated with Behcet's syndrome

INITIAL CRITERIA: Apremilast (Otezla®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of ulcer of the mouth associated with Behcet's syndrome; and
2. Member has active oral ulcers; and
3. Member is 18 years of age or older; and
4. Prescribed by or in consultation with a rheumatologist or dermatologist; and
5. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate systemic corticosteroids, topical corticosteroids or topical sucralfate; and
6. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
7. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA Apremilast (Otezla®) is medically necessary when BOTH of the following are met:

1. There is documentation of positive clinical response to therapy as evidenced by ONE of the following:
 - a. Reduction in pain from oral ulcers from baseline; or
 - b. Reduction in number of oral ulcers from baseline; and
2. ONE of the following:
 - a. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
 - b. Member is continuing on the established dose and frequency previously approved

Reauthorization duration: 12 months

DRUG	DOSE
Apremilast (Otezla®)	Loading dose: 5-day titration - Starter pack Day 1 10mg, Day 2 20mg, Day 3 30mg, Day 4 40mg, Day 5 60mg Maintenance dose: 30 mg twice daily

Deficiency of Interleukin-1 Receptor Antagonist

INITIAL CRITERIA: Rilonacept (Arcalyst®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes) confirming the use for the maintenance of remission of Deficiency of Interleukin-1 Receptor Antagonist (DIRA); and
2. Member is currently in remission (e.g., no fever, skin rash, and bone pain; no radiological evidence of active bone lesions; C-reactive protein [CRP] less than 5 mg/L); and
3. Member weights at least 10kg; and
4. Prescribed by or in consultation with a rheumatologist or pediatric specialist; and
5. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonist); and
6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Anakinra (Kineret®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of Deficiency of Interleukin-1 Receptor Antagonist (DIRA); and
2. Prescribed by or in consultation with a rheumatologist or pediatric specialist; and

3. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonist); and
4. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA Rilonacept (Arcalyst®) or anakinra (Kineret®) is medically necessary when BOTH of the following are met:

1. There is documentation of positive clinical response to therapy; and
2. ONE of the following:
 - a. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
 - b. Member is continuing on the established dose and frequency previously approved

Reauthorization duration: 12 months

DRUG	DOSE
Rilonacept (Arcalyst®)	Adults and pediatric patients weighing 10 kg or more: 4.4mg/kg up to a maximum of 320 mg (160 mg at 2 different sites on the same day) once weekly
Anakinra (Kineret®)	1 to 2 mg/kg daily; adjust dose in 0.5 to 1 mg/kg increments as needed to a maximum of 8 mg/kg daily

Recurrent pericarditis

INITIAL CRITERIA: Rilonacept (Arcalyst®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming use for the treatment of recurrent pericarditis as evidenced by at least 2 episodes that occur a minimum of 4 to 6 weeks apart and reduction in risk of recurrence; and
2. Member is 12 years of age or older; and
3. Submission of medical records (e.g., chart notes) confirming inadequate response or inability to tolerate at least one of the following:
 - a. NSAID (e.g., ibuprofen, naproxen); or
 - b. Colchicine; or
 - c. Corticosteroids (e.g., prednisone); and
4. Prescribed by or in consultation with a cardiologist; and
5. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA Rilonacept (Arcalyst®) is medically necessary when BOTH of the following are met:

1. There is documentation of positive clinical response to therapy; and
2. ONE of the following:
 - a. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or

b. Member is continuing on the established dose and frequency previously approved
Reauthorization duration: 12 months

DRUG	DOSE
Rilonacept (Arcalyst®)	Initial dose: 320mg given as 2 separate injections (160 [2mL] per injection) on the same day at 2 different sites. Maintenance dose: 160mg once weekly. (Begin maintenance dose 1 week following loading dose).

Systemic sclerosis-associated interstitial lung disease

INITIAL CRITERIA: preferred tocilizumab product³ is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of Systemic Sclerosis-Associated Interstitial Lung Disease (SSc-ILD) confirmed by a High-Resolution CT scan or biopsy; and
2. Member is 18 years of age or older; and
3. Prescribed by or in consultation with a pulmonologist or rheumatologist; and
4. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
5. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Preferred tocilizumab product³ is medically necessary when BOTH of the following are met:

1. There is documentation of positive clinical response to therapy; and
2. ONE of the following:
 - a. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
 - b. Member is continuing on the established dose and frequency previously approved

Reauthorization duration: 12 months

DRUG	DOSE
Tocilizumab (Actemra®) and its biosimilars	162mg once every week

Active enthesitis-related arthritis

INITIAL CRITERIA: Secukinumab (Cosentyx®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of active enthesitis-related arthritis (ERA); and
2. Member is 4 years of age or older; and
3. Prescribed by or in consultation with a rheumatologist; and
4. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate TWO different nonsteroidal anti-inflammatory drugs (NSAIDs) (e.g., ibuprofen, naproxen) at maximally tolerated doses; and
5. No concurrent therapy with any other biologic DMARD (i.e., tumor necrosis factor antagonists); and
6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Secukinumab (Cosentyx®) is medically necessary when BOTH of the following are met:

1. There is documentation of positive clinical response to therapy as evidenced by at least one of the following:
 - a. Reduction in the total active (swollen and tender) joint count from baseline; or
 - b. Improvement in symptoms (e.g., pain, stiffness, inflammation) from baseline; and
2. ONE of the following:
 - a. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
 - b. Member is continuing on the established dose and frequency previously approved

Reauthorization duration: 12 months

DRUG	DOSE
Secukinumab (Cosentyx®)	Pediatrics 4 years or older: <50kg: 75mg at weeks 0, 1, 2, 3, 4, followed by 75mg every 4 weeks ≥50kg: 150mg at weeks 0, 1, 2, 3, 4 followed by 150mg every 4 weeks

Atopic dermatitis

INITIAL CRITERIA: Upadacitinib (Rinvoq™) is medically necessary when ALL of the following are met:

1. Diagnosis of refractory, moderate to severe atopic dermatitis; and
2. One of the following:
 - a. Involvement of at least 10% body surface area (BSA); or
 - b. SCORing Atopic Dermatitis (SCORAD) index value of at least 25; and
3. Member is 12 years of age or older; and
4. Prescribed by or in consultation with a dermatologist, allergist or immunologist; and
5. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate ONE of the following:
 - a. Topical steroids, medium potency or higher; or
 - b. Topical tacrolimus; or
 - c. Topical pimecrolimus; or
 - d. Eucrisa™; and
 - e. Opzelura; and
6. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate ONE systemic drug product for the treatment of atopic dermatitis (example include, but are not limited to Adbry [tralokinumab-ldrm], Dupixent [dupilumab], etc.); and
7. No concurrent therapy with any other biologic agents (e.g., JAK inhibitors); and
8. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Abrocitinib (Cibinqo™) is medically necessary when ALL of the following are met:

1. Diagnosis of refractory, moderate to severe atopic dermatitis; and
2. One of the following:
 - a. Involvement of at least 10% body surface area (BSA); or

- b. SCORing Atopic Dermatitis (SCORAD) index value of at least 25; and
- 3. Member is 12 years of age or older; and
- 4. Prescribed by or in consultation with a dermatologist, allergist or immunologist; and
- 5. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate ONE of the following:
 - a. Topical steroids, medium potency or higher; or
 - b. Topical tacrolimus; or
 - c. Topical pimecrolimus; or
 - d. Eucrisa™; and
 - e. Opzelura; and
- 6. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate ONE systemic drug product for the treatment of atopic dermatitis (examples include, but are not limited to Adbry [tralokinumab-ldrm], Dupixent [dupilumab], etc.); and
- 7. No concurrent therapy with any other biologic agents (e.g., JAK inhibitors); and
- 8. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Tralokinumab-idrm (Adbry™) is medically necessary when ALL of the following are met:

- 1. Member is 12 years of age or older; and
- 2. Diagnosis of moderate-severe atopic dermatitis; and
- 3. One of the following:
 - a. Involvement of at least 10% body surface area (BSA); or
 - b. SCORing Atopic Dermatitis (SCORAD) index value of at least 25; and
- 4. Prescribed by or in consultation with a dermatologist, allergist or immunologist; and
- 5. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate ONE of the following:
 - a. Topical steroids, medium potency or higher; or
 - b. Topical tacrolimus; or
 - c. Topical pimecrolimus; or
 - d. Eucrisa™; and
 - e. Opzelura; and
- 6. No concurrent therapy with any other biologic agents; and
- 7. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Lebrikizumab-lbkz (Ebglyss™), nemolizumab-ilto (Nemluvio®) is medically necessary when ALL of the following are met:

- 1. Member is 12 years of age or older; and
- 2. Diagnosis of moderate-severe atopic dermatitis; and
- 3. One of the following:
 - 1. Involvement of at least 10% body surface area (BSA); or
 - 2. SCORing Atopic Dermatitis (SCORAD) index value of at least 25; and
- 4. Prescribed by or in consultation with a dermatologist, allergist or immunologist; and
- 5. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate ONE of the following:

1. Topical steroids, medium potency or higher; or
2. Topical tacrolimus; or
3. Topical pimecrolimus; or
4. Eucrisa®; and
5. Opzelura; and
6. ONE of the following:
 1. Paid claims or submission of medical records (e.g., chart notes) confirming the member has had an inadequate response or inability to tolerate TWO of the following:
 1. Adbry (tralokinumab-idrm)
 2. Dupixent (dupilumab)
 3. Cibinqo (abrocitinib)
 4. Rinvoq (upadacitinib); or
 2. Paid claims or submission of medical records (e.g., chart notes) confirming a continuation of therapy with the requested drug, defined as no more than a 45-day gap in therapy; and
7. No concurrent therapy with any other biologic agents; and
8. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Upadacitinib (Rinvoq™), abrocitinib (Cibinqo™), tralokinumab-idrm (Adbry™), lebrikizumab-lbkz (Ebglyss™), nemolizumab-ilto (Nemluvio®) is medically necessary when BOTH of the following are met:

1. Documentation of positive clinical response to therapy (e.g., reduction in body surface area involvement, reduction in pruritus severity); and
2. ONE of the following:
 1. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
 2. Member is continuing on the established dose and frequency previously approved

Reauthorization duration: 12 months

DRUG	DOSE
Upadacitinib (Rinvoq®)	Pediatric Patients 12 Years of Age and Older Weighing at Least 40 kg and Adults Less Than 65 Years of Age: 15 mg PO once daily; may increase to 30 mg once daily if inadequate response Adults 65 Years of Age and Older: 15 mg PO once daily
Tralokinumab-idrm (Adbry®)	600 mg SQ (four 150-mg injections) followed by 300 mg SQ (two 150 mg injections) every other week. After 16 weeks of treatment, for patient with body weight below 100 kg who achieved clear or almost clear skin, may consider 300 mg SQ every 4 weeks
Abrocitinib (Cibinqo®)	100 mg PO once daily. If inadequate response is not achieved after 12 weeks, consider increasing to 200mg PO once daily. Discontinue if inadequate response after dosage increase

Lebrikizumab-ibkz (Ebglyss™)	500 mg (two 250 mg injections) at week 0 and week 2, followed by 250mg (one injection) every 2 weeks until week 16 or later, when adequate clinical response is achieved. Maintenance: 250 mg every 4 weeks
Nemolizumab-ilto (Nemluvio®)	Initial: 60mg (two 30mg injections) Maintenance: 30mg every 4 weeks

Multiple sclerosis

INITIAL CRITERIA: Ozanimod (Zeposia®) is medically necessary when BOTH of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming diagnosis of a relapsing form of multiple sclerosis (MS) (e.g., clinically isolated syndrome, relapsing-remitting disease, secondary progressive disease, including active disease with new brain lesions); and
2. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Ozanimod (Zeposia®) is medically necessary when both of the following are met:

1. Documentation of positive clinical response to therapy (e.g., stability in radiologic disease activity, clinical relapses, disease progression); and
2. ONE of the following:
 1. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
 2. Member is continuing on the established dose and frequency previously approved

Reauthorization duration: 12 months

DRUG	DOSE
Ozanimod (Zeposia®)	Initial dose: 0.23 mg PO once daily on days 1 through 4; then 0.46 mg once daily on days 5 through 7 Maintenance dose: 0.92 mg once daily starting on day 8

Alopecia Areata

INITIAL CRITERIA: Baricitinib (Olmiant®) is medically necessary when all of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of alopecia areata; and
2. Member is 18 years of age or older; and
3. Member has at least 50% scalp hair loss; and
4. Other causes of hair loss have been ruled out (e.g., androgenetic alopecia, trichotillomania, tinea capitis, psoriasis); and
5. Prescribed by or in consultation with a dermatologist; and
6. No concurrent therapy with any other biological agent (e.g., JAK inhibitors); and
7. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Ritlecitinib (Litfulo™) is medically necessary when all of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of alopecia areata; and
2. Member is 12 years of age or older; and
3. Member has at least 50% scalp hair loss; and
4. Other causes of hair loss have been ruled out (e.g., androgenetic alopecia, trichotillomania, tinea capitis, psoriasis); and
5. Prescribed by or in consultation with a dermatologist; and
6. No concurrent therapy with any other biological agent (e.g., JAK inhibitors); and
7. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Baricitinib (Olmiant®), Ritlecitinib (Litfulo™) is medically necessary when BOTH of the following are met:

1. Documentation of positive clinical response to therapy; and
2. ONE of the following:
 - a. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
 - b. Member is continuing on the established dose and frequency previously approved

Reauthorization duration: 12 months

DRUG	DOSE
Baricitinib (Olmiant®)	Initial dose: 2mg PO once daily; may increase to 4mg PO once daily if inadequate response or in patients with nearly complete or complete scalp hair loss; decrease dose to 2mg PO daily after adequate response
Litfulo (ritlecitinib)	50mg orally once daily

Polymyalgia Rheumatica

INITIAL CRITERIA: Sarilumab (Kevzara®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes) confirming a diagnosis of polymyalgia rheumatica (PMR); and
2. Paid claims or submission of medical records (e.g., chart notes) confirming that the member had an inadequate response or inability to tolerate corticosteroids (e.g., prednisone); and
3. Prescribed by or in consultation with a rheumatologist; and
4. Member is 18 years of age or older; and
5. No concurrent therapy with other biologic DMARD (i.e., tumor necrosis factor antagonists); and
6. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Sarilumab (Kevzara®) is medically necessary when BOTH of the following are met:

1. Documentation of positive clinical response to therapy as evidenced by at least one of the following:
 - a. Improvement in symptoms (e.g., pain, stiffness) or lab values (e.g., C-reactive protein) from baseline; or

- b. Reduced need for corticosteroids (e.g., Prednisone), and
- 2. ONE of the following:
 - a. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
 - b. Member is continuing on the established dose and frequency previously approved

Reauthorization duration: 12 months

DRUG

Sarilumab (Kevzara®)

DOSE

200 mg SQ, once every two weeks in combination with a tapering course of corticosteroids

Prurigo Nodularis

INITIAL CRITERIA: Nemolizumab-ilto (Nemluvio®) is medically necessary when ALL of the following are met:

1. Submission of documentation (e.g., chart notes) confirming a diagnosis of Prurigo Nodularis (PN); and
2. Member is 18 years of age or older; and
3. Member has at least 20 nodular lesions; and
4. Paid claims or submission of documentation (e.g., chart notes) confirming inadequate response or inability to tolerate one previous PN treatment (e.g., topical corticosteroids, topical calcineurin inhibitors, topical capsaicin); and
5. ONE of the following:
 - a. Paid claims or submission of documentation (e.g., chart notes) confirming inadequate response or inability to tolerate dupilumab (Dupixent); or
 - b. Paid claims or submission of documentation (e.g., chart notes) confirming a continuation of therapy with the requested drug, defined as no more than a 45-day gap in therapy; and
6. Prescribed by or in consultation with allergist, immunologist or dermatologist; and
7. No concurrent therapy with any other biologic agents; and
8. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Nemolizumab-ilto (Nemluvio®) is medically necessary when ALL of the following are met:

1. Documentation of a positive clinical response to therapy as evidenced by at least ONE of the following:
 - a. Reduction in the number of nodular lesions from baseline; or
 - b. Improvement in symptoms (e.g., pruritus, inflammation) from baseline; and
2. ONE of the following:
 - a. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
 - b. Member is continuing on the established dose and frequency previously approved

Reauthorization duration: 12 months

DRUG

DOSE

Nemolizumab-ilto (Nemluvio®)

Adults weighing less than 90kg: initial dose of 60mg (two 30mg injections), followed by 30mg given every 4 weeks

Adults weighing 90kg or more: initial dose of 60mg (two 30mg injections), followed by 60mg given every 4 weeks

Approval Date: Jun- 05-2025

Title: Insulin human, inhalation (Afrezza®)

Applicable Drugs:

Brand Name	Generic Name
Afrezza®	Insulin human, inhalation

Policy:

INITIAL CRITERIA: Afrezza® is medically necessary when ALL of the following are met:

1. Member is 18 years of age or older; and
2. One of the following:
 - a. Both of the following:
 1. Diagnosis of type I diabetes mellitus; and
 2. Used in combination with a long-acting insulin (e.g., Lantus)
 - b. Diagnosis of type II diabetes mellitus; and
3. Spirometry (FEV₁) completed prior to initiation of therapy to identify potential lung disease (must provide the result); and
4. Member is a non-smoker for a minimum of 6 months; and
5. Absence of chronic lung disease such as asthma or chronic obstructive pulmonary disease; and
6. Prescribed by or in consultation with an endocrinologist

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Afrezza® is medically necessary when the following are met:

1. There is documentation of spirometry value (FEV₁) has not declined $\geq 20\%$ from baseline; and
2. There is documentation of positive clinical response to therapy

Reauthorization duration: 2 years

P&T Approval Date: Sep-12-2024

Title: Insulin Policy

Applicable Drugs:

Brand Name	Generic Name
Basaglar TMPO®	Insulin Glargine
Humalog TMPO®	Insulin Lispro
Insulin aspart	
Insulin glargine	
Levemir®	Insulin Detemir
Lyumjev TMPO®	Insulin Lispro-aabc
Novolin® Relion	Insulin Regular
Novolog® Relion	Insulin aspart
Semglee®	Insulin Glargine-yfgn
Tresiba®	Insulin Degludec
Insulin Degludec	

Policy:

Humalog TMPO®, Lyumjev TMPO®, Novolog Relion, Novolin Relion or Insulin aspart is medically necessary when ALL of the following are met:

1. Diagnosis of diabetes mellitus; and
2. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate TWO of the following:
 - a. Novolin®
 - b. Novolog®
 - c. Humalog®/Insulin lispro

- d. Lyumjev®
- e. Fiasp®
- f. Apidra®
- g. Admelog®
- h. Humulin®

Authorization duration: 2 years

Basaglar TMPO®, Levemir®, Tresiba®, Insulin Degludec, Insulin glargine-YFGN/Semglee®, or Insulin Glargine is medically necessary when ALL of the following are met:

1. Diagnosis of diabetes mellitus; and
2. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate THREE of the following:
 - a. Lantus®
 - b. Toujeo®
 - c. Basaglar®
 - d. Rezvoglar®

Authorization duration: 2 years

P&T Approval Date: Sep-12-2024

Title: Interferon Gamma-1b (Actimmune)

Applicable Drugs:

Brand Name	Generic Name
Actimmune®	Interferon gamma-1b

Policy:

INITIAL CRITERIA: Interferon gamma-1b (Actimmune®) is medically necessary when ONE of the following is met:

1. Diagnosis of chronic granulomatous disease (CGD); or
2. Diagnosis of severe, malignant osteopetrosis (SMO)

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA: Interferon gamma-1b (Actimmune®) is medically necessary when there is documentation of positive clinical response to therapy (i.e., delay of malignant osteopetrosis disease progression; reduction in the frequency and severity of serious infections associated with Chronic Granulomatous Disease)

Reauthorization duration: 2 years

P&T Approval Date: Sep-12-2024

Title: Interleukin-5 (IL-5) Antibody Agents

Applicable Drugs:

Brand Name	Generic Name
Nucala®	Mepolizumab
Fasenra®	Benralizumab

Policy:

Severe Asthma

INITIAL CRITERIA: Mepolizumab (Nucala®) is medically necessary when ALL of the following are met:

1. Submission of documentation (e.g., chart notes, lab values) confirming diagnosis of severe asthma with eosinophilic phenotype as defined by ONE of the following:
 1. Blood eosinophil levels are at least 150 cells/microliter at initiation of therapy (measured within 6 weeks of dosing); or
 2. Blood eosinophil levels at least 300 cells/microliter within the past 12 months; and
2. Member is 6 years of age or older; and
3. One of the following:
 1. Member has had at least two or more asthma exacerbations requiring systemic corticosteroids within the past 12 months; or
 2. Prior asthma-related hospitalization within the past 12 months; and
4. Prescribed by or in consultation with pulmonologist or allergy/immunology specialist; and
5. ONE of the following:
 1. Member is 6 to less than 12 years of age and paid claim or submission of documentation (e.g., chart notes) confirming the member is currently being treated or has a contraindication or intolerance to one of the following:
 1. Medium-dose inhaled corticosteroids (e.g., greater than 100-200mcg fluticasone propionate equivalent/day) and ONE additional controller medication (e.g., leukotriene receptor antagonist [LTRA] (e.g., montelukast), long-acting beta-2 agonist [LABA] (e.g., salmeterol), long-acting muscarinic antagonist [LAMA] (e.g., tiotropium)); or
 2. One medium-dose combination ICS/LABA product (e.g., Advair [fluticasone propionate/salmeterol], Bre Ellipta [fluticasone furoate/vilanterol], Symbicort [budesonide/formoterol]); or
 2. Member is 12 years of age or older and paid claims or submission of documentation (e.g., chart notes) confirming that the member is currently treated or has a contraindication or intolerance to ONE of the following:
 1. High dose inhaled corticosteroids (ICS) (e.g., greater than or equal to 500 mcg fluticasone propionate equivalents/day) and ONE additional asthma controller medication (e.g., leukotriene receptor antagonist [LTRA] (e.g., montelukast), long-acting beta 2 agonist [LABA] (e.g., salmeterol), long-acting muscarinic antagonist [LAMA] (e.g., tiotropium)); or
 2. One maximally dosed combination ICS/LABA product (e.g., Advair® [fluticasone propionate/salmeterol], Bre Ellipta [fluticasone furoate/vilanterol], Symbicort® [budesonide/formoterol]); and
6. No concurrent therapy with any other biologic agents; and

7. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

INITIAL CRITERIA: Benralizumab (Fasenra®) is medically necessary when ALL of the following are met:

1. Submission of documentation (e.g., chart notes, lab values) confirming diagnosis of severe asthma with eosinophilic phenotype as defined by ONE of the following:
 1. Blood eosinophil levels are at least 150 cells/microliter at initiation of therapy (measured within 6 weeks of dosing); or
 2. Blood eosinophil levels at least 300 cells/microliter within the past 12 months; and
2. One of the following:
 1. Member has had at least two or more asthma exacerbations requiring systemic corticosteroids within the past 12 months; or
 2. Prior asthma-related hospitalization within the past 12 months; and
3. ONE of the following:
 1. Member is 6 to less than 12 years of age and paid claim or submission of documentation (e.g., chart notes) confirming the member is currently being treated or has a contraindication or intolerance to one of the following:
 1. Medium-dose inhaled corticosteroids greater than 100-200mcg fluticasone propionate equivalent/day) and ONE additional controller medication (e.g., leukotriene receptor antagonist [LTRA] (e.g., montelukast), long-acting beta-2 agonist [LABA] (e.g., salmeterol), long-acting muscarinic antagonist [LAMA] (e.g., tiotropium)); or
 2. One medium-dose combination ICS/LABA product (e.g., Advair [fluticasone propionate/salmeterol], Bre Ellipta [fluticasone furoate/vilanterol], Symbicort [budesonide/formoterol]); or
 2. Member is 12 years of age or older and paid claims or submission of documentation (e.g., chart notes) confirming that the member is currently being treated or has a contraindication or intolerance to ONE of the following:
 1. High dose inhaled corticosteroids (ICS) (e.g., greater than or equal to 500 mcg fluticasone propionate equivalents/day) and ONE additional asthma controller medication (e.g., leukotriene receptor antagonist [LTRA] (e.g., montelukast), long-acting beta 2 agonist [LABA] (e.g., salmeterol), long-acting muscarinic antagonist [LAMA] (e.g., tiotropium)); or
 2. One maximally dosed combination ICS/LABA product (e.g., Advair® [fluticasone propionate/salmeterol], Bre Ellipta [fluticasone furoate/vilanterol], Symbicort® [budesonide/formoterol]); and
4. Member is 6 years of age or older; and
5. Prescribed by or in consultation with pulmonologist or allergist/immunologist; and
6. No concurrent therapy with any other biologic agents; and
7. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 12 months

CONTINUATION CRITERIA: Mepolizumab (Nucala®) or benralizumab (Fasenra®) is medically necessary when ALL of the following are met:

1. Submission of documentation (e.g., chart notes) confirming a positive clinical response (e.g., reduction in exacerbations, improvement in forced expiratory volume in 1 second [FEV1], decreased use of rescue medications); and
2. ONE of the following:
 1. Member is 6 to less than 12 years of age and paid claim or submission of documentation (e.g., chart notes) confirming the member is currently being treated or has a contraindication or intolerance to one of the following:

1. Medium-dose inhaled corticosteroids (e.g., greater than 100-200mcg fluticasone propionate equivalent/day) with or without ONE additional controller medication (e.g., leukotriene receptor antagonist [LTRA] (e.g., montelukast, long-acting beta-2 agonist [LABA] (e.g., salmeterol), long-acting muscarinic antagonist [LAMA] (e.g., tiotropium)); or
2. One medium-dose combination ICS/LABA product (e.g., Advair [fluticasone propionate/salmeterol], Bre Ellipta [fluticasone furoate/vilanterol], Symbicort [budesonide/formoterol]); or
2. Member is 12 years of age or older and paid claims or submission of documentation (e.g., chart notes) confirming that the member is currently being treated or has a contraindication or intolerance to ONE of the following:
 1. High dose inhaled corticosteroids (ICS) (e.g., greater than 500mcg fluticasone propionate equivalents/day); with or without ONE additional asthma controller medication [e.g., leukotriene receptor antagonist [LTRA] (e.g., montelukast), long-acting beta 2 agonist [LABA] (e.g., salmeterol), long-acting muscarinic antagonist [LAMA] (e.g., tiotropium)]; or
 2. One maximally dosed combination ICS/LABA product (e.g., Advair® [fluticasone propionate/salmeterol]; Bre Ellipta [fluticasone furoate/vilanterol], Symbicort® (budesonide/formoterol)); and
3. Prescribed by or in consultation with pulmonologist or allergist/immunologist; and
4. No concurrent therapy with any other biologic agents; and
5. ONE of the following:
 1. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; and
 2. Member is continuing on the established dose and frequency previously approved

Continuation authorization duration: 12 months

Mepolizumab (Nucala®)	DOSE
Adults and pediatric patients aged 12 and older	100 mg every 4 weeks
Pediatric patients aged 6 to 11 years	40 mg every 4 weeks
Benralizumab (Fasenra®)	DOSE
Adults and pediatric patients aged 12 and older	Initial: 30 mg every 4 weeks for the first 3 doses Maintenance: 30 mg every 8 weeks
Pediatric patients 6 years to 11 years of age	Weighing Less Than 35 kg: the recommended dosage is 10 mg every 4 weeks for first 3 doses followed by once every 8 weeks thereafter. Weighing 35 kg or More: the recommended dosage is 30 mg every 4 weeks for first 3 doses followed by once every 8 weeks thereafter.

Eosinophilic Granulomatosis with Polyangiitis (EGPA)

INITIAL CRITERIA: Mepolizumab (Nucala®), benralizumab (Fasenra®) is medically necessary when ALL of the following are met:

1. Submission of documentation (e.g., chart notes) confirming a diagnosis of Eosinophilic Granulomatosis with Polyangiitis (EGPA); and
2. Paid claims or submission of medical records (e.g., chart notes) confirming that member's disease has relapsed or is refractory to standard of care therapy (i.e., prednisolone, prednisone); and
3. Member is currently receiving corticosteroid therapy (e.g., prednisolone, prednisone); and

4. Member is 18 or older; and
5. Prescribed by or in consultation with pulmonologist, rheumatologist or allergy/immunology specialist; and
6. No concurrent therapy with any other biologic agents; and
7. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial Authorization Duration: 12 months

REAUTHORIZATION CRITERIA: Mepolizumab (Nucala®), benralizumab (Fasenra®) is medically necessary when ALL of the following are met:

1. Submission of documentation (e.g., chart notes) confirming a positive clinical response to therapy (e.g., increase in remission time); and
2. Prescribed by or in consultation with a pulmonologist, rheumatologist or allergy/immunology specialist; and
3. No concurrent therapy with any other biologic agents; and
4. ONE of the following:
 - a. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
 - b. Member is continuing on the established dose and frequency previously approved

Reauthorization duration: 12 months

Mepolizumab (Nucala®)	DOSE
Adults	300 mg as 3 separate 100-mg injections once every 4 weeks
Benralizumab (Fasenra®)	Dose
Adults	30 mg every 4 weeks

Hypereosinophilic Syndrome (HES)

INITIAL CRITERIA: Mepolizumab (Nucala®) is medically necessary when ALL of the following are met:

1. Submission of documentation (e.g., chart notes) confirming diagnosis of Hypereosinophilic Syndrome (HES); and
2. All of the following:
 1. Member has been diagnosed for at least 6 months; and
 2. Verification that other non-hematologic secondary causes have been ruled out (e.g., drug hypersensitivity, parasitic helminth infection, HIV infection, non-hematologic malignancy); and
 3. Submission of documentation (e.g., chart notes, lab value) confirming that the member is FIP1-like1-platelet derived growth factor receptor alpha kinase (FIP1L1-PDGFRα kinase)-negative; and
3. Member is 12 years old or older; and
4. Submission of documentation (e.g., chart notes, lab value) confirming member has uncontrolled HES defined by both of the following:
 1. Pre-treatment blood eosinophil count greater than or equal to 1000 cells/microliter; and
 2. Member has experienced 2 or more flares within the past 12 months; and
5. Paid claims or submission of documentation (e.g., chart notes) confirming inadequate response or inability to tolerate ONE of the following:
 1. Corticosteroid therapy (e.g., prednisone); or
 2. Cytotoxic/immunosuppressive therapy (e.g., hydroxyurea, cyclosporine, imatinib); and
6. Prescribed by or in consultation with one of the following:
 1. Allergist/Immunologist; or
 2. Hematologist; and

7. No concurrent therapy with any other biologic agents; and
8. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Mepolizumab (Nucala®) is medically necessary when ALL of the following are met:

1. Submission of documentation of positive clinical response (e.g., reduction in corticosteroid use, reduction of blood eosinophil count, reduction in flares); and
2. Prescribed by or in consultation with one of the following:
 - a. Allergist/Immunologist; or
 - b. Hematologist; and
3. No concurrent therapy with any other biologic agents; and
4. ONE of the following:
 - a. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
 - b. Member is continuing on the established dose and frequency previously approved

Reauthorization duration: 12 months

Mepolizumab (Nucala®)	DOSE
Adults and pediatric patients aged 12 and older	300 mg as 3 separate 100-mg injections once every 4 weeks

Chronic rhinosinusitis with nasal polyps (CRSwNP)

INITIAL CRITERIA: Mepolizumab (Nucala®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes) confirming a diagnosis of chronic rhinosinusitis with nasal polyps (CRSwNP); and
2. Member is 18 years of age or older; and
3. Paid claims or submission of medical records (e.g., chart notes) confirming an inadequate response or inability to tolerate at least a 2-month treatment with intranasal corticosteroids (e.g., fluticasone); and
4. Used in combination with another agent for CRSwNP; and
5. Prescribed by or in consultation with an allergist, immunologist, or Ear Nose Throat specialist; and
6. No concurrent therapy with any other biologic agents; and
7. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Mepolizumab (Nucala®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes) confirming a documentation of positive clinical response to therapy (e.g., reduction in nasal polyps score [NPS: 0-8 scale], improvement in nasal obstruction symptoms via visual analog scale [VAS: 0-10 scale]); and
2. Used in combination with another agent for CRSwNP; and
3. Prescribed by or in consultation with an allergist, immunologist, or Ear Nose Throat specialist; and
4. No concurrent therapy with any other biologic agents; and
5. ONE of the following:
 - a. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
 - b. Member is continuing on the established dose and frequency previously approved

Reauthorization duration: 12 months

Mepolizumab (Nucala®)	DOSE
Adults	100 mg every 4 weeks

P&T Approval Date: March 20, 2025

Title: Interstitial Lung Disease Agents

Applicable Drugs:

Brand name	Generic name
Ofev®	nintedanib
Esbriet®	pirfenidone

Policy:

Idiopathic Pulmonary Fibrosis (IPF)

INITIAL CRITERIA: Pirfenidone (Esbriet®) or Nintedanib (Ofev®) is approved when ALL of the following are met:

1. Diagnosis of Idiopathic Pulmonary Fibrosis (IPF); and
2. Member is 18 years of age or older; and
3. Diagnosis was confirmed by BOTH of the following:
 1. High resolution CT scan or biopsy; and
 2. Member does not have evidence or suspicion of an alternative interstitial lung disease diagnosis; and
4. Prescribed by or in consultation with a pulmonologist or lung transplant specialist

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Pirfenidone (Esbriet®) or Nintedanib (Ofev®) is re-approved when there is documentation of positive clinical response to therapy (e.g., member has experienced stabilization from baseline or a less than 10% decline in forced vital capacity (FVC))

Reauthorization duration: 12 months

Systemic Sclerosis Associated Interstitial Lung Disease (SSc-ILD)

INITIAL CRITERIA: Nintedanib (Ofev®) is approved when ALL of the following are met:

1. Diagnosis of Systemic Sclerosis Associated Interstitial Lung Disease (SSc-ILD); and
2. Member is 18 years of age or older; and

3. Diagnosis was confirmed by BOTH of the following:
 1. High resolution CT scan or biopsy; and
 2. Member does not have evidence or suspicion of an alternative interstitial lung disease diagnosis; and
4. Prescribed by or in consultation with a pulmonologist or lung transplant specialist

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Nintedanib (Ofev®) is re-approved when there is documentation of positive clinical response to therapy (e.g., member has experienced stabilization from baseline or a less than 10% decline in forced vital capacity (FVC))

Reauthorization duration: 12 months

Chronic Fibrosing Interstitial Lung Disease (ILDs) with a progressive phenotype

INITIAL CRITERIA: Nintedanib (Ofev®) is approved when ALL of the following are met:

1. Diagnosis of Chronic Fibrosing Interstitial Lung Disease (ILDs) with a progressive phenotype; and
2. Member is 18 years of age or older; and
3. Disease has a progressive phenotype as observed by one of the following:
 1. Decline of forced vital capacity (FVC); or
 2. Worsening of respiratory symptoms; or
 3. Increased extent of fibrosis seen on imaging; and
4. Diagnosis was confirmed by BOTH of the following:
 1. High resolution CT scan or biopsy; and
 2. Member does not have evidence or suspicion of an alternative interstitial lung disease diagnosis; and
5. Prescribed by or in consultation with a pulmonologist or lung transplant specialist

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Nintedanib (Ofev®) is re-approved when there is documentation of positive clinical response to therapy (e.g. member has experienced stabilization from baseline or a less than 10% decline in forced vital capacity (FVC))

Reauthorization duration: 12 months

P&T Approval Date: March 20, 2025

Title: Intranasal Corticosteroids

Applicable Drugs:

Beconase AQ®	beclomethasone
Dymista®	azelactine hydrochloride and fluticasone propionate
Qnasl®	beclomethasone dipropionate
Qnasl®Childrens	beclomethasone dipropionate
Xhance™	Fluticasone propionate
Ryaltris®	olopatadine hydrochloride and mometasone furoate monohydrate

Policy:

Nasal polyps

INITIAL CRITERIA: Beconase AQ®, or fluticasone propionate (Xhance™) is approved when BOTH of the following are met:

1. Diagnosis of nasal polyps; and
2. Submission of documentation (e.g., chart note) or paid claim history showing inadequate response or inability to tolerate generic fluticasone propionate (trial for at least 90 days within the previous 365 days)

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Beconase AQ®, or fluticasone propionate (Xhance®) is reapproved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 12 months

Allergic Rhinitis

INITIAL CRITERIA: Beconase AQ®, Children's Qnasl®, azelastine hydrochloride and fluticasone propionate (Dymista), Qnasl®, or Ryaltris® is approved when BOTH of the following are met:

1. Diagnosis of allergic rhinitis; and
2. Inadequate response or inability to tolerate BOTH of the following generic nasal sprays:

1. Flunisolide; and
2. Fluticasone propionate

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Beconase AQ®, Children's Qnasl®*, azelastine hydrochloride and fluticasone propionate (Dymista®), Qnasl®, or Ryaltris® is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 12 months

*Fluticasone propionate is approved for children under 6 years of age

Chronic rhinosinusitis without nasal polyps

INITIAL CRITERIA: Fluticasone propionate (Xhance™) is approved when BOTH of the following are met:

1. Diagnosis of chronic rhinosinusitis without nasal polyps; and
2. Submission of documentation (e.g., chart notes) or paid claim history showing inadequate response or inability to tolerate generic fluticasone propionate (trial of at least 90 days within the previous 365 days)

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Fluticasone propionate (Xhance™) is medically necessary with documentation of positive clinical response to therapy

Reauthorization duration: 12 months

P&T Approval Date: March 20, 2025

Title: Leniolisib (Joenja)

Applicable Drugs:

Brand Name	Generic Name
Joenja®	Leniolisib

Policy:

INITIAL CRITERIA: Leniolisib (Joenja®) is medically necessary when all of the following are met:

1. Diagnosis of activated phosphoinositide 3-kinase delta syndrome (APDS); and
2. Molecular genetic testing confirms mutations in the PIK3CD or PIK3R1 gene; and
3. Member is 12 years of age or older; and
4. Member weighs greater than or equal to 45kg; and
5. Both of the following:
 1. Presence of nodal and/or extranodal proliferation (e.g., lymphadenopathy, splenomegaly, hepatomegaly); and
 2. Presence of other clinical findings and manifestations consistent with APDS (e.g., recurrent sino-pulmonary infections, bronchiectasis, enteropathy); and
6. Inadequate response or inability to tolerate at least one standard of care treatment for APDS (e.g., Immunoglobulin replacement therapy, antimicrobial prophylaxis [e.g., azithromycin, Bactrim], rituximab, tacrolimus, etc.); and
7. Prescribed by or in consultation with one of the following:
 1. Hematologist; or
 2. Immunologist; or
 3. Geneticist

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Leniolisib (Joenja®) is medically necessary with documentation of positive clinical response to therapy (e.g., reduced lymph node size, increased naïve B-cell percentage, decreased severity or frequency of infections/hospitalizations)

Reauthorization duration: 12 months

P&T Approval Date: Dec-12-2024

Title: Lonafarnib (Zokinvy)

Applicable Drugs:

Brand Name	Generic Name
Zokinvy™	Lonafarnib

Policy:

INITIAL CRITERIA Lonafarnib (Zokinvy™) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming one of the following:
 1. Diagnosis of Hutchinson-Gilford Progeria Syndrome; or
 2. Genetic testing results confirming a LMNA mutation that results in the production of progerin; or
 3. Processing-deficient Progeroid Laminopathies with one of the following:
 1. Genetic testing results confirming member has a heterozygous LMNA mutation with progerin-like protein accumulation; or
 2. Genetic testing results confirming member has a homozygous or compound heterozygous ZMPSTE24 mutations; and
2. Member is 12 months of age or older; and
3. Member has a body surface area of 0.39 m² and above; and
4. Prescribed by or in consultation with a specialist with expertise in the diagnosis and management of Progeria

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA Lonafarnib (Zokinvy™) is medically necessary when all of the following have been met:

1. Documentation that member has had clinical benefit with the requested drug; and
2. Prescribed by or in consultation with a specialist with expertise in the diagnosis and management of Progeria

Reauthorization duration: 2 years

P&T Approval Date: Dec-12-2024

Title: Mannitol (Bronchitol®)

Applicable Drugs:

Brand Name	Generic Name
Bronchitol®	Mannitol

Policy:

INITIAL CRITERIA: Mannitol (Bronchitol®) is approved when all of the following are met:

1. Diagnosis of cystic fibrosis; and
2. Member is 18 years of age or older; and
3. Member has passed the Bronchitol Tolerance Test (BTT); and
4. Member has inadequate response or inability to tolerate ONE of the following:
 1. Inhaled hypertonic saline; or
 2. Pulmozyme (dornase alfa); and
5. Prescribed by or in consultation with one of the following:
 1. Pulmonologist; or
 2. Specialist associated with a cystic fibrosis care center

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA: Mannitol (Bronchitol®) is re-approved when there is documentation of positive clinical response to therapy (e.g. improvement in lung function [forced expiratory volume in one second {FEV1}])

Reauthorization duration: 2 years

P&T Approval Date: March 20, 2025

Title: Maralixibat (Livmarli)

Applicable Drugs:

Brand Name	Generic Name
Livmarli™	maralixibat

Policy:

Alagille Syndrome (ALGS)

INITIAL CRITERIA Maralixibat (Livmarli®) is medically necessary when ALL of the following are met:

1. Diagnosis of Alagille Syndrome (ALGS) as confirmed by BOTH of the following:
 1. Molecular genetic testing confirms mutations in the JAG1 or NOTCH2 gene; and
 2. One of the following:
 1. Total serum bile acid > 3x the upper limit of normal (ULN); or
 2. Conjugated bilirubin > 1 mg/dL; or
 3. Fat soluble vitamin deficiency otherwise unexplainable; or
 4. Gamma-glutamyl transpeptidase (GGT) > 3x ULN; and
2. Member is experiencing moderate to severe cholestatic pruritus; and
3. Member is 3 months of age or older; and
4. Prescribed by or in consultation with a hepatologist or gastroenterologist; and
5. Member has had an inadequate response or inability to tolerate at least two of the following treatments used for the relief of pruritus:
 1. Ursodeoxycholic acid (e.g., Ursodiol); or
 2. Antihistamines (e.g., diphenhydramine, hydroxyzine); or
 3. Rifampin; or
 4. Bile acid sequestrants (e.g., cholestyramine, colestipol, colesevelam)

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA Maralixibat (Livmarli™) is medically necessary with

documentation of positive clinical response to therapy (e.g., reduced bile acids, reduced pruritus severity score)

Reauthorization duration: 2 years

Progressive Familial Intrahepatic Cholestasis (PFIC)

INITIAL CRITERIA: Maralixibat (Livmarli™) is medically necessary when ALL of the following are met:

1. Both of the following:
 1. Diagnosis of Progressive familial intrahepatic cholestasis (PFIC); and
 2. Molecular genetic testing confirms mutations in the ATP8B1, ABCB11, ABCB4, TJP2, NR1H4, or MYO5B; and
2. Member is experiencing both of the following:
 1. Moderate to severe pruritus; and
 2. Member has a serum bile acid concentration above the upper limit of the normal reference for the reporting laboratory; and
3. Member is 12 months of age or older; and
4. Member has had an inadequate response to at least two of the following treatments used for the relief of pruritus:
 1. Ursodeoxycholic acid (e.g., Ursodiol)
 2. Antihistamines (e.g., diphenhydramine, hydroxyzine)
 3. Rifampin
 4. Bile acid sequestrants (e.g., Questran, colestid, Welchol); and
5. Prescribed by or in consultation with one of the following:
 1. Hepatologist; or
 2. Gastroenterologist

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Maralixibat (Livmarli™) is medically necessary with documentation of positive clinical response to therapy (e.g., reduced serum bile acids, improved pruritus)

Reauthorization duration: 2 years

P&T Approval Date: Dec-12-2024

Title: Mavacamten (Camzyos)

Applicable Drugs:

Brand Name	Generic Name
Camzyos™	Mavacamten

Policy:

INITIAL CRITERIA: Mavacamten (Camzyos™) is approved when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of symptomatic New York Heart Association (NYHA) class II-III obstructive hypertrophic cardiomyopathy (HCM); and
2. Member is 18 years of age or older; and
3. Member's baseline left ventricular ejection fraction (LVEF) is greater than or equal to 55%; and
4. Member has Valsalva left ventricular outflow tract (LVOT) peak gradient greater than or equal to 50 mmHg at rest or with provocation; and
5. Inadequate response or inability to tolerate BOTH of the following at a maximally tolerated dose:
 - a. Non-vasodilating One beta blocker (e.g., bisoprolol, propranolol); and
 - b. Calcium channel blocker (e.g., verapamil, diltiazem); and
6. Prescribed by or in consultation with a cardiologist

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Mavacamten (Camzyos™) is re-approved when ALL of the following are met:

1. Documentation of positive clinical response to therapy (e.g., improved symptom relief); and

2. Member's left ventricular ejection fraction (LVEF) is greater than or equal to 50%; and
3. Prescribed by or in consultation with a cardiologist.

Reauthorization duration: 12 months

P&T Approval Date: Jul-01-2024

Title: Mavorixafor (Xolremdi)

Applicable Drugs:

Brand Name	Generic Name
Xolremdi	Mavorixafor

Policy:

INITIAL CTITERIA: Mavorixafor (Xolremdi™) is medically necessary when ALL of the following are met:

1. Diagnosis of WHIM (warts, hypogammaglobulinemia, infections and myelokathexis) syndrome; and
2. Member has genotype confirmed variant of CXCR4 as detected by an FDA-approved test or a test performed at a facility approved by Clinical Laboratory Improvement Amendments (CLIA); and
3. Member has an absolute neutrophil count (ANC) less than or equal to 500 cells /μL; and
4. Member is 12 years of age or older; and
5. Prescribed by or in consultation with one of the following:
 1. Immunologist
 2. Hematologist
 3. Geneticist
 4. Allergist

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Mavorixafor (Xolremdi™) is medically necessary with documentation of positive clinical response to therapy (e.g., improvement in ANC, reduction in infections)

Reauthorization duration: 12 months

P&T Approval Date: Sep-12-2024

Title: Mecasermin (Increlex®)

Applicable Drugs:

Brand Name	Generic Name
Increlex®	mecasermin

Policy:

INITIAL CRITERIA: Mecasermin (Increlex®) is medically necessary when all of the following are met:

1. Diagnosis of growth failure in children with ONE of the following:
 - a. All of the following:
 1. Severe primary insulin-like growth factor-1 deficiency (IGF-D); and
 2. Height standard deviation (SD) score of less than or equal to 3.0 SD scores below normal (growing at below the third percentile for age and sex); and
 3. Baseline IGF-1 (SD) score of less than or equal to 3.0 SD scores below normal (based on age- and sex-related reference ranges); and
 4. Normal or elevated GH level (based on GH stimulation testing); or
 - b. Both of the following:
 1. Growth hormone (GH) gene deletion who have developed neutralizing antibodies to GH; and
 2. Measured titers of GH-neutralizing antibodies; and
2. Member is 2 years of age or older; and
3. Open epiphyses (bone growth plates) (bone age less than 14 years for girls and less than 16 years for boys); and
4. Prescribed by or in consultation with an endocrinologist

Initial Authorization duration: 12 months

CONTINUATION CRITERIA: Continuation of mecasermin (Increlex®) is medically necessary when all of the following are met:

1. Growth velocity greater than or equal to 2 cm/year; and

2. Yearly evaluation by an endocrinologist; and
3. BOTH of the following
 - a. Expected adult height is not obtained; and
 - b. Documentation of expected adult height goal

Continuation duration: 12 months

P&T Approval Date: Sep-12-2024

Title: Medical injectable medications covered under the pharmacy benefit

Policy:

Coverage is subject to the terms, conditions, and limitations of the member's contract.

The following medications are covered under the medical benefit:

1. Cyanocobalamin (vitamin B12) injection
2. Heparin injection
3. Hydrocortisone injection
4. Methotrexate injection (vial)
5. Non-insulin syringes/needles

A benefit exception will be made to cover cyanocobalamin injection, heparin injection, hydrocortisone injection, methotrexate vials under the prescription drug benefit when ALL of the following are met:

1. The requested drug is being used for a Food and Drug Administration approved indication or compendium supported indication as outlined in Off-label Use policy; and
2. The prescriber assumes responsibility for teaching the member proper preparation, administration and disposal; and
3. The prescriber provides a statement indicating the reason prescription drug benefit products are not an option, and
4. ONE of the following:
 1. Provider does not stock the requested medication; or
 2. Access at the provider's office is not feasible due to frequency of administration

A benefit exception will be made to cover non-insulin syringes/needles under the prescription drug benefit when required to administer an injectable medication and not supplied with the product.

Coverage is subject to the terms of the member's prescription drug benefit, including but not limited to cost-share.

Authorization duration: 2 years

P&T Approval Date: Jul-01-2024

Field Name	Field Description
Prior Authorization Group Description	Medications without Drug or Class Specific Criteria
Drugs	- Medications without drug or class specific prior authorization criteria - Brand drugs and reference biologics when a therapeutic equivalent generic drug or biosimilar/interchangeable biologic is available ***The Oncology Drugs prior authorization criteria will be applied to oncology drugs without drug or class specific criteria***
Covered Uses	Medically accepted indications are defined using the following sources: the Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), or disease state specific standard of care guidelines.
Exclusion Criteria	N/A
Required Medical Information	See “Other Criteria”
Age Restrictions	According to package insert
Prescriber Restrictions	N/A
Coverage Duration	If all of the conditions are met, requests will be approved for up to 12 months (depending on the diagnosis and usual treatment duration).
Other Criteria	<u>Initial Authorization:</u> All Requests: - The drug is requested for an appropriate use (per the references outlined in “Covered Uses”) - The dose requested is appropriate for the requested use (per the references outlined in “Covered Uses”) - Patient meets one of the three following criteria: - Documented trial and failure or intolerance of two alternative formulary/preferred medications appropriate for the requested use (per the references outlined in “Covered Uses” or has a medical reason why these drug(s) cannot be used [e.g. intolerance, contraindication]). For medications where there is only one preferred agent, only that agent must have been ineffective or not tolerated. - No other preferred medication has a medically accepted use for the patient’s specific diagnosis as referenced in the medical compendia. - All other preferred medications are contraindicated based on the patient’s diagnosis, other medical conditions, or other medication therapy. Brand drugs with a therapeutically equivalent (A-rated) generic drug currently available: - The provider either verbally or in writing has submitted a medical or member specific reason why the brand name drug is required based on the member’s condition or treatment history; AND if the member had side effects or a reaction to the generic drug, the provider has completed and submitted an FDA MedWatch form to justify the member’s need to avoid this drug. The MedWatch form must be included with the prior authorization request Form FDA 3500 – Voluntary Reporting

Revision/Review Date 11/2024	Reference biologic drugs with either a biosimilar or interchangeable biologic drug currently available: • The prescriber has verbally or in writing submitted a medical or member specific reason why the reference biologic is required based on the member’s condition or treatment history; AND if the member had side effects or a reaction to two (if available) biosimilar or interchangeable biologics, the provider has completed and submitted an FDA MedWatch form to justify the member’s need to avoid these drugs. The MedWatch form must be included with the prior authorization • The currently available biosimilar product(s) does not have the same appropriate use (per the references outlined in “Covered Uses”) as the reference biologic drug being requested <u>Form FDA 3500 – Voluntary Reporting</u> Reauthorization: • Documentation of provider attestation that demonstrates a clinical benefit • The requested drug is for a medically accepted dose as outlined in Covered Uses Physician/clinical reviewer must override criteria when, in his/her professional judgment, the requested item is medically necessary.

Title: Metabolic Disorder agents (Strensiq, Xuriden)

Applicable Drugs:

Brand Name	Generic Name
Strensiq® Xuriden®	asfotase alfa uridine triacetate

Policy:

Perinatal/infantile or juvenile-onset hypophosphatasia

INITIAL CRITERIA: Asfotase alfa (Strensiq®) is medically necessary when ALL of the following are met:

1. Submission of documentation (e.g., chart note) confirming diagnosis of perinatal/infantile or juvenile-onset hypophosphatasia (HPP); and
2. Prescribed by or in consultation with a medical geneticist or other specialist that treats inborn errors of metabolism (e.g., endocrinologist, rheumatologist, geneticist, orthopedist); and
3. For member requesting the 80mg/0.8ml vial: submission of documentation confirming the member's weight is greater than or equal to 40kg; and
4. Submission of medical records (e.g., chart notes) documenting onset of clinical signs and symptoms of hypophosphatasia prior to age 18 years (e.g., respiratory insufficiency, vitamin B6 responsive seizures, hypotonia, failure to thrive, delayed walking, waddling gait, dental abnormalities, low trauma fractures); and
5. Submission of medical records (e.g., chart notes) documenting radiographic evidence supporting the diagnosis of hypophosphatasia at the age of onset prior to age 18 (e.g., infantile rickets, craniosynostosis, non-traumatic fractures, osteoporosis or low bone mineral content for age [as detected by DEXA]); and
6. Submission of medical records (e.g., chart notes) documenting one of the following:
 - a. Both of the following:
 1. Patient has low level activity of serum alkaline phosphatase (ALP) evidenced by an ALP level below the age and gender-adjusted normal range; and

2. Patient has an elevated level of tissue non-specific alkaline phosphatase (TNSALP) substrate (e.g., serum pyridoxal 5'-phosphate [PLP] level, serum or urine phosphoethanolamine [PEA] level, urinary inorganic pyrophosphate [PPi level]); or
 - b. Confirmation of tissue-nonspecific alkaline phosphatase (TNSALP) gene mutation by ALPL genomic DNA testing; and
7. Requested dose will not exceed the following: (Note to prescriber: Three times a week dosing leads to less waste and may lead to less injection site reactions compared to six times a week dosing)
 - b. 9 mg/kg per week for perinatal/infantile-onset HPP
 - c. 6 mg/kg per week for juvenile-onset HPP

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA: Asfotase alfa (Strensiq®) is medically necessary when ALL of the following are met:

1. There is positive clinical response to therapy as evidenced by one of the following:
 1. Improvement and/or stabilization of clinical signs and/or symptoms of hypophosphatasia (e.g., respiratory status [ventilator free survival], growth) or radiographic findings (e.g., skeletal manifestations); or
 2. Clinically relevant decrease from baseline in tissue non-specific alkaline phosphatase (TNSALP) substrate (e.g., serum pyridoxal 5'-phosphate [PLP] level, serum or urine phosphoethanolamine [PEA] level, urinary inorganic pyrophosphate [PPi level]); and
2. Prescribed by or in consultation with a medical geneticist or other specialist that treats inborn errors of metabolism (e.g., endocrinologist, rheumatologist, geneticist, orthopedist); and
3. Requested dose will not exceed the following: (Note to prescriber: Three times a week dosing leads to less waste and may lead to less injection site reactions compared to six times a week dosing)
 1. 9 mg/kg per week for perinatal/infantile-onset HPP
 2. 6 mg/kg per week for juvenile-onset HPP; and
4. For member requesting the 80mg/0.8ml vial: submission of documentation confirming the member's weight is greater than or equal to 40kg

Reauthorization duration: 2 years

Hereditary orotic aciduria

INITIAL CRITERIA: Uridine triacetate (Xuriden®) is medically necessary when ALL of the following are met:

1. Submission of documentation (e.g., chart note) confirming diagnosis of hereditary orotic aciduria; and
2. Prescribed by or in consultation with a medical geneticist or other specialist that treats inborn errors of metabolism

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA: Uridine triacetate (Xuriden®) is medically necessary when there is positive clinical response to therapy

Reauthorization duration: 2 years

P&T Approval Date: Dec-12-2024

Title: Metreleptin (Myalept®)

Brand Name	Generic Name
Myalept®	metreleptin

Policy:

INITIAL CRITERIA: Metreleptin (Myalept®) is medically necessary when ALL of the following are met:

1. Diagnosis of congenital or acquired generalized lipodystrophy (excluding other forms of lipodystrophy); and
2. Prescribed as adjunct to diet as replacement therapy; and
3. Member is refractory to current standards of care for lipid and diabetic management; and
4. Prescribed by or in consultation with an endocrinologist; and
5. Documentation demonstrates that member has at least one of the following metabolic abnormalities:
 - a. Insulin resistance (defined as requiring more than 200 units per day)
 - b. Hypertriglyceridemia
 - c. Diabetes

Initial Authorization duration: 12 months

CONTINUATION CRITERIA: Continuation of metreleptin (Myalept®) is medically necessary when there is documentation of positive clinical response to metreleptin (Myalept®) therapy (e.g., sustained reduction in Hemoglobin A1c or triglycerides from baseline)

Continuation authorization duration: 2 years

P&T Approval Date: Sep-12-2024

Title: Migraine and Headache Agents

Applicable Drugs:

Brand Name	Generic Name
Maxalt [®] /Maxalt [®] MLT	Rizatriptan
Amerge [®]	Naratriptan
Frova [®]	Frovatriptan
Imitrex [®] , Tosymra [®] , Onzetra [®] Xsail, Zembrace [®] Symtouch	Sumatriptan
Relpax [®]	Eletriptan
Zomig [®] / Zomig [®] ZMT	Zolmitriptan
Treximet [®]	Sumatriptan/naproxen
D.H.E. 45 [®] , Migranal [®] , Trudhesa [™]	Dihydroergotamine mesylate
Nurtec [™] ODT	Rimegepant
Ubrelvy [™]	Ubrogepant
Reyvow [®]	Lasmiditan
Aimovig [™]	Erenumab
Ajovy [™]	Fremanezumab
Emgality [™]	Galcanezumab
Qulipta [™]	Atogepant
Zavzpret [™]	zavegepant

Policy:

Acute Treatment of Migraine

INITIAL CRITERIA: Frova®, Imitrex®, Tosymra®, Relpax®, Onzetra® Xsail, Zembrace® Symtouch, zolmitriptan nasal spray, or Zomig®/zolmitriptan Zomig® ZMT is medically necessary when ALL of the following are met:

1. Diagnosis of migraine headache; and
2. Use in the age group shown in the table below; and
3. Inadequate response or inability to tolerate two generic triptans (e.g., eletriptan, naratriptan, rizatriptan, zolmitriptan, sumatriptan) as appropriate for the member's age

Drug	Age Recommendation
Rizatriptan	Age 6 and up
Zolmitriptan (Zomig®/Zomig® ZMT)	Age 12 and up
Eletriptan (Relpax®)	Age 18 and up
Naratriptan	Age 18 and up
Sumatriptan (Imitrex®, Onzetra® Xsail, Zembrace® Symtouch, Tosymra®)	Age 18 and up
Frovatriptan (Frova®)	Age 18 and up

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA: Frova®, Imitrex®, Tosymra®, Relpax®, Onzetra® Xsail, Zembrace® Symtouch, zolmitriptan nasal spray or Zomig®/Zomig® ZMT is medically necessary when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

INITIAL CRITERIA: Sumatriptan/naproxen (Treximet®) is medically necessary when ALL of the following are met:

1. Diagnosis of migraine headache; and
2. Member is 12 years of age or older; and
3. Inadequate response or inability to tolerate three generic triptans (e.g., eletriptan, naratriptan, rizatriptan, zolmitriptan, sumatriptan); and
4. Inadequate response to concurrent administration of sumatriptan and naproxen as separate products

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA: Sumatriptan/naproxen (Treximet®) is medically necessary when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

INITIAL CRITERIA: Dihydroergotamine mesylate (D.H.E. 45®) injection is medically necessary when ALL of the following are met:

1. Prescribed by or in consultation with one of the following specialists:

- a. Neurologist; or
 - b. Pain specialist; or
 - c. Headache specialist certified by the United Council of Neurologic Subspecialties; and
2. Diagnosis of acute treatment of migraine or cluster headaches; and
3. Member is 18 years of age or older; and
4. Member has been instructed on proper preparation, injection, and disposal of medication; and
5. ONE of the following:
 - a. Inadequate response or inability to tolerate two, oral or nasal, triptans; or
 - b. Triptan overuse, defined as using triptans greater than 8 days per month; and
6. For brand D.H.E. 45 only, inadequate response or inability to tolerate generic dihydroergotamine injection or it is not available; and
7. If member has 4 or more headache days per month, member must be currently treated with one of the following, unless there is a contraindication or intolerance to these medications:
 - a. An antidepressant (i.e., Elavil [amitriptyline] or Effexor [venlafaxine])
 - b. An anticonvulsant (i.e., Depakote/Depakote ER [divalproex sodium] or Topamax [topiramate])
 - c. A beta-blocker (i.e., atenolol, propranolol, nadolol, timolol, or metoprolol)
 - d. Atacand (candesartan)

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA: Dihydroergotamine mesylate (D.H.E 45®) injection is medically necessary when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

INITIAL CRITERIA: Dihydroergotamine mesylate (Migranal®) or dihydroergotamine mesylate HFA (Trudhesa™) is medically necessary when ALL of the following are met:

1. Diagnosis of moderate to severe migraine headache with or without aura; and
2. Inadequate response or inability to tolerate TWO, oral or nasal, triptans; and
3. If member has 4 or more headache days per month, member must be currently treated with one of the following, unless there is a contraindication or intolerance to these medications:
 - a. An antidepressant (i.e., Elavil [amitriptyline] or Effexor [venlafaxine])
 - b. An anticonvulsant (i.e., Depakote/Depakote ER [divalproex sodium] or Topamax [topiramate])
 - c. A beta-blocker (i.e., atenolol, propranolol, nadolol, timolol, or metoprolol)
 - d. Atacand (candesartan); and
4. Prescribed by or in consultation with one of the following specialists:
 - a. Neurologist; or
 - b. Pain specialist; or
 - c. Headache specialist certified by the United Council of Neurologic Subspecialties; and
5. For dihydroergotamine mesylate HFA (Trudhesa) only, inadequate response or inability to tolerate generic dihydroergotamine mesylate nasal spray

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA: Dihydroergotamine mesylate (Migranal®) or dihydroergotamine mesylate HFA (Trudhesa™) is medically necessary when ALL of the following are met:

1. Documentation of positive clinical response to therapy; and

2. Prescribed by or in consultation with one of the following specialists:
 1. Neurologist; or
 2. Pain specialist; or
 3. Headache specialist certified by the United Council of Neurologic Subspecialties; and
3. For dihydroergotamine mesylate HFA (Trudhesa) only, inadequate response or inability to tolerate generic dihydroergotamine mesylate nasal spray

Reauthorization duration: 2 years

INITIAL CRITERIA: Rimegepant (Nurtec™ ODT), ubrogepant (Ubrelvy™), zavegepant (Zavzpret) or lasmiditan (Reyvow®) is medically necessary when all of the following are met:

1. Diagnosis of migraine with or without aura; and
2. Will be used for the acute treatment of migraine; and
3. For ubrogepant (Ubrelvy™), zavegepant (Zavzpret™), lasmiditan (Reyvow®) only, will not be used for preventative treatment of migraine; and
4. Member is 18 years of age or older; and
5. Inadequate response or inability to tolerate two triptans (e.g., eletriptan, rizatriptan, sumatriptan); and
6. If the member has 4 or more headache days per month, the member must be on current treatment or have inability to tolerate one of the following:
 - a. Elavil (amitriptyline) or Effexor (venlafaxine); or
 - b. Depakote/Depakote ER (divalproex sodium) or Topamax (topiramate); or
 - c. Beta blocker (i.e., atenolol, propranolol, nadolol, timolol, or metoprolol); or
 - d. Atacand (candesartan); and
7. Medication will not be used in combination with another CGRP antagonist for the acute treatment of migraines; and
8. For Lasmiditan (Reyvow®) and zavegepant (Zavzpret) only, inadequate response or inability to tolerate BOTH rimegepant (Nurtec™ ODT) and ubrogepant (Ubrelvy™)

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Rimegepant (Nurtec™ ODT), ubrogepant (Ubrelvy™), zavegepant (Zavzpret) or lasmiditan (Reyvow®) is medically necessary when all of the following are met:

1. Member has experienced a positive response to therapy (e.g., reduction in pain, photophobia, phonophobia, nausea); and
2. For ubrogepant (Ubrelvy™), zavegepant (Zavzpret™), lasmiditan (Reyvow®) only, will not be used for preventative treatment of migraine; and
3. Medication will not be used in combination with another CGRP antagonist for the acute treatment of migraines

Reauthorization duration: 2 years

Preventative Treatment of Episodic or Chronic Migraine with Injectable CGRP Antagonists

INITIAL CRITERIA: Erenumab (Aimovig™), fremanezumab (Ajovy™), or galcanezumab (Emgality™) 120mg/ml is medically necessary when ALL of the following are met:

1. Member is 18 years of age or older; and
2. ONE of the following:

1. Diagnosis of episodic migraines defined as 4-14 headache days per month and inadequate response or inability to tolerate at least a two-month trial of TWO of the following prophylactic medications:
 1. Topiramate
 2. Divalproex sodium/ valproic acid
 3. Beta-blocker: metoprolol, propranolol, timolol, atenolol, nadolol
 4. Tricyclic antidepressants: amitriptyline, nortriptyline
 5. SNRI antidepressants: venlafaxine, duloxetine; or
 6. Candesartan (Atacand); or
2. Diagnosis of chronic migraines defined as 15 or more headache days per month and inadequate response or inability to tolerate at least a two-month trial of TWO of the following prophylactic medications:
 1. Topiramate
 2. Divalproex sodium/valproic acid
 3. Beta-blocker: metoprolol, propranolol, timolol, atenolol, nadolol
 4. Tricyclic antidepressants: amitriptyline, nortriptyline
 5. SNRI antidepressants: venlafaxine, duloxetine; or
 6. Trial of additional prophylactic medications does not apply if member has previously been treated with Onabotulinumtoxin A (Botox) for migraines; and
3. Medication overuse headache has been considered, and potentially offending medication(s) have been discontinued; and
4. Medication will not be used in combination with another CGRP inhibitor for the preventive treatment of migraines; and
5. For galcanezumab (Emgality™ 120mg/ml) only, inadequate response or inability to tolerate BOTH erenumab (Aimovig™) and fremanezumab (Ajovy™)

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Erenumab (Aimovig™), fremanezumab (Ajovy™), or galcanezumab (Emgality™) 120mg/ml is medically necessary when ALL of the following are met:

1. Documentation of response to therapy as defined by 50% reduction in headache days per month from baseline (defined as at least 4 hours duration and moderate intensity); and
2. For galcanezumab (Emgality™ 120mg/ml) only, inadequate response or inability to tolerate BOTH erenumab (Aimovig™) and fremanezumab (Ajovy™); and
3. Use of acute migraine medication (e.g., nonsteroidal anti-inflammatory drugs (NSAID) (e.g., ibuprofen, naproxen), triptans (e.g., eletriptan, rizatriptan, sumatriptan) has decreased since the start of CGRP therapy; and
4. For Chronic migraine only: member continues to be monitored for medication overuse headache (MOH); and
5. Medication will not be used in combination with another CGRP inhibitor for the preventive treatment of migraines

Reauthorization duration: 2 years

Preventative Treatment of Episodic Migraines with Oral CGRP Antagonist

INITIAL CRITERIA: Rimegepant (Nurtec™ ODT) or atogepant (Qulipta™) is medically necessary when all of the following are met:

1. Both of the following:
 1. Diagnosis of episodic migraines; and
 2. One of the following:
 1. For Nurtec ODT only, member has 4 to 18 migraine days per month, but no more than 18 headache days per month; or
 2. For Qulipta only, Member has 4 to 14 migraine days per month, but no more than 14 headache days per month; and
2. Member is 18 years of age or older; and
3. Two of the following:
 1. Inadequate response or inability to tolerate at least a two-month trial of Elavil (amitriptyline) or Effexor (venlafaxine); or
 2. Inadequate response or inability to tolerate at least a two-month trial of Depakote/Depakote ER (divalproex sodium) or Topamax (topiramate); or
 3. Inadequate response or inability to tolerate at least a two-month trial of one of the following beta blockers: atenolol, propranolol, nadolol, timolol, or metoprolol; and
 4. Inadequate response or inability to tolerate at least a two-month trial of Atacand (candesartan); and
4. Medication will not be used in combination with another CGRP antagonist for the preventative treatment of migraines

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Rimegepant (Nurtec™ ODT) or atogepant (Qulipta™) is medically necessary when all of the following are met:

1. Member has experienced a positive response to therapy, demonstrated by a reduction in headache frequency and/or intensity; and
2. Use of acute migraine medications [e.g., nonsteroidal anti-inflammatory drugs (NSAIDs) (e.g., ibuprofen, naproxen), triptans (e.g., eletriptan, rizatriptan, sumatriptan)] has decreased since the start of CGRP therapy; and
3. Medication will not be used in combination with another CGRP antagonist for the preventative treatment of migraines

Reauthorization duration: 2 years

Preventive treatment of Chronic Migraine with Oral CGRP Antagonist

INITIAL CRITERIA: Atogepant (Qulipta™) is medically necessary when all of the following are met:

1. Diagnosis of chronic migraines defined as 15 or more headache days per month, of which at least 8 must be migraine days for at least 3 months; and
2. Inadequate response or inability to tolerate at least two-month trial of TWO of the following prophylactic medications:
 - a. Tricyclic antidepressants: amitriptyline, nortriptyline
 - b. Topiramate
 - c. Divalproex sodium/valproic acid

- d. Beta blocker: metoprolol, propranolol, timolol, atenolol, nadolol
 - e. SNRI antidepressants; venlafaxine, duloxetine
 - f. Candesartan (Atacand)
3. Trial of additional prophylactic medications does not apply if member has previously been treated with Onabotulinumtoxin A (Botox) for migraines; and
 4. Member is 18 years of age or older; and
 5. Medication will not be used in combination with another CGRP inhibitor for the preventative treatment of migraines; and
 6. Medication overuse headache has been considered, and potentially offending medication(s) have been discontinued

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Atogepant (Qulipta™) is medically necessary when all of the following are met:

1. Member has experienced a positive response to therapy, demonstrated by a reduction in headache frequency and/or intensity; and
2. Use of acute migraine medications [e.g., nonsteroidal anti-inflammatory drugs (NSAIDs) (e.g., ibuprofen, naproxen), triptans (e.g., eletriptan, rizatriptan, sumatriptan)] has decreased since the start of CGRP therapy; and
3. Member continues to be monitored for medication overuse headache (MOH); and
4. Medication will not be used in combination with another CGRP inhibitor for the preventative treatment of migraines

Reauthorization duration: 2 years

Episodic Cluster Headaches

INITIAL CRITERIA: Galcanezumab (Emgality™) 100mg/ml is medically necessary when ALL of the following are met:

1. Diagnosis of episodic cluster headache; and
2. Member has experienced at least 2 cluster periods lasting 7 days to 365 days, separated by pain-free periods lasting at least three months; and
3. Member is 18 years of age or older; and
4. Medication will not be used in combination with another CGRP antagonist

Initial authorization duration: 3 months

REAUTHORIZATION CRITERIA: Galcanezumab (Emgality™) 100mg/ml is medically necessary when ALL of the following are met:

1. Member has experienced a positive clinical response to therapy, demonstrated by a reduction in headache frequency and/or intensity; and
2. Medication will not be used in combination with another CGRP antagonist

Reauthorization duration: 12 months

P&T Approval Date: March 20, 2025

Title: Mitapivat (Pyrukynd)

Applicable Drugs:

Brand Name	Generic Name
Pyrukynd	Mitapivat

Policy:

INITIAL CRITERIA: Mitapivat (Pyrukynd®) is approved when ALL of the following are met:

1. Diagnosis of hemolytic anemia confirmed by the presence of chronic hemolysis (e.g., increased indirect bilirubin, elevated lactated dehydrogenase [LDH], decreased haptoglobin, increased reticulocyte count); and
2. Diagnosis of pyruvate kinase deficiency confirmed by molecular testing of ALL of the following mutations on the PLKR gene:
 - a. Presence of at least 2 variant alleles in the pyruvate kinase liver and red blood cell (PKLR) gene, of which at least 1 was a missense variant; and
 - b. Member is not homozygous for the c.1436G>A (p.R479H) variant; and
 - c. Member does not have 2 non-missense variants (without the presence of another missense variant) in the PKLR gene; and
3. Hemoglobin is less than or equal to 10g/dL; and
4. Member has symptomatic anemia or is transfusion dependent; and
5. Other causes of hemolytic anemias (e.g., infections, toxins, drugs) were ruled out; and
6. Member is 18 years of age and older; and
7. Prescribed by or in consultation with a hematologist

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Mitapivat (Pyrukynd®) re-approved when ALL of the following are met:

1. Documentation of positive clinical response to therapy (e.g., hemoglobin greater than or equal to 1.5g/dL from baseline sustained on 2 or more follow ups (weeks 16, 20 and 24) during the fixed dose period without transfusions; reduction in transfusions of greater than or equal to 33% in the number of red blood cell units transfused during the fixed dose period compared with the member's historical transfusion burden; improvement in markers of hemolysis from baseline (e.g., bilirubin, lactated dehydrogenase [LDH], haptoglobin, reticulocyte count)); and
2. Prescribed by or in consultation with a hematologist

Reauthorization duration: 12 months

P&T Approval Date: Jul-01-2024

Title: Nedosiran (Rivfloza™)

Applicable Drugs:

Brand Name	Generic Name
Rivfloza™	Nedosiran

Policy:

INITIAL CRITERIA: Nedosiran (Rivfloza™) is approved when ALL of the following are met:

1. Diagnosis of primary hyperoxaluria type 1 (PH1); and
2. Disease has been confirmed by both of the following:
 1. One of the following:
 1. Elevated urinary oxalate excretion; or
 2. Elevated plasma oxalate concentration; or
 3. Spot urinary oxalate to creatinine molar ratio greater than normal for age; and
 2. One of the following:
 1. Genetic testing demonstrating a mutation in the alanine: glyoxylate aminotransferase (AGXT) gene; or
 2. Liver biopsy demonstrating absence or reduced alanine: glyoxylate aminotransferase (AGT) activity; and
3. Member is 9 years of age or older; and
4. Member has preserved kidney function (e.g., eGFR greater than or equal to 30 ml/min/1.72m²); and
5. Member has not received a liver transplant; and
6. Prescribed by or in consultation with one of the following:
 1. Hepatologist
 2. Nephrologist
 3. Urologist
 4. Geneticist

5. Specialist with expertise in the treatment of PH1

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Nedosiran (Rivfloza™) is re-approved when ALL of the following are met:

1. Member demonstrates positive clinical response to therapy (e.g., decreased urinary oxalate excretion, decreased plasma oxalate concentration); and
2. Member has not received a liver transplant; and
3. Prescribed by or in consultation with one of the following:
 1. Hepatologist
 2. Nephrologist
 3. Urologist
 4. Geneticist
 5. Specialist with expertise in the treatment of PH1

Reauthorization duration: 12 months

P&T Approval Date: Jul-01-2024

Title: Non-FDA Approved Products

Policy:

Coverage is subject to the terms, conditions, and limitations of the member's contract.

Prescription drugs that are commercially available but not approved by the FDA are not considered a covered benefit.

Some prescription drugs that are not FDA approved, and not otherwise excluded, will be covered under the pharmacy benefit for certain plans as required by the Patient Protection and Affordable Care Act (PPACA) or as defined in the member's benefit booklet. These items include but may not be limited to the following products as listed:

- Prenatal vitamins, oral
- Preventative vitamins and minerals as required by the PPACA
- Cholecalciferol (vitamin D3) 50,000 units*
- Sulfuric acid/phenolsulfonic acid solution*

Some prescription drugs that came to market prior to 1938, prior to the current FDA approval process, and not otherwise excluded, will be covered under the prescription drug benefit if they are deemed medically accepted as defined in the Off-Label Use policy. These items include but may not be limited to the following products as listed:

- Aluminum chloride topical
- Hydrocortisone suppositories
- Hyoscyamine
- Phenobarbital
- Opium tincture
- Morphine suppositories
- Sodium chloride for inhalation
- Homatropine ophthalmic
- Thyroid products (e.g., Armour Thyroid, Nature-Thyroid, NP Thyroid, WP Thyroid)
- Phenazopyridine HCL (Pyridium) 100mg and 200mg tablets
- Nitro-time CPCR

- Salsalate tablet

*Exceptions will be made for these products to meet essential health benefit requirements

P&T Approval Date: Jul-01-2024

Title: Octreotide Products

Applicable Drugs:

Brand Name	Generic Name
Mycapssa	Octreotide

Policy:

ACROMEGALY

INITIAL CRITERIA: Octreotide acetate or octreotide (Mycapssa™) is medically necessary when ALL the following are met:

1. Member is 18 years of age or older; and
2. Diagnosis of acromegaly; and
3. Prescribed by or in conjunction with an endocrinologist; and
4. One of the following:
 1. Inadequate response to surgery or pituitary irradiation; or
 2. Not a candidate for surgical resection or pituitary irradiation; and
5. Inadequate response or inability to tolerate a dopamine agonist (e.g., bromocriptine or cabergoline) at maximally tolerated doses; and
6. For Mycapssa™ only, member has responded to and tolerated treatment with Octreotide or Lanreotide products (e.g., Somatulline Depot, Sandostatin, Sandostatin LAR depot).

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Octreotide acetate or octreotide (Mycapssa™) is medically necessary with documentation of positive clinical response to therapy (e.g., reduction or normalization of IFG-I or Growth Hormone level for same age and sex)

Reauthorization duration: 2 years

CARCINOID TUMORS, FOR SYMPTOMATIC TREATMENT OF DIARRHEA OR FLUSHING

INITIAL CRITERIA: Octreotide acetate is medically necessary when ALL the following are met:

1. Diagnosis of metastatic carcinoid tumor; and

2. Member requires symptomatic treatment of severe diarrhea or flushing episodes; and
3. Member is 18 years of age or older

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Octreotide acetate is medically necessary with documentation of an improvement in the number of diarrhea or flushing episodes.

Reauthorization duration: 2 years

VASOACTIVE INTESTINAL PEPTIDE TUMORS, FOR SYMPTOMATIC TREATMENT OF DIARRHEA

INITIAL CRITERIA: Octreotide acetate is medically necessary when ALL the following are met:

1. Diagnosis of vasoactive intestinal peptide tumor; and
2. Member requires the treatment of profuse watery diarrhea, and
3. Member is 18 years of age or older

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Octreotide acetate is medically necessary with documentation of an improvement in the number of diarrhea episodes.

Reauthorization duration: 2 years

P&T Approval Date: Sep-12-2024

Title: Odevixibat (Bylvay)

Applicable Drugs:

Brand Name	Generic Name
Bylvay™	odevixibat

Policy:

Progressive Familial Intrahepatic Cholestasis (PFIC)

INITIAL CRITERIA: Odevixibat (Bylvay™) is medically necessary when ALL of the following are met:

1. Diagnosis of pruritus associated with progressive familial intrahepatic cholestasis (PFIC); and
2. Confirmed molecular diagnosis of PFIC type 1, 2, or 3; and
3. Member is 3 months of age or older; and
4. Member is experiencing both of the following:
 1. Moderate to severe pruritus; and
 2. Serum bile acid concentration above the upper limit of the normal reference for the reporting laboratory; and
5. Prescribed dose is consistent with FDA-approved package labeling and does not exceed a total daily dose of 6mg; and
6. Prescribed by or in consultation with a hepatologist or gastroenterologist; and
7. Inadequate response or inability to tolerate at least TWO of the following treatments used for the relief of pruritus:
 1. Ursodeoxycholic acid (e.g., Ursodiol)
 2. Antihistamines (e.g., diphenhydramine, hydroxyzine)
 3. Rifampin
 4. Bile acid sequestrants (e.g., Questran, Colestid, Welchol)

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Odevixibat (Bylvay™) is medically necessary when BOTH of the following are met:

1. Documentation of positive clinical response to therapy (e.g., improvement in pruritus symptoms, reduced serum bile acids); and
2. Prescribed dose is consistent with FDA-approved package labeling and does not exceed a total daily dose of 6mg

Reauthorization duration: 2 years

Alagille Syndrome (ALGS)

INITIAL CRITERIA: Odevixibat (Bylvay™) is medically necessary when ALL of the following are met:

1. Diagnosis of Alagille Syndrome (ALGS); and
2. Molecular genetic testing confirms mutations in the JAG1 or NOTCH2 gene; and
3. Member is experiencing both of the following:
 - a. Moderate to severe pruritus; and
 - b. Serum bile acid concentration above the upper limit of the normal reference for the reporting laboratory; and
4. Inadequate response or inability to tolerate at least TWO of the following treatments used for the relief of pruritus:
 - a. Ursodeoxycholic acid (e.g., Ursodiol)
 - b. Antihistamines (e.g., diphenhydramine, hydroxyzine)
 - c. Rifampin
 - d. Bile acid sequestrants (e.g., cholestyramine, colestipol, colesevelam); and
5. Member is 12 months of age or older; and
6. Prescribed by or in consultation with a hepatologist or gastroenterologist

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Odevixibat (Bylvay™) is medically necessary when there is documentation of positive clinical response to therapy (e.g., reduced bile acids, reduced pruritus severity score)

Reauthorization duration: 2 years

P&T Approval Date: Dec-12-2024

Title: Off-Label Use

Policy:

Off-label uses are medically accepted and thus approved when BOTH of the following are met:

1. Request is NOT for an excluded benefit (e.g., cosmetic); and
2. ONE of the following:
 1. The narrative text in American Hospital Formulary Service--Drug Information (AHFS-DI®) is supportive of the use; or
 2. The use is classified as Category 1 or 2A by National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium™; or
 3. The use is classified as Class I or Class IIa in Micromedex®; or
 4. Adequate published clinical research (supplied by the provider) as defined below:

Authorization duration: 1 year

PUBLISHED CLINICAL RESEARCH

In order for an off-label use to be supported by published clinical research, all of the following criteria must be met:

A. The prescription drug or biologic must have been studied in at least two clinical trials conducted at different centers and the results must have been published in a national or international peer-reviewed journals with an editorial committee composed of physicians. Peer-reviewed medical literature includes scientific, medical, and pharmaceutical publications. It does not include in-house publications of pharmaceutical manufacturing companies or abstracts (including meeting abstracts).

1. A use is considered supported by clinical research when it appears in at least two Phase III clinical trials that have definitively demonstrated its safety and effectiveness as an appropriate medical treatment for the condition. If no Phase III trial evidence is available, at least two Phase II clinical trials with reasonably large patient samples showing consistent results of safety and efficacy may be considered in certain instances (e.g. rare diseases in which a Phase III study might be difficult to complete in a reasonable period of time after completion of the Phase II studies. Or when overwhelmingly good evidence of safety and effectiveness is noted in Phase II studies)

B. Reliable evidence must demonstrate that the proposed off label use for the specified medical condition is safe and effective and that the beneficial effects of the treatment outweigh its risks.

C. In determining whether there is supportive clinical evidence for a particular use of a prescription drug or biologic, the Company considers the quality of the evidence in published,

peer-reviewed medical literature. Among other things, such consideration involves the assessment of the following:

1. The prevalence and life history of the disease when evaluating the adequacy of the number of subjects and the response rate
2. The effect on the individual's well-being and other responses to therapy that indicate effectiveness (e.g. reduction in mortality, morbidity, and signs and symptoms)
3. Whether the clinical characteristics of the beneficiary and the indication are adequately represented in the published evidence
4. Whether the study is appropriate to address the clinical question, such as:
 1. If the study design is appropriate to address investigative questions (e.g. in some clinical studies, it may be unnecessary or not feasible to use randomized, double-blind trial, placebos, or crossover)
 2. If non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs
 3. Generally, case reports are considered uncontrolled, are based on anecdotal information, and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
5. The off-label use is supported by published clinical research and the results have been published in major, peer-reviewed medical journals such as, but not limited to:

American Journal of Medicine	Gynecologic Oncology
American Journal of Psychiatry	International Journal of Radiation, Oncology, Biology and Physics
Annals of Internal Medicine	Journal of Clinical Oncology
Annals of Oncology	Journal of Obstetrics and Gynecology
Annals of Surgical Oncology	Journal of Pediatrics
Archives of Pediatric and Adolescent Medicine	Journal of the National Cancer Institute

Biology of Blood and Marrow Transplantation	Journal of the National Comprehensive Cancer Network (NCCN)
British Journal of Cancer	Journal of Urology
British Journal of Hematology	Lancet
British Medical Journal	Lancet Oncology
Cancer	Leukemia
Clinical Cancer Research	Pediatrics
Drugs	Radiation Oncology
European Journal of Cancer	The Journal of the American Medical Association
Bone Marrow Transplantation	The New England Journal of Medicine

EXPERIMENTAL/INVESTIGATIONAL

Prescription drugs that are considered experimental/investigational are not covered because the safety and/or efficacy of the drug for those purposes cannot be established by a review of the available published peer reviewed literature. Prescription drugs and biologics are considered experimental/investigational for any of the following:

1. The prescription drug or biologic has not received FDA approval for any use
2. The off-label use of the prescription drug or biologic does not meet the medical necessity criteria listed in this policy or in any other specific Company Pharmacy Policy addressing a drug and/or biologic (i.e. the off-label use is not recognized by the appropriate compendia or published clinical research). This includes products granted orphan designation by the FDA.
3. The FDA determined the prescription drug or biologic to be contraindicated for specific condition(s) or specific off-labels use(s)
4. The off-label use is not medically accepted or not indicated by a compendium for specific conditions (i.e. the indication is Category 3 in NCCN, Class III in Micromedex®) or when the narrative text in AHFS-DI® is not supportive)

- a. The absence of narrative text for an off-label use is considered neither supportive nor non-supportive

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include but are not limited to records from the professional provider's office, hospital, nursing home, home health agency, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the service.

P&T Approval Date: Mar-20-2025

Title: Omalizumab (Xolair)-Pharmacy

Applicable Drugs:

Brand Name	Generic Name
Xolair®	Omalizumab

Policy:

Allergic asthma

INITIAL CRITERIA: Omalizumab (Xolair®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of moderate to severe persistent allergic asthma; and
2. Submission of documentation (e.g., chart notes, lab values) confirming a positive skin test or in vitro reactivity to a perennial aeroallergen; and
3. One of the following:
 1. Both of the following:
 1. Member is 12 years of age or older; and
 2. Submission of documentation (e.g., chart notes, lab values) confirming pre- treatment serum immunoglobulin IgE level between 30 to 700 IU/mL; or
 2. Both of the following:
 1. Member is 6 years to less than 12 years of age; and
 2. Submission of documentation (e.g., chart notes, lab values) confirming pre-treatment serum immunoglobulin IgE level between 30 to 1300 IU/mL; and
4. ONE of the following:
 1. Member is 6 to less than 12 years of age and paid claims or submission of documentation (e.g., chart notes) confirming the member is currently being treated or has a contraindication or intolerance to one of the following:
 1. Medium-dose inhaled corticosteroids greater than 100-200mcg fluticasone propionate equivalent/day) and ONE additional controller medication (e.g., leukotriene receptor antagonist [LTRA] (e.g., montelukast), long-acting beta-2 agonist [LABA] (e.g., salmeterol), long-acting muscarinic antagonist [LAMA] (e.g., tiotropium); or
 2. One medium-dose combination ICS/LABA product (e.g., Advair [fluticasone propionate/salmeterol], Breo Ellipta [fluticasone furoate/vilanterol], Symbicort [budesonide/formoterol]); or
 2. Member is 12 years of age or older and paid claims or submission of documentation (e.g., chart notes) confirming that the member is currently being treated or has a contraindication or intolerance to ONE of the following
 1. High dose inhaled corticosteroid (ICS) (e.g. greater than or equal to 500 mcg fluticasone propionate equivalent/day); and ONE additional asthma controller medication (e.g. leukotriene receptor antagonist [LTRA] (e.g., montelukast), long-acting beta-2 agonist [LABA] (e.g., salmeterol), long-acting muscarinic antagonist [LAMA] (e.g., tiotropium)); or
 2. One maximally dosed combination ICS/ LABA product (e.g. Advair [fluticasone propionate/salmeterol], Breo Ellipta [fluticasone/vilanterol], Symbicort [budesonide/formoterol]); and
5. Prescribed by or in consultation with one of the following:
 1. Pulmonologist; or

2. Allergist/ immunologist; and
6. Treatment will be initiated in a healthcare setting with at least 3 doses administered under the supervision of a healthcare provider; and
7. No concurrent therapy with any other biologic agents; and
8. Dosing and frequency does not exceed maximum FDA recommendation for indication requested

Initial authorization duration: 12 months

CONTINUATION CRITERIA: Omalizumab (Xolair®) is medically necessary when ALL of the following are met:

1. Submission of documentation (e.g., chart notes) confirming a positive clinical response to therapy (e.g., reduction in exacerbations, improvement in forced expiratory volume in 1 second [FEV1], decreased use of rescue medications); and
2. Prescribed by or in consultation with one of the following:
 1. Pulmonologist; or
 2. Allergist/Immunologist; and
3. ONE of the following:
 1. Member is 6 to less than 12 years of age and paid claim or submission of documentation (e.g., chart notes) confirming the member is currently being treated or has a contraindication or intolerance to one of the following:
 1. Medium-dose inhaled corticosteroids (e.g., greater than 100-200mcg fluticasone propionate equivalent/day) with or without ONE additional controller medication (e.g., leukotriene receptor antagonist [LTRA] (e.g., montelukast), long-acting beta-2 agonist [LABA] (e.g., salmeterol), long-acting muscarinic antagonist [LAMA] (e.g., tiotropium)); or
 2. One medium-dose combination ICS/LABA product (e.g., Advair [fluticasone propionate/salmeterol], Breo Ellipta [fluticasone furoate/vilanterol], Symbicort [budesonide/formoterol]); or
 2. Member is 12 years of age or older and paid claims or submission of documentation (e.g., chart notes) confirming that the member is currently being treated or has a contraindication or intolerance to one of the following:
 1. High dose inhaled corticosteroid (ICS) (e.g., greater than or equal to 500 mcg fluticasone propionate equivalent/day) with or without ONE additional asthma controller medication (e.g., leukotriene receptor antagonist [LTRA] (e.g., montelukast), long-acting beta-2 agonist [LABA] (e.g., salmeterol), long-acting muscarinic antagonist [LAMA] (e.g., tiotropium)); or
 2. One maximally dosed combination ICS/ LABA product (e.g., Advair [fluticasone propionate/salmeterol], Breo Ellipta [fluticasone/vilanterol], Symbicort [budesonide/formoterol]); and
4. No concurrent therapy with any other biologic agents; and
5. ONE of the following:
 1. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
 2. Member is continuing on the established dose and frequency previously approved

Continuation approval duration: 12 months

DOSE	
Adults and pediatric patients 6 years of age and older	75 to 375 mg every 2 or 4 weeks. Determine dose (mg) and dosing frequency by serum total IgE level, measured before the start of treatment, and body weight (kg). Refer to omalizumab (Xolair®) Prescribing Information for additional information.

Chronic Spontaneous Urticaria

INITIAL CRITERIA Omalizumab (Xolair®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of chronic spontaneous urticaria; and
 2. Member is 12 years of age or older; and
 3. Paid claims or submission of documentation (e.g., chart notes) confirming an inadequate response or inability to tolerate one second- generation antihistamine (e.g., desloratadine) at maximally tolerated dose in addition to ONE of the following:
 - a. Substituting to a different second- generation antihistamine; or
 - b. H2 antagonist (e.g., famotidine, cimetidine); or
 - c. Doxepin; or
 - d. Leukotriene receptor antagonist (e.g., montelukast); or
 - e. Systemic corticosteroids; or
 - f. cyclosporine; and
 4. Paid claims or submission of documentation (e.g., chart notes) confirming that Xolair will be used concurrently with an H1 antihistamine, unless there is a contraindication or intolerance to H1 antihistamine; and
 5. Prescribed by or in consultation with one of the following:
 - a. Allergist/ immunologist; or
 - b. Dermatologist; and
 6. Treatment will be initiated in a healthcare setting with at least 3 doses administered under the supervision of a healthcare provider; and
 7. No concurrent therapy with any other biologic agents; and
 8. Dosing and frequency does not exceed maximum FDA recommendation for indication requested
- Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Omalizumab (Xolair®) is medically necessary when ALL of the following are met:

1. Member's disease status has been re-evaluated since the last authorization to confirm the member's condition warrants continued treatment; and
 2. Submission of documentation (e.g., chart notes) confirming that the member has experienced at least one of the following:
 - a. Reduction in itching severity from baseline; or
 - b. Reduction in the number of hives from baseline; and
 3. Prescribed by or in consultation with one of the following:
 - a. Dermatologist; or
 - b. Allergist/Immunologist; and
 4. No concurrent therapy with any other biologic agents; and
 5. ONE of the following:
 - a. Dosing and frequency does not exceed maximum FDA recommendation for indication requested; or
 - b. Member is continuing on the established dose and frequency previously approved
- Reauthorization duration: 12 months

DOSE	
Adults and pediatric patients 12 years of age and older	150 mg or 300 mg every 4 weeks. Dosing in CSU is not dependent on serum IgE level or body weight.

Chronic Rhinosinusitis with Nasal Polyps

INITIAL CRITERIA: Omalizumab (Xolair®) is medically necessary when ALL of the following are met:

1. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of chronic rhinosinusitis with nasal polyps (CRSwNP); and
2. Member has baseline serum IgE level of between 30 IU/mL and 1500 IU/mL; and

3. Paid claims or submission of documentation confirming an inadequate response or inability to tolerate at least a 2-month treatment with intranasal corticosteroid; and
 4. Used in combination with another agent for nasal polyps (e.g. intranasal corticosteroid); and
 5. Prescribed by or in consultation with one of the following:
 - a. Allergist/Immunologist; or
 - b. ENT specialist; or
 - c. Pulmonologist; and
 6. Treatment will be initiated in a healthcare setting with at least 3 doses administered under the supervision of a healthcare provider; and
 7. No concurrent therapy with any other biologic agents; and
 8. Dosing and frequency does not exceed maximum FDA recommendation for indication requested
- Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Omalizumab (Xolair®) is medically necessary when ALL of the following are met:

1. Documentation of positive clinical response to therapy (e.g., reduction in nasal polyps score [NPS: 0-8 scale], improvement in nasal congestion/obstruction score [NCS: 0-3 scale]); and
2. Used in combination with another agent for nasal polyps (e.g. intranasal corticosteroid); and
3. Prescribed by or in consultation with one of the following:
 - a. Allergist/immunologist; or
 - b. ENT specialist; or
 - c. Pulmonologist; and
4. No concurrent therapy with any other biologic agents; and
5. ONE of the following:
 - a. Dosing and frequency does not exceed maximum FDA recommendation for indication requested; or
 - b. Member is continuing on the established dose and frequency previously approved

Reauthorization duration: 12 months

DOSE	
Adults	75 to 600 mg every 2 or 4 weeks. Determine dose (mg) and dosing frequency by serum total IgE level, measured before the start of treatment, and body weight (kg). Refer to omalizumab (Xolair®) Prescribing Information for additional information.

IgE-Mediated Food Allergy

INITIAL CRITERIA: Omalizumab (Xolair®) is medically necessary when ALL of the following are met:

1. Submission of documentation (e.g., chart note, lab values) confirming ONE of the following:
 1. BOTH of the following:
 1. Diagnosis of IgE mediated food allergy as evidenced by one of the following:
 1. Positive skin prick test (defined as greater than or equal to 4 mm wheal greater than saline control) to food; or
 2. Positive food specific IgE (greater than or equal to 6 kUA/L); or
 3. Positive oral food challenge, defined as experiencing dose- limiting symptoms at a single dose of less than or equal to 300 mg of food protein; and
 2. Clinical history of IgE mediated food allergy; or
 2. Member has a history of severe allergic response, including anaphylaxis, following exposure to one or more foods; and
2. Member is 1 year of age or older; and

3. Used in conjunction with food allergen avoidance; and
4. Submission of documentation (e.g., chart notes, lab values) confirming both of the following:
 1. Baseline (pre-Xolair treatment) serum total IgE level is greater than or equal to 30 IU/ml and less than or equal to 1850 IU/ml; and
 2. Dosing is according to serum total IgE levels and body weight; and
5. Prescribed by or in consultation with allergist or immunologist; and
6. No concurrent therapy with any other biologic agents; and
7. Dosing and frequency does not exceed maximum FDA recommendation for indication requested

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Omalizumab (Xolair®) is medically necessary when ALL of the following are met:

1. Submission of documentation (e.g., chart notes, lab values) confirming a positive clinical response to therapy (e.g., reduction of type 1 allergic reactions, including anaphylaxis, following accidental exposure to one or more foods); and
2. Used in conjunction with food allergen avoidance; and
3. Submission of documentation (e.g., chart notes, lab values) confirming that dosing will continue to be based on body weight and pretreatment total IgE serum levels (Note: Dose should only be adjusted during therapy due to significant changes in member's body weight); and
4. No concurrent therapy with any other biologic agents; and
5. ONE of the following:
 - a. Dosing and frequency does not exceed maximum FDA recommendation for indication requested; or
 - b. Member is continuing on the established dose and frequency previously approved

Reauthorization duration: 12 months

DOSE	
Adults and pediatric patients aged 1 year and older	75mg to 600mg every 2 or 4 weeks. Determine dose (mg) and dosing frequency by serum total IgE level (IU/ml), measured before the start of treatment, and body weight (kg). See the dose determination chart in the Prescribing Information.

P&T Approval Date: March 20, 2025

Title: Omaveloxolone (Skyclarys®)

Applicable Drugs:

Brand Name	Generic Name
Skyclarys®	Omaveloxolone

Policy:

INITIAL CRITERIA: Omaveloxolone (Skyclarys®) is approved when all of the following are met:

1. Diagnosis of Friedreich ataxia as confirmed via genetic testing demonstrating mutation in FXN gene; and
2. Member has a Modified Friedreich's Ataxia Rating Scale (mFARS) score of greater than or equal to 20 and less than or equal to 80; and
3. Member has B-type natriuretic peptide value less than or equal to 200 pg/ml; and
4. Member is 16 years of age or older; and
5. Prescribed by or in consultation with one of the following:
 1. Neurologist; or
 2. Neurogeneticist; or
 3. Physiatrist (Physical Medicine and Rehabilitation Specialist)

Initial authorization duration: 1 year

CONTINUATION CRITERIA: Omaveloxolone (Skyclarys®) is re-approved when BOTH of the following are met:

1. Documentation of positive clinical response to therapy as evidenced by one of the following:
 1. A decrease in the rate of progression of Modified FA rating scale (mFARS) score; or
 2. An increase in peak work (in Watts/kg) during exercise testing from baseline; and
2. Prescribed by or in consultation with one of the following:
 1. Neurologist; or
 2. Neurogeneticist; or

3. Physiatrist (Physical Medicine and Rehabilitation Specialist)

Reauthorization duration: 1 year

P&T Approval Date: Mar-20-2025

Title: Oncology agents

Applicable Drugs:

Brand Name	Generic Name
Gleevec®	imatinib mesylate
Voranigo®	Vorasidenib
Nexavar®	sorafenib
Revlimid®	lenalidomide
Sprycel®	dasatinib
Sutent®	sunitinib malate
Tarceva®	erlotinib
Thalomid®	thalidomide
Zolinza®	vorinostat
Tykerb®	lapatinib
Tasigna®	nilotinib
Hycamtin®	topotecan
Temodar®	temozolimide
Afinitor®, Torpenz	everolimus
Oforta®	fludarabine Phosphate
Votrient®	pazopanib

Caprelsa®	vandetanib
Zytiga®	abiraterone
Zelboraf®	vemurafenib
Xalkori®	crizotinib
Jakafi®	ruxolitinib
Inlyta®	axitinib
Erivedge®	vismodegib
Xtandi®	enzalutamide
Bosulif®	bosutinib
Stivarga®	regorafenib
Iclusig®	ponatinib
Cometriq®, Cabometyx®	cabozantinib
Pomalyst®	pomalidomide
Tafinlar®	dabrafenib
Mekinist®	trametinib
Gilotrif®	afatinib
Imbruvica®	ibrutinib
Zykadia®	ceritinib
Zydelig®	idelalisib

Lynparza®	olaparib
Ibrance®	palbociclib
Lenvima®	lenvatinib
Lonsurf®	trifluridine/tipiracil
Odomzo®	sonidegib
Alecensa®	alectinib
Cotellic®	cobimetinib
Ninlaro®	ixazomib
Tagrisso®	osimertinib
Venclexta®	venetoclax
Rubraca®	rucaparib
Kisqali®	ribociclib
Zejula®	niraparib
Alunbrig®	brigatinib
Nerlyx®	neratinib
Rydapt®	midostaurin
Idhifa®	enasidenib
Verzenio®	abemaciclib
Calquence®	acalabrutinib
Tibsovo®	ivosidenib

Mektovi®	binimetinib
braftovi®	encorafenib
Erleada™	apalutamide
Copiktra™	duvelisib
Vizimpro®	dacomitinib
Talzenna®	talazoparib
Lorbrena®	lorlatinib
Daurismo™	glasdegib
Vitrakvi®	larotrectinib
Xospata®	gilteritinib
Balversa®	erdafitinib
Piqray®	alpelisib
Xpovio™	selinexor
Targretin® oral capsule and topical gel	bexarotene
Nubeqa®	darolutamide
Turalio™	pexidartinib
Rozlytrek™	entrectinib
Inrebic®	fedratinib

Ayvakit™	avapritinib
Brukina®	Zanubrutinib
Koselugo™	selumetinib
Tazverik™	tazemetostat
Tukysa™	tucatinib
Pemazyre™	pemigatinib
Qinlock®	ripretinib
Retevmo™	selpercatinib
Tabrecta™	capmatinib
Iressa®	Gefitinib
	tretinoin capsules
Gavreto™	Pralsetinib
Inqovi®	Deciabine and cedazuridine
Onureg®	azacitidine
Orgovyx™	relugolix
Tepmetko®	tepotinib
Ukoniq™	umbralisib
Fotivda®	tivozanib
Truseltiq™	infigratinib

Lumakras™	sotorasib
Valchlor®	mechlorethamine
Exkivity™	mobocertinib
Welireg™	belzutifan
Besremi®	ropeginterferon alfa-2b-njft
Scemblix®	asciminib
Vonjo™	Pacritinib
Panretin®	Alitretinoin
Krazati™	Adagrasib
Lytgobi®	Futibatinib
Rezlidhia™	Olutasidenib
Jaypirca™	Pirtobrutinib
Orserdu™	Elacestrant
Akeega™	Niraparib/abiraterone
Ojjaara®	momelotinib
Vanflyta®	quizartinib
Augtyro™	repotrectinib
Fruzaqla™	fruquintinib
Iwilfin™	eflornithine

Ogsiveo®	nirogacestat
Truqap™	capivasertib
Lazcluze™	lazertinib
Itovebi™	inavolisib
Revuforj	revumenib

Policy:

A. Oncology agents are medically necessary when ONE of the following is met:

1. Drug is FDA approved for indication and regimen requested, including confirmation by genetic and/or biomarker testing when appropriate; or
2. The indication and regimen are classified as Category 1 or 2A by National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium™; or
3. The narrative text in American Hospital Formulary Service--Drug Information (AHFS-DI®) is supportive of the use; or
4. The indication is classified as Class I or Class IIa in Micromedex®

B. Ibrance®, Imbruvica® 140mg, 280mg tablet, Yonsa® or Zytiga® is medically necessary when BOTH of the following are met:

1. One of the following:
 - a. Drug is FDA approved for indication and regimen requested, including confirmation by genetic and/or biomarker testing when appropriate; or
 - b. The indication and regimen are classified as Category 1 or 2A by National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium™; or
 - c. The narrative text in American Hospital Formulary Service—Drug Information (AHFS-DI®) is supportive of the use; or
 - d. The indication is classified as Class I or Class IIa in Micromedex®; and
2. ONE of the following:
 - a. For Brand Yonsa® only; ,: inadequate response or inability to tolerate Xtandi®; or
 - b. For Brand Zytiga® only: inadequate response or inability to tolerate Xtandi® or Erleada®; or
 - c. For Brand Ibrance® only, inadequate response or inability to tolerate Kisqali® and Verzenio®; or

- d. For Imbruvica® 140mg, 280mg tablet only, inadequate response or inability to tolerate Imbruvica® 140mg capsule; or
- e. For Brand Yonsa®, Brand Zytiga®, Brand Ibrance®, Imbruvica® 140mg, 280mg tablet only, request is for continuation of therapy

Authorization duration: 2 years

P&T Approval Date: Mar-20-2025

Title: Onychomycosis agents

Applicable Drugs:

Brand Name	Generic Name
Jublia®	Efinaconazole
Kerydin®	Tavaborole
Ciclodan®	Ciclopirox

Policy:

Efinaconazole (Jublia®), tavaborole (Kerydin®), or ciclopirox (Ciclodan®) 8% topical solution is medically necessary when ALL of the following are met:

1. Diagnosis of onychomycosis confirmed by one of the following:
 - a. Positive potassium hydroxide (KOH) preparation; or
 - b. Culture; or
 - c. Histology and
2. The member does not have dermatophytomas or lunula (matrix) involvement; and
3. Inadequate response or inability to tolerate BOTH of the following:
 - a. oral generic terbinafine; and
 - b. oral generic itraconazole OR topical generic ciclopirox; and
4. One of the following:
 - a. For efinaconazole (Jublia®) and tavaborole (Kerydin®) only, member is 6 years of age or older; or
 - b. For ciclopirox (Ciclodan®) 8% topical solution only, member is 12 years of age or older; and
5. For Brand Kerydin only, inadequate response or inability to tolerate generic tavaborole

Authorization duration: 1 year

P&T Approval Date: Dec-12-2024

Title: Opioids

Policy:

PRIOR AUTHORIZATION

I. Transmucosal Immediate Release Fentanyl (TIRF) Product fentanyl citrate is considered medically necessary when:

A. INITIAL CRITERIA [Authorization duration: 1 year]: Transmucosal Immediate Release Fentanyl (TIRF) Products are considered medically necessary when there is documentation of ALL of the following:

1. Use for breakthrough pain associated with active cancer treatment or cancer not in remission in members who are receiving long-acting opioid therapy; and
2. Member is 18 years of age or older (16 years of age and older for fentanyl citrate); and
3. Member is tolerant to current opioid therapy (i.e., adherence to one of the following regimens for one week or longer: 25mcg of transdermal fentanyl hourly, 30mg of oxycodone daily, 60mg of oral morphine daily, 8mg of oral hydromorphone daily, 25mg of oral oxymorphone daily; or an equianalgesic dose of another opioid)

B. REAUTHORIZATION CRITERIA [Authorization duration: 1 year]: Transmucosal Immediate Release Fentanyl (TIRF) product is re-approved when there is documentation of continued use for breakthrough pain associated with active cancer treatment or cancer not in remission in members who are currently receiving long-acting opioid therapy

II. Opioid regimens containing greater than 90 morphine milligram equivalents per day, long acting opioids, and short acting opioids for continuation beyond 30 days [Authorization duration: 1 year] - are considered medically necessary as follows:

A. INITIAL CRITERIA: The requested product or regimen is considered medically necessary when there is ONE of the following:

1. Pain associated with active cancer treatment, cancer not in remission, or sickle cell anemia (regardless of age); OR
2. Severe, persistent chronic pain with documentation of diagnosis associated with pain and ALL of the following:

1. Documentation of a current patient-prescriber opioid treatment agreement (signed within one year of request); and
2. ONE of the following

1. Documentation of a current patient-prescriber opioid treatment agreement (signed within one year of request); and
2. documentation that a urine drug screen (UDS) will be performed by prescriber within 1 year of request.

III. Appropriate Utilization with Medication Assistant Treatments (MAT) for opioid use disorder - [Authorization duration: 2 months] - Opioid analgesics will require prior authorization for medical necessity when filled within two months of a paid claim for either buprenorphine/naloxone (Bunavail®/Suboxone®/Zubsolv®) or buprenorphine sublingual tablet. Opioid analgesic products are approved in patients that have received buprenorphine/naloxone or buprenorphine in the previous two months when there is documentation of a treatment plan showing discontinuation of buprenorphine containing MAT.

DAYS' SUPPLY AND QUANTITY LIMITS

I. Day supply limit Criteria

A. Short-acting opioids for short term use (greater than two 5-day fills within 60 days for 18 and older, and greater than two 3-day fills within 60 days for age less than 18) [Authorization duration: 1 month for a 30 days' supply] - an exception is approved when ALL of the following are met:

INITIAL CRITERIA

1. Diagnosis of acute pain; and
2. Prescriber reviewed member's history in state Prescription Drug Monitoring Program website; and
3. Prescriber counseled member (or member's representative) on risk of addiction; and
4. Substance abuse screening done by prescriber

REAUTHORIZATION CRITERIA see Opioid regimens containing greater than 90 morphine milligram equivalents per day, long acting opioids, and short acting low dose opioids for continuation beyond additional 30 days Prior Authorization criteria under section under section II.A above

B. Opioid containing cough and cold products are limited to two five (5) day fills within 60 days for 18 and older and two 3-day fills within 60 days for age less than 18 - an exception is approved when

INITIAL CRITERIA: there is documentation of inadequate response or inability to tolerate non-opioid therapies for the indication [Authorization duration 1 month]

EAUTHORIZATION CRITERIA: Documentation the underlying etiology of cough has been identified and treated, if applicable (e.g., allergic rhinitis, asthma, GERD) [Authorization duration 6 months]

C. Butalbital containing headache products are limited to one five (5) day fill within 30 days. Opioid containing headache products are limited to one three (3) day fill within 30 days for less than 18 years of age, an exception is approved as follows:

INITIAL CRITERIA [Authorization duration: 3 months]: All of the following:

- 1. Diagnosis of one of the following:**
 - 1. Tension-type or muscular headache**
 - 2. Migraine headache**
- 2. Member is 12 years of age or older**
- 3. Inadequate response or inability to tolerate TWO of the following:**
 - 1. At least two triptans**
 - 2. Non-steroid anti-inflammatory drugs (e.g., ibuprofen, naproxen)**
 - 3. Neuroleptics (e.g., prochlorperazine, metoclopramide)**
 - 4. Dihydroergotamine**

REAUTHORIZATION CRITERIA: [Authorization duration: 1 year]: All of the following:

- 1. Diagnosis of one of the following:**
 - 1. Tension-type or muscular headache**
 - 2. Migraine headache**
- 2. Member is 12 years of age or older**
- 3. Prescribed by or in consultation with a neurologist or a headache specialist, or pain specialist**
- 4. Inadequate response or inability to tolerate NSAIDs**
- 5. Ongoing assessment of medication-overuse headache**

II. Quantity limit Criteria –

A. Opioid pain products [authorization duration = 1 year] An increased quantity of an opioid medication is approved when there is documentation of ALL of the following:

1. Current patient-prescriber opioid treatment agreement (signed within one year of request); and
2. The requested dose and frequency do not exceed FDA approved dosing or are supported by compendia; and
3. ONE of the following:
 1. The dose cannot be achieved with commercially available clinical dosage forms; or
 2. Documentation indicating medical necessity for a quantity that exceeds the plan limit (e.g. GI malabsorption).

B. Cough and cold products [Authorization duration: 1 month for initial; 6 months for reauthorizations] - An increased quantity of an opioid containing cough and cold medication is approved when there is documentation of ALL of the following:

1. The requested dose and frequency do not exceed FDA approved dosing or are supported by compendia; and
2. Documentation of diagnosis requiring long-term therapy with requested cough/ cold medications; and
3. Inadequate response or inability to tolerate non-opioid therapies for the indication

C. Butalbital containing headache products [Authorization duration:1 year] - An increased quantity of a butalbital containing headache medication is approved when there is documentation of ALL of the following:

1. The requested dose and frequency do not exceed FDA approved dosing or are supported by compendia; and
2. Inadequate response or inability to tolerate prophylactic therapy; and
3. Prescribed by or in consultation with a neurologist, headache specialist or pain specialist.

D. Buprenorphine/ naloxone (Bunavail®/Suboxone®/Zubsolv®) and buprenorphine sublingual tablet [Authorization duration: 6 months]: buprenorphine/ naloxone or buprenorphine for the treatment of opioid use disorder are approved in quantities greater than those specified in the policy when ALL of the following are met:

1. The requested dose and frequency do not exceed FDA approved dosing or are supported by compendia; and

2. The dose cannot be achieved with commercially available dosage forms; and
3. Inadequate response to lower doses

All products containing the active ingredients in the chart below are subject to the following:

- Opioid regimens containing greater than 90 morphine milligram equivalents per day
- Appropriate Utilization with Medication Assistant Treatments (MAT) for opioid use disorder

Active ingredient
Benzhydrocodone
Codeine
Dihydrocodeine
Fentanyl
Hydrocodone
Hydromorphone
Levorphanol
Meperidine
Methadone
Morphine
Opium
Oxycodone
Oxymorphone
Tapentadol

Tramadol

The table below identifies medications that are found in the following sections of this policy:

- Transmucosal Immediate Release Fentanyl (TIRF) Products (¥ identifies impacted medications)
- Opioid regimens containing greater than 90 morphine milligram equivalents per day, long acting opioids, and short acting low dose opioids for continuation beyond 30days (*identifies impacted long acting opioids)
- Days' Supply and Quantity Limits

Drug Name	Days' Supply Limit	Maximum Quantity per Day	Quantity limit per rolling 30 days, unless otherwise specified (tablet, capsule)
Acetaminophen/codeine #2 300/15mg tab	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	12	
Acetaminophen/codeine #3 300/30mg tab	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	12	

Acetaminophen/codeine #4 300/60mg tab	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	6	
Acetaminophen/codeine liquid	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	90mL	
Benzhydrocodone/acetaminophen (Apadaz®)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	12	
Buprenorphine film* (Belbuca®)	No	2	
Buprenorphine patch* (Butrans®)	No		4 patches
Buprenorphine sublingual tablet 2mg	No	4	
Buprenorphine sublingual tablet 8mg	No	3	
Buprenorphine/naloxone (Suboxone® 2/0.5mg, 4/1mg)	No	4	

Buprenorphine/ naloxone (Suboxone® 8/2mg)	No	3	
Buprenorphine/ naloxone (Suboxone® 12/3mg)	No	2	
Buprenorphine/naloxone (Zubsolv® 1.4/0.36mg, 2.9-0.71mg)	No	4	
Buprenorphine/naloxone (Zubsolv® 5.7/1.4mg, 0.7/0.18mg)	No	3	
Buprenorphine/naloxone (Zubsolv® 8.6/2.1mg)	No	2	
Buprenorphine/naloxone (Zubsolv® 11.4-2.9mg)	No	1	
Buprenorphine/naloxone 2.1/0.3mg	No	4	
Buprenorphine/naloxone 4.2/0.7mg	No	3	
Buprenorphine/naloxone 6.3/1mg	No	1	
Butalbital/apap (Allzital®)	one 5-day fill per 30 days	6	
Butalbital/apap/caffeine without codeine (Esgic®, Fioricet®)	one 5-day fill per 30 days	6	
Butalbital/apap/caffeine with codeine (Esgic®, Fioricet®/codeine)	one 5-day fill per 30 days for 18 and over; one 3-day fill per 30 days for less than 18	6	

Butalbital/asa/caffeine without codeine	one 5-day fill per 30 days	6	
Butalbital/asa/caffeine with codeine	one 5-day fill per 30 days for 18 and over; one 3-day fill per 30 days for less than 18	6	
Carisoprodol/ aspirin/ codeine	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	8	
Codeine sulfate tablets 15mg, 30mg	two 5-day fills per 60 for 18 and older; two 3-day fills per 60 days for less than 18	12	
Codeine sulfate tablets 60mg	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	6	

Codeine/chlorpheniramine (Tuxarin® ER)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	2	
Codeine/chlorpheniramine tablets	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	20mL	
Codeine/ chlorpheniramine solution	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	60mL	
Dihydrocodeine/ acetaminophen/ caffeine (Trezix®)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	10	
Fentanyl IR [¥] (Actiq®, Fentora®)	No	4	
Fentanyl nasal solution [¥]	No	1	

Fentanyl patch*	No		15 patches
Guaifenesin/ codeine (Coditussin® AC)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	60mL	
Guaifenesin/ codeine (MAR-COF® CG)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	45mL	
Guaifenesin/ codeine	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	90mL	
Hydrocodone bitartrate ER* (Hysingla® ER)	No	1	
Hydrocodone bitartrate ER*	No	2	
Hydrocodone/acetaminophen 2.5/325mg, 5/300mg, 7.5/300mg, 5/325mg, 7.5/325mg tab (Xodol®)	two 5-day fills per 60 days for 18 and older; two 3-day	12	

	fills per 60 days for less than 18		
Hydrocodone/apap 10/325mg, 10/300mg tab (Xodol®)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	6	
Hydrocodone/apap liquid (10mg/325mg/15ml, 2.5mg/167mg/5ml, 5mg/333mg/10ml, 7.5mg/325mg/15ml, 10mg/300mg/15ml)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	90mL	
Hydrocodone/chlorpheniramine	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	10mL	
Hydrocodone/chlorpheniramine	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	2	

Hydrocodone/ homatropine (Hydromet®)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	30mL	
Hydrocodone/ homatropine	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	6	
Hydrocodone/ibuprofen	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	5	
Hydromorphone (Dilaudid®)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	6	
Hydromorphone 1mg/1ml liquid (Dilaudid®)	two 5-day fills per 60 days for 18	12mL	

	and older; two 3-day fills per 60 days for less than 18		
Hydromorphone extended release* (Exalgo®)	No	2	
Levorphanol tartrate 2mg	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	6	
Levorphanol tartrate 3mg	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	4	
Meperidine 50mg/5ml liquid	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	67mL	
Meperidine HCL (Demerol®)	two 5-day fills per 60 days for 18	6	

	and older; two 3-day fills per 60 days for less than 18		
Methadone* tabs 5mg, 10mg	No	6	
Methadone solution* 5mg/5ml	No	60mL	
Methadone solution* 10mg/5ml	No	30mL	
Methadone solution* (Methadose concentrate, Methadose sugar-free concentrate) 10mg/1ml	No	6mL	
Morphine 10mg/5ml liquid	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	45 mL	
Morphine 20mg/5ml liquid	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	23 mL	
Morphine concentrate 20mg/1ml, 10mg/0.5ml, 5mg/0.25ml liquid	two 5-day fills per 60 days for 18 and older;	6mL	

	two 3-day fills per 60 days for less than 18		
Morphine sulfate IR (MSIR®)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	6	
Morphine sulfate ER capsules*	No	1	
Morphine sulfate ER capsules*	No	2	
Morphine sulfate SR*	No	3	
Morphine sulfate SR* (MS Contin®)	No	3	
Morphine sulfate/naltrexone*	No	2	
Morphine suppositories 5mg	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	18	
Morphine suppositories 10mg	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60	6	

	days for less than 18		
Morphine suppositories 20mg, 30mg	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	6	
Opium tincture	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	N/A	
Oxycodone 7.5mg tab (Oxaydo®)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	8	
Oxycodone HCL (Oxy® IR/Roxicodone®/Oxaydo®, Roxybond®) 5mg caps/tabs	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	12	

Oxycodone HCL (Oxy® IR/Roxicodone®, Roxybond®), 10mg, 15 mg, 30mg caps/tabs	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	6	
Oxycodone 5mg/5ml liquid	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	60 mL	
Oxycodone highly concentrated liquid 20mg/1ml liquid	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	6mL	
Oxycodone HCL ER* (Oxycontin®)	No	3	
Oxycodone ER* (Xtampza® ER)	No	2	
Oxycodone/Acetaminophen, Endocet® (Percocet®, Nalocet®, Prolate®) 2.5/325mg tab, 2.5/300mg tab, 5/300mg, 5/325mg tab	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	12	

Oxycodone/Acetaminophen (Prolate®) 7.5/300mg tab, 10/300mg tab	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	6	
Oxycodone/acetaminophen 7.5/325mg tab (Endocet®/Percocet®)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	8	
Oxycodone/acetaminophen 10/325mg tab (Endocet®/Percocet®)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	6	
Oxycodone/acetaminophen 5mg/325mg/5ml liquid	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	60	

Oxycodone/aspirin 4.8355/325mg tab	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	12	
Oxycodone/Acetaminophen (Prolate®) 10-300mg/5ml soln	Two 5-days fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	30 ml	
Oxymorphone HCL	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	6	
Oxymorphone HCL ER*	No	3	
Phenylephrine/ brompheniramine/ codeine	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	90mL	

Phenylephrine/ chlorpheniramine/ codeine (Capcof®)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	60mL	
Phenylephrine/ dexchlorpheniramine/ codeine (Pro-red® AC)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	60mL	
Promethazine/codeine 6.25-10mg/5mL syrup	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	30mL	
Pseudoephedrine/ brompheniramine/ codeine (MAR-COF® BP)	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	60mL	
Pseudoephedrine/codeine/ guaifenesin solution 30-10-100 MG/5ML	two 5-day fills per 60 days for 18	40mL	

	and older; two 3-day fills per 60 days for less than 18		
Pseudoephedrine/ dextbrompheniramine/ codeine	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	60mL	
Tapentadol (Nucynta®) 50mg	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	4	
Tapentadol (Nucynta®) 75mg, 100mg	two 5-day fills per 60 days for 18 and older; two 3-day fills per 60 days for less than 18	6	
Tapentadol ER* (Nucynta® ER)	No	2	
Tramadol 50mg, 25mg		8	
Tramadol 75mg		5	
Tramadol (Conzip®)		1	

Tramadol/acetaminophen		8	
Tramadol/celecoxib (Seglantis®)	No	4	
Tramadol 100 mg		4	
Tramadol (Qdolo®)		80ml	

P&T Approval Date: Mar-20-2025

Title: Oral Anti-infective Agents

Applicable Drugs:

Brand Name	Generic Name
Cresemba®	isavuconazonium
Sirturo®	bedaquiline
Sivextro®	tedizolid
	Pretomanid
Nuzyra®	omadacycline

Policy:

BEDAQUILINE (SIRTURO®)

Bedaquiline (Sirturo®) is approved when ALL of the following are met:

1. Diagnosis of pulmonary multi-drug resistant tuberculosis (MDR-TB), for which an effective treatment regimen cannot otherwise be established; and
2. Member is 5 years of age or older and weighing at least 15kg; and
3. Prescribed by or in consultation with an infection disease specialist or pulmonologists; and
4. Bedaquiline is used as combination therapy as defined by ONE of the following:
 - a. With at least 3 other drugs to which the member's MDR-TB isolate has been shown to be susceptible in vitro; or
 - b. With at least 4 other drugs to which the patient's MDR-TB isolate is likely to be susceptible

Authorization duration: 24 weeks

ISAVUCONAZONIUM (CRESEMBA®)

Isavuconazonium (Cresemba®) is approved when ALL of the following are met:

1. Member is 18 years of age or older; and
2. Prescribed by or in consultation with an infectious diseases specialist; and
3. Diagnosis of ONE of the following:
 - a. Treatment of invasive aspergillosis and inadequate response or inability to tolerate voriconazole; or
 - b. Treatment of invasive mucormycosis

Authorization duration: 12 months

TEDIZOLID (SIVEXTRO®)

Tedizolid (Sivextro®) is approved when ALL of the following are met:

1. Member is 12 years of age or older; and
2. Prescribed by or in consultation with an infectious diseases specialist; and
3. Documentation of use for the treatment of acute bacterial skin and skin structure infections (ABSSSI) caused by susceptible isolates of Gram-positive microorganisms and ONE of the following:
 - a. Inadequate response or inability to tolerate ALL antibiotics to which the organism is susceptible; or
 - b. Tedizolid is the only antibiotic to which the organism is susceptible; or
 - c. There is a contraindication to using an alternative antibiotic to which the organism is susceptible to (e.g., drug-drug interaction concern with the alternative antibiotic and member's existing drug regimen)

Authorization duration: 4 weeks

PRETOMANID

Pretomanid is approved when ALL of the following are met:

1. Diagnosis of pulmonary extensively drug resistant (XDR), treatment-intolerant or nonresponsive multidrug-resistant (MDR) tuberculosis (TB); and

2. Medication will be used as part of combination regiment with bedaquiline (Sirturo®) and linezolid; and
3. Member is 18 years of age or older; and
4. Prescribed by or in consultation with an infectious disease specialist

Authorization duration: 26 weeks

OMADACYCLINE (NUZYRA®)

Omadacycline (Nuzyra®) is approved when ALL of the following are met:

1. Member is 18 years of age or older; and
2. Prescribed by or in consultation with an infectious disease specialist; and
3. One of the following:
 - a. Documentation of use for the treatment of community-acquired bacterial pneumonia; or
 - b. Documentation of use for the treatment of acute bacterial skin and skin structure infections (ABSSSI); and
4. ONE of the following:
 - a. Inadequate response or inability to tolerate ALL antibiotics to which the organism is susceptible; or
 - b. Omadacycline is the only antibiotic to which the organism is susceptible; or
 - c. There is a contraindication to using an alternative antibiotic to which the organism is susceptible to (e.g., drug-drug interaction concern with the alternative antibiotic and member's existing drug regimen)

Authorization duration: 4 weeks

P&T Approval Date: Jul-01-2024

Title: Oteseconazole (Vivjoa)

Applicable Drugs:

Brand Name	Generic Name
Vivjoa	oteseconazole

Policy:

INITIAL CRITERIA: Oteseconazole (Vivjoa™) is approved when ALL of the following are met:

1. Diagnosis of recurrent vulvovaginal candidiasis (RVVC); and
2. Member is not of reproductive potential; and
3. Diagnosis of RVVC is confirmed by ONE of the following:
 - a. Positive potassium hydroxide (KOH) preparation; or
 - b. Vaginal fungal culture; and
4. Member has experienced 3 or more symptomatic episodes of vulvovaginal candidiasis (VVC) within the past 12 months; and
5. Inadequate response or inability to tolerate BOTH of the following:
 - a. One intravaginal product (e.g., clotrimazole, miconazole, terconazole); and
 - b. Oral fluconazole

Authorization duration: 4 months

P&T Approval Date: Jul-01-2024

Title: Oxymetazoline (Upneeq™)

Applicable Drugs:

Brand Name	Generic Name
Upneeq™	Oxymetazoline hydrochloride

Policy:

INITIAL CRITERIA: Oxymetazoline (Upneeq™) is approved when ALL of the following are met:

1. Diagnosis of acquired blepharoptosis; and
2. Request is not for an excluded benefit (i.e. cosmetic - solely for lifting the eyelid to improve appearance); and
3. Member has obstructed visual field in primary gaze or down gaze due to blepharoptosis; and
4. One of the following:
 - a. Marginal reflex distance-1 (MRD-1) is less than or equal to 2mm in primary gaze; or
 - b. Marginal reflex distance-1 (MRD-1) is less than or equal to 2mm in down gaze; or
 - c. Superior visual field loss of at least 12 degrees or 24 percent; and
5. Other treatable causes of blepharoptosis have been ruled out (e.g., recent botulinum toxin injection, myasthenia gravis); and
6. Prescribed by or in consultation with an ophthalmologist or optometrist

Initial authorization duration: 3 months

REAUTHORIZATION CRITERIA: Oxymetazoline (Upneeq™) is re-approved when BOTH of the following are met:

1. Documentation of positive clinical response to therapy (e.g., improvement in superior visual field, increase in Marginal reflex distance-1 [MRD-1]); and
2. One of the following:

- a. Marginal reflex distance-1 (MRD-1) is less than or equal to 2mm in primary gaze;
or
- b. Marginal reflex distance-1 (MRD-1) is less than or equal to 2mm in down gaze; or
- c. Superior visual field loss of at least 12 degrees or 24 percent

Reauthorization duration: 12 months

P&T Approval Date: Jul-01-2024

Title: Palopegteriparatide (Yorvipath®)

Applicable Drugs:

Brand Name	Generic Name
Yorvipath®	palopegteriparatide

Policy:

INITIAL CRITERIA: Palopegteriparatide (Yorvipath®) is medically necessary when ALL of the following are met:

1. Diagnosis of hypoparathyroidism; and
2. Requested drug is not being used in the setting of acute post-surgical hypoparathyroidism; and
3. Member has achieved albumin-corrected serum calcium of at least 7.8 mg/dL using calcium and active vitamin D (e.g., calcitriol) treatment; and
4. Prescribed by or in consultation with an endocrinologist or nephrologist

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Palopegteriparatide (Yorvipath®) medically necessary when there is documentation of positive clinical response to therapy as evidenced by maintenance of normalized calcium levels compared to baseline

Reauthorization duration: 12 months

P&T Approval Date: Dec-12-2024

Title: Palovarotene (Sohonos®)

Applicable Drugs:

Brand Name	Generic Name
Sohonos®	palovarotene

Policy:

INITIAL CRITERIA: Palovarotene (Sohonos) is approved when all of the following are met:

1. Diagnosis of Fibrodysplasia Ossificans Progressiva (FOP); and
2. Molecular genetic testing confirms mutations in the ACVR1 gene; and
3. One of the following:
 1. Both of the following:
 1. Member is female; and
 2. Member is 8 years of age or older; or
 2. Both of the following:
 1. Member is male; and
 2. Member is 10 years of age or older; and
4. Prescribed by or in consultation with one of the following:
 1. Geneticist; or
 2. Orthopedic physician

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Palovarotene (Sohonos) is re-approved if documentation is provided that member demonstrates positive clinical response to therapy (e.g., reduction in volume in new abnormal bone growth)

Reauthorization duration: 12 months

P&T Approval Date: Mar-20-2025

Title: Peanut immunotherapy (Palforzia)

Applicable Drugs:

Brand Name	Generic Name
Palforzia®	Peanut immunotherapy

Policy:

INITIAL CRITERIA Peanut immunotherapy (Palforzia®) is medically necessary when ALL of the following are met:

1. Diagnosis of peanut allergy as documented by all of the following:
 - a. Serum peanut-specific IgE level of greater than or equal to 0.35kUA/L; and
 - b. Mean wheal diameter that is at least 3mm larger than the negative control on skin-prick testing for peanut; and
2. Member does not have any of the following:
 - a. History of eosinophilic esophagitis (EoE) or eosinophilic gastrointestinal disease; or
 - b. History of severe or life-threatening episode(s) of anaphylaxis or anaphylactic shock within the past 2 months; or
 - c. Severe or poorly controlled asthma; and
3. One of the following:
 - a. Member is 1 to 17 years of age and in the initial dose escalation phase of therapy; or
 - b. Member is 1 years of age or older and in the up-dosing or maintenance phase of therapy; and
4. Prescribed by or in consultation with an allergist/immunologist

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA Peanut immunotherapy (Palforzia®) is medically necessary when prescribed by or in consultation with allergist/immunologist.

Reauthorization duration: 12 months

P&T Approval Date: Dec-12-2024

Title: Peginterferon alfa-2a (Pegasys®)

Applicable Drugs:

Brand Name	Generic Name
Pegasys	peginterferon alfa-2a

Policy:

Chronic Hepatitis C (CHC)

INITIAL CRITERIA: Peginterferon alfa-2a (Pegasys®) is approved when ALL of the following are met:

1. Diagnosis of Chronic Hepatitis C (CHC); and
2. Member is without decompensated liver disease (defined as Child-Pugh Class B or C); and
3. One of the following:
 1. Used in combination with one of the following:
 1. Sovaldi (sofosbuvir); or
 2. Ribavirin; or
 2. Inadequate response or inability to tolerate all other HCV agents (e.g., Sovaldi (sofosbuvir), ribavirin); and
4. Prescribed by or in consultation with one of the following:
 1. Hepatologist
 2. Gastroenterologist
 3. Infectious disease specialist
 4. HIV specialist certified through the American Academy of HIV medicine

Initial authorization duration: 28 weeks

REAUTHORIZATION CRITERIA: Peginterferon alfa-2a (Pegasys®) is re-approved when ALL of the following are met:

1. Member has an undetectable HCV RNA at week 24; and

2. Additional treatment weeks of peginterferon are required to complete treatment regimen; and
3. Member has not exceeded 48 weeks of therapy with peginterferon; and
4. Prescribed by or in consultation with one of the following:
 1. Hepatologist
 2. Gastroenterologist
 3. Infection disease specialist
 4. HIV specialist certified through the American Academy of HIV medicine

Reauthorization duration: 20 weeks

Chronic Hepatitis B (CHB)

Peginterferon alfa-2a (Pegasys®) is approved when BOTH of the following are met:

1. Diagnosis of chronic hepatitis B infection; and
2. Member is without decompensated liver disease (defined as Child-Pugh Class B or C)

Authorization duration: 48 weeks

P&T Approval Date: Mar-14-2024

Title: Pegvaliase-pqpz (Palynziq™)

Applicable Drugs:

Brand Name	Generic Name
Palynziq™	Pegvaliase-pqpz

Policy:

INITIAL CRITERIA: Pegvaliase-pqpz (Palynziq™) is medically necessary when ALL of the following are met:

1. Member is 18 years of age or older, and
2. Member has diagnosis of phenylketonuria with uncontrolled blood phenylalanine concentration of greater than 600 micromol/L on existing management (e.g., medical foods, Kuvan®); and
3. Member will continue to have phenylalanine blood levels measured every 4 weeks until a maintenance dose is established and periodically thereafter; and
4. ONE of the following:
 1. Member has had an inadequate response or inability to tolerate the generic sapropterin; or
 2. Member is not a candidate for generic sapropterin therapy due to the presence of two null mutations in trans

Initial Authorization duration: 6 months

CONTINUATION CRITERIA: Pegvaliase-pqpz (Palynziq™) is medically necessary when there is documentation of a positive clinical response to Pegvaliase-pqpz (Palynziq™) therapy (i.e., reduction in blood phenylalanine concentrations).

Continuation authorization duration: 2 years

P&T Approval Date: Sep-12-2024

Title: Pegvisomant (Somavert®)

Applicable Drugs:

Brand Name	Generic Name
Somavert®	Pegvisomant

Policy:

INITIAL CRITERIA: Pegvisomant (Somavert®) is medically necessary when ALL the following are met:

1. Diagnosis of acromegaly; and
2. One of the following:
 - a. Inadequate response to surgery or pituitary irradiation; or
 - b. Not a candidate for surgical resection or pituitary irradiation; and
3. Inadequate response or inability to tolerate a dopamine agonist (e.g., bromocriptine or cabergoline) at maximally tolerated doses; and
4. Prescribed by or in consultation with an endocrinologist; and
5. Member is 18 years of age or older

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Pegvisomant (Somavert®) is medically necessary when there is documentation of positive clinical response to Somavert® therapy (i.e., reduction or normalization of IGF-1)

Reauthorization duration: 2 years

P&T Approval Date: Sep-12-2024

Title: Pentosan polysulfate (Elmiron)

Applicable Drugs:

Brand Name	Generic Name
Elmiron®	pentosan polysulfate sodium

Policy:

INITIAL CRITERIA: Pentosan polysulfate sodium (Elmiron®) is medically necessary when ALL of the following are met:

1. Diagnosis of interstitial cystitis/ bladder pain syndrome and BOTH of the following:
 - a. Pain, pressure, or discomfort associated with lower urinary tract symptoms for 6 weeks or longer; and
 - b. Absence of infection or other identifiable cause; and
2. Inadequate response to conservative therapy (e.g., bladder training, pelvic floor rehab, biofeedback, etc.); and
3. Member is 16 years of age or older; and
4. Inadequate response or inability to tolerate ONE of the following:
 - a. Amitriptyline; or
 - b. Cimetidine; or
 - c. Hydroxyzine

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Pentosan polysulfate sodium (Elmiron®) is medically necessary when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

P&T Approval Date: Dec-12-2024

Title: Phenoxybenzamine (Dibenzyl[®])

Applicable Drugs:

Brand name	Generic name
Dibenzyl [®]	phenoxybenzamine

Policy:

INITIAL CRITERIA: Phenoxybenzamine (Dibenzyl[®]) is medically necessary when ALL of the following are met:

1. Diagnosis of pheochromocytoma; and
2. Member is 18 years of age or older; and
3. Prescribed by or in consultation with a nephrologist, endocrinologist or endocrine surgeon; and
4. For brand Dibenzyl[®] only, inadequate response or inability to tolerate generic phenoxybenzamine; and
5. Medication is being used for preoperative preparation; and
6. Treatment will also include a high-sodium diet and fluid intake; and
7. Inadequate response or inability to tolerate to one of the following
 1. Doxazosin; or
 2. Terazosin; or
 3. Prazosin.

Initial Authorization duration: 6 months

REAUTHORIZATION CRITERIA: Phenoxybenzamine (Dibenzyl[®]) is medically necessary when both of the following are met:

1. Documentation of positive clinical response; and
2. Yearly evaluation by prescriber for long-term use

Reauthorization duration: 12 months

P&T Approval Date: Sep-12-2024

Title: Pilocarpine (Vuity™, Qlosi™)

Applicable Drugs:

Brand Name	Generic Name
Vuity™, Qlosi™	Pilocarpine

Policy:

INITIAL CRITERIA: Pilocarpine (Vuity™, Qlosi™) is medically necessary when ALL of the following are met:

1. Diagnosis of presbyopia; and
2. Prescribed by or in consultation with ONE of the following:
 - a. Ophthalmologist; or
 - b. Optometrist; and
3. Member is unable to use corrective lenses (e.g., eyeglasses or contact lenses)

Initial authorization duration: 1 month

REAUTHORIZATION CRITERIA: Pilocarpine (Vuity™, Qlosi™) is medically necessary when BOTH of the following are met:

1. Documentation of positive clinical response to therapy (e.g., improvement in near vision in low light conditions without loss of distance vision); and
2. Prescribed by or in consultation with one of the following:
 - a. Ophthalmologist; or
 - b. Optometrist

Reauthorization duration: 6 months

P&T Approval Date: Mar-20-2025

Title: Pimavanserin (Nuplazid)

Applicable Drugs:

Brand Name	Generic Name
Nuplazid®	pimavanserin

Policy:

INITIAL CRITERIA: Pimavanserin (Nuplazid®) is medically necessary when ALL of the following are met:

1. Diagnosis of hallucinations and delusions associated with Parkinson's disease; and
2. Trial of dose adjustment or withdrawal of antiparkinsonian medications (anticholinergics, amantadine, dopamine agonists, COMT inhibitors, selegiline) prior to treatment with pimavanserin; and
3. Inadequate response or inability to tolerate clozapine or quetiapine; and
4. Member is 18 years of age or older

Initial Authorization duration: 6 months

REAUTHORIZATION CRITERIA: Pimavanserin (Nuplazid®) is medically necessary when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

P&T Approval Date: Dec-12-2024

Title: Prescription Drugs or Biologics With an Accelerated Approval

Policy:

Coverage is subject to the terms, conditions, and limitations of the member's contract.

Prescription drugs or biologics that receive an accelerated approval are considered a benefit contract exclusion for most plans, and, therefore, not eligible for reimbursement consideration for a period of 18 months following the US food and Drug Administration (FDA) accelerated approval date when ALL of the following are met:

1. The drug does not have a final, standard, traditional FDA approval, and
2. The accelerated approval was based on a surrogate endpoint, and
3. The FDA indicates that a confirmatory trial is necessary to demonstrate clinical benefits.

During the 18-month consideration period, the Company will evaluate any new reliable data. By the end of this consideration period of 18 months, the Company will provide a coverage position based on the current status of those reliable data.

This exclusion does not apply to prescription drugs or biologics under the following circumstances :

1. The prescription drugs or biologics are an anti-cancer treatment, or
2. Coverage is required based on a federal or state mandate/regulation.

Individual benefits must be verified.

NOTE: For plans that do not have a benefit contract exclusion for prescription drugs or biologics that receive an accelerated approval with insufficient reliable evidence of effectiveness, refer to the applicable medical necessity policies for additional information.

P&T Approval Date: Dec-12-2024

Title: Prescription Vitamins, Dietary Supplements, and Medical Foods

Policy:

Coverage is subject to the terms, conditions, and limitations of the member's contract.

Prescription vitamins, dietary supplements, and medical foods are not covered under the pharmacy benefit.

An exception to allow coverage under the member's plan will be in place for prescription medication that are either mandated when used as a preventive medication as described in the Patient Protection and Affordable Care Act (PPACA) or medically necessary for the treatment of a specific illness as determined by the plan.

The following prescription products are covered under the member's prescription benefit:

Products	Clinical Use
Calcitriol oral	Management of secondary hyperparathyroidism and resultant metabolic bone disease in patients with moderate to severe chronic renal failure (creatinine clearance 15 to 55 mL/min) not yet on dialysis.
Cholecalciferol (vitamin D3) 50,000 units	Treatment of hypoparathyroidism, refractory rickets, also known as vitamin D resistant rickets, and familial hypophosphatemia. This is an over the counter preparation included to meet essential health benefit requirements.
Cyanocobalamin inhaled	Maintenance of normal hematologic status in pernicious anemia patients who are in remission following intramuscular (IM) vitamin B12 therapy and who have no nervous system involvement
Dialysis vitamins oral as identified by indication in product label	Wasting syndrome in chronic renal failure, uremia, and impaired metabolic function of the kidney
Doxercalciferol oral	Secondary hyperparathyroidism (dialysis patients): Treatment of secondary hyperparathyroidism in patients with chronic kidney disease on dialysis. Secondary hyperparathyroidism (predialysis patients):

	Treatment of secondary hyperparathyroidism in patients with stage 3 or 4 chronic kidney disease.
Ergocalciferol oral	Treatment of hypoparathyroidism, refractory rickets, also known as vitamin D resistant rickets, and familial hypophosphatemia.
Paricalcitol oral	Hyperparathyroidism: For the prevention and treatment of secondary hyperparathyroidism associated with chronic kidney disease stage 3 and 4, and chronic kidney disease stage 5 in patients on hemodialysis or peritoneal dialysis.
Pediatric vitamins	Nutritional supplement for children
Phytonadione oral	Anticoagulant-induced prothrombin deficiency caused by coumarin or indandione derivatives. Coagulation disorders: Phytonadione is indicated in the following coagulation disorders which are due to faulty formation of factors II, VII, IX and X when caused by vitamin K deficiency or interference with vitamin K activity.
Potassium aminobenzoate oral	The treatment of scleroderma, dermatomyositis, morphea, linear scleroderma, pemphigus, and Peyronie's disease.
Prenatal vitamins	Nutritional supplement used prior to conception, during pregnancy, and in the postnatal period
Prescription electrolytes	Electrolyte repleters (i.e., potassium) and electrolyte depleters (i.e., calcium acetate)

P&T Approval Date: Jul-01-2024

Title: Primary Biliary Cholangitis (PBC) Agents

Applicable Drugs:

Brand Name	Generic Name
Ocaliva®	Obeticholic acid
Iqirvo®	Elafibranor
Livdelzi®	Seladelpar

Policy:

INITIAL CRITERIA: Obeticholic acid (Ocaliva®) is medically necessary when ALL of the following are met:

1. Diagnosis of primary biliary cholangitis (PBC) (also known as primary biliary cirrhosis); and
2. Member is 18 years of age or older; and
3. One of the following:
 1. Both of the following:
 1. Member has failed to achieve an alkaline phosphatase (ALP) level of less than 1.67 times the upper limit of normal (ULN) after at least 12 consecutive months of treatment with ursodeoxycholic acid (UDCA) (e.g., Urso, Urso Forte, ursodiol); and
 2. Used in combination with ursodeoxycholic acid (UDCA); or
 2. History of contraindication or intolerance ursodeoxycholic acid (UDCA); and
4. Prescribed by or in consultation with hepatologist or gastroenterologist; and
5. Member does not have evidence of advanced cirrhosis (i.e., cirrhosis with current or prior evidence of hepatic decompensation including encephalopathy or coagulopathy); and
6. Member does not have evidence of portal hypertension (e.g., ascites, gastroesophageal varices, persistent thrombocytopenia); and
7. Obeticholic acid (Ocaliva®) will not be used in combination with elafibranor (Iqirvo®) or seladelpar (Livdelzi®)

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Obeticholic acid (Ocaliva®) is medically necessary when ALL of the following are met:

1. Documentation of positive clinical response to therapy (e.g., a reduction in ALP level from pre-treatment baseline); and
2. Member does not have evidence of advanced cirrhosis (i.e., cirrhosis with current or prior evidence of hepatic decompensation including encephalopathy or coagulopathy); and
3. Member does not have evidence of portal hypertension (e.g., ascites, gastroesophageal varices, persistent thrombocytopenia); and
4. Obeticholic acid (Ocaliva®) will not be used in combination with elafibranor (Iqirvo®) or seladelpar (Livdelzi®)

Reauthorization duration: 12 months

INITIAL CRITERIA: Elafibranor (Iqirvo®) is medically necessary when ALL of the following are met:

1. Diagnosis of primary biliary cholangitis (PBC) (also known as primary biliary cirrhosis); and
2. Member is 18 years of age or older; and
3. One of the following:
 1. Both of the following:
 1. Member has failed to achieve an alkaline phosphatase (ALP) level of less than 1.67 times the upper limit of normal (ULN) after treatment with ursodeoxycholic acid (UDCA) (e.g., Urso, Urso Forte, ursodiol); and
 2. Used in combination with ursodeoxycholic acid (UDCA); or
 2. History of contraindication or intolerance to ursodeoxycholic acid (UDCA), and
4. Prescribed by or in consultation with hepatologist or gastroenterologist; and
5. Elafibranor (Iqirvo®) will not be used in combination with obeticholic acid (Ocaliva®) or with seladelpar (Livdelzi®)

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Elafibranor (Iqirvo®) is medically necessary when both of the following are met:

1. Documentation of positive clinical response to therapy (e.g., ALP level less than 1.67 times ULN, total bilirubin less than or equal to ULN, ALP decrease greater than or equal to 15% from baseline); and
2. Elafibranor (Iqirvo®) will not be used in combination with obeticholic acid (Ocaliva®) or with seladelpar (Livdelzi®)

Reauthorization duration: 12 months

INITIAL CRITERIA: Seladelpar (Livdelzi®) is medically necessary when ALL of the following are met:

1. Diagnosis of primary biliary cholangitis (PBC) (also known as primary biliary cirrhosis); and
2. Member is 18 years of age and older; and
3. One of the following:
 1. Both of the following:
 1. Member has failed to achieve an alkaline phosphatase (ALP) level of less than 1.67 times the upper limit of normal (ULN) after treatment with ursodeoxycholic acid (UDCA) (e.g., Urso, Urso Forte, ursodiol); and
 2. Used in combination with ursodeoxycholic acid (UDCA); or
 2. History of contraindication or intolerance to ursodeoxycholic acid (UDCA); and
4. Prescribed by or in consultation with hepatologist or gastroenterologist; and
5. Seladelpar (Livdelzi®) will not be used in combination with obeticholic acid (Ocaliva®) or elafibranor (Iqirvo®)

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Seladelpar (Livdelzi®) is medically necessary when both of the following are met:

1. Documentation of positive clinical response to therapy (e.g., ALP level less than 1.67 times ULN, total bilirubin less than or equal to ULN, ALP decrease greater than or equal to 15% from baseline); and
2. Seladelpar (Livdelzi®) will not be used in combination with obeticholic acid (Ocaliva®) or elafibranor (Iqirvo®)

Reauthorization duration: 12 months

P&T Approval Date: Dec-12-2024

Title: Prior Authorization Requirement for Select Drugs policy

Policy:

A medication with alternative or alternatives is medically necessary when ALL of the following are met:

1. FDA approved, or compendia supported indication; and
2. Request is not for an excluded benefit (i.e., cosmetic); and

3. Inadequate response or inability to tolerate the alternative(s)

Authorization duration: 1 year

Target	Prerequisite(s)	Category
Vasotec®, Zestril®, Altace®, Accupril®, Lotrel®, Epaned®	3 generic angiotensin-converting enzyme (ACE) inhibitors (e.g., lisinopril, enalapril)	ACE-Inhibitors
Absorica [LD] ®	2 of the following: Amnesteem®, Claravis®, Myorisan®, Zenatane®	Acne agents
Daytrana®, amphetamine ER 1.25mg/ml suspension [Adzenys® ER], Adzenys XR-ODT®, Dyanavel XR®, Mydayis®, Cotempla®, Evekeo ODT, Zenzedi®, Xelstry™, Vyvanse®, methylphenidate (Relexxii®) tab ER osmotic release	2 generic ADHD stimulants (e.g., methylphenidate, amphetamines, etc.)	ADHD
Concerta®, Dexedrine® spansule, Desoxyn®, Ritalin, Ritalin LA®, Focalin XR®, Adderall®, Adderall XR®, Kapvay®, Intuniv®, Strattera®	generic equivalent of requested brand	ADHD
Azstarys®	One generic ADHD stimulants (e.g., methylphenidate, amphetamines, etc.)	ADHD
Quillichew®, Quillivant®, Aptensio®, Jornay PM®, Adhansia XR®, Metadate CD®	Generic methylphenidate	ADHD
Qelbree™, Onyda™ XR	ONE of the following: generic atomoxetine, generic guanfacine ER, generic clonidine ER	ADHD
Alrex®, Alocril®, Zerviate™, Bepreve®	Two of the following generics: azelastine, cromolyn sodium, epinastine), olopatadine	Allergic conjunctivitis
Aricept®, Adlarity®	Generic donepezil tablets	Alzheimer's Disease
Atacand [HCT]®, Avapro [Avalide]®, Cozaar [Hyzaar]®, Diovan [HCT]®, Micardis [HCT]®, Exforge [HCT]®, Benicar [HCT]®, Azor®, Tribenzor®, Edarbi®, Edarbyclor®, Tekturna [HCT]®,	3 generic angiotensin receptor blockers or combinations (e.g., losartan, olmesartan, valsartan tablet, etc.)	Angiotensin II receptor antagonists

Patanase®	Both of the following: fluticasone and flunisolide	Antiallergic agents
Rythmol® SR	Generic propafenone	Antiarrhythmics
Mysoline®	Generic primidone	Anticonvulsants
Lamictal®	generic lamotrigine	anticonvulsants
Keppra®, Elepsia™ XR, Spritam®	generic levetiracetam	anticonvulsants
Briviact®, Xcopri®	One of the following generics: lamotrigine IR, levetiracetam IR, levetiracetam ER, oxcarbazepine IR, topiramate IR OR continuation of therapy with the requested drug	anticonvulsants
Lyrica®	Generic pregabalin	anticonvulsants
Topamax® [sprinkle]	topiramate	Anticonvulsants
Trokendi XR®, topiramate ER [Qudexy XR®], Eprontia™	Generic topiramate	Anticonvulsants
Oxcarbazepine ER [Oxtellar XR®]	generic oxcarbazepine	Anticonvulsants
Aptiom®	Three generic anticonvulsants OR continuation of therapy with Aptiom®	Anticonvulsants
Tegretol®, Tegretol XR®, Carbatrol®	generic carbamazepine	Anticonvulsants
Neurontin®	Generic gabapentin	Anticonvulsants
Felbatol®	Generic felbamate	Anticonvulsants
Zonegran®, Zonisade® suspension	Generic zonisamide	Anticonvulsants
Trileptal®	Generic oxcarbazepine	Anticonvulsants
Motpoly XR	Three generic anticonvulsants OR continuation of therapy with Motpoly XR	Anticonvulsants
Wellbutrin SR®, Wellbutrin XL®, Prozac®, Lexapro®, Zoloft®, Effexor XR®, Aplenzin®, bupropion ER 450mg [Forfivo® XL], Pexeva®, Pristiq®, Celexa®, Citalopram capsule, Sertraline capsule, Paxil [CR]®, Venlafaxine besylate tab ER	3 generic antidepressants (e.g., citalopram tablet, venlafaxine, bupropion, sertraline tablet, etc.)	Antidepressants
Symbyax®	Generic equivalent of requested brand	Antidepressants
Fetzima®, Viibryd®, Auvelity™	3 generic antidepressants (e.g., citalopram tablet, venlafaxine, bupropion, sertraline tablet, etc.) OR	Antidepressants

	continuous therapy with requested agent for a minimum of 2 weeks	
Trintellix®	2 generic antidepressants (e.g., citalopram tablet, venlafaxine, bupropion, sertraline tablet, etc.) OR continuous therapy with requested agent for a minimum of 2 weeks	Antidepressants
Cymbalta®, Drizalma®	Duloxetine	Antidepressants
Duetact®	Generic pioglitazone-glimepiride	Anti-diabetic
Actos®	Generic pioglitazone	Anti-diabetics
Glucotrol®, Amaryl®	3 generic sulfonylureas (e.g., glipizide, glyburide, glimepiride)	Anti-diabetics
Metformin tab 625mg	ONE of the following: metformin IR 500mg, 850mg, metformin 1000mg	Anti-diabetics
Riomet®	Metformin oral solution	Anti-diabetics
Xultophy	Soliqua	Anti-diabetics
Symlin®	Insulin within 180 days	Anti-diabetics
Non-preferred diabetic testing supplies (test strips and meters)	Contour®	Anti-diabetics
Nesina®, Oseni®, Kazano®, Onglyza®, Kombiglyze®, Sitagliptin [Zituvio], Sitagliptin/Metformin [Zituvimet, Zituvimet XR]	Two of the following: Januvia® or Janumet® AND Tradjenta® or Jentaduo®	Anti-diabetics
Metformin tab ER Osmotic	Generic Glucophage XR (Metformin ER) tablets	Anti-diabetics
Qtern®, Steglatro™, Steglujan™, Segluromet™, Invokana®, Invokamet® [XR], bexagliflozin [Brenzavvy™], dapagliflozin, dapagliflozin/metformin ER	Minimum of 3-months trial with ONE of the following: Jardiance, Synjardy [XR], Glyxambi or Trijardy XR AND minimum of 3-months trial with ONE of the following: Farxiga or Xigduo XR	Anti-diabetics
Mytesi®	HIV therapy and ONE of the following: loperamide or diphenoxylate/ atropine	Antidiarrheal

Compro®	Generic prochlorperazine suppository	Anti-emetics
Sancuso®	One of the following: generic granisetron, generic ondansetron, aprepitant	Anti-emetics
Alphagan® P, Azopt®, Combigan®, Cosopt®, Cosopt® PF, Iopidine®, Istalol®, Timoptic® Ocudose	Minimum of 30-day trial with the generic equivalent of the requested brand	Anti-glaucoma agents
Betoptic®-S	Two generic ophthalmic beta blockers (e.g., timolol, betaxolol, levobunolol)	Anti-glaucoma agents
Allopurinol 200mg tablets	Generic allopurinol 100mg tablet	Anti-gout
Colchicine capsules [Mitigare®], Colcris®, Gloperba®	colchicine tablets	Anti-gout
Febuxostat, Zyloprim®	generic allopurinol	Anti-gout
Uloric®	Both allopurinol and generic febuxostat	Anti-gout
Clemastine fumarate syrup	Both of the following: 2 second-generation generic antihistamines (e.g., loratadine, desloratadine, etc..) and generic clemastine fumarate tablets	Antihistamine
Clarinetx®, Clarinetx-D®, Dexchlorpheniramine/Ryclora®	BOTH of the following generics (desloratadine, carbinoxamine/Ryvent®)	Antihistamines
Bystolic®	Generic nebivolol	Antihypertensives
Clonidine ER [Nexiclon™ XR]	Both of the following generics: clonidine tablets and clonidine patches	Antihypertensives
Bethkis®, Kitabis®, Tobî® Nebulizer solution	Generic tobramycin nebulizer solution	Anti-infective
Firvanq®	Generic vancomycin 25mg/ml or 50mg/ml oral solution	Anti-infective
Nuessa™, Cleocin® ovules, Cleocin® cream	ONE of the following: generic metronidazole gel or generic clindamycin cream	Anti-infective
Likmez™	Generic metronidazole	Anti-infective
Solosec®	Both of the following: (1) generic metronidazole vaginal gel or generic clindamycin	Anti-infective

	vaginal gel AND (2) metronidazole tablets or tinidazole tablets	
Vandazole™	ONE of the following: generic metronidazole vaginal gel or generic clindamycin vaginal gel	Anti-infective
Noxafil	Generic posaconazole	Anti-infectives
Zyvox	generic linezolid	Anti-infectives
Brexafemme®, Diflucan®	Generic fluconazole	Anti-infectives
Monurol®	Generic Fosfomycin tromethamine	Anti-infectives
Arimidex®	Generic anastrozole	Antineoplastic
Eulexin®	Generic flutamide	Antineoplastic
Jylamvo®	Generic methotrexate tablets	Antineoplastics
Sensipar®	Generic cinacalcet	Antiparathyroid agent
Effient®, Plavix®	Generic equivalent of the requested brand	Antiplatelets
Abilify Mycite®, Fanapt®, Caplyta™, Secuado®, Lybalvi™, Opipza™, Cobenfy™	2 generic antipsychotic agents (e.g., aripiprazole, paliperidone, quetiapine, risperidone, etc.) OR continuation of therapy with requested medication	antipsychotics
Abilify®, Geodon®, Risperdal®, Saphris®, Seroquel® [XR], Invega®, Zyprexa® [Zydis]	2 generic antipsychotic agents (e.g., aripiprazole, paliperidone, quetiapine, risperidone, etc.)	antipsychotics
Latuda®	Generic lurasidone tablets	antipsychotics
Xerese® cream	Generic acyclovir cream	Antiviral
Valtrex®	generic valacyclovir	Antivirals
Ativan®, Valium®, Xanax®, Xanax® XR, Klonopin®, Loreev™ XR	3 generic benzodiazepines (e.g., lorazepam, diazepam, alprazolam, clonazepam, etc.)	Benzodiazepine
Inderal LA®, Tenormin®, Tenoretic®, Kapsargo™, Coreg [CR]®, InnoPran XL®, Inderal XL®	3 generic beta blockers (e.g., propranolol, atenolol, metoprolol, etc.)	Beta blockers
Questran®, Welchol™ tablet, Welchol™ packet, Colestid®	2 generic bile acid sequestrants (e.g., colestipol, cholestyramine, colesevelam)	Bile acid sequestrants

Binosto®, Actonel®, Boniva®	2 generic bone resorption inhibitors (e.g., risedronate, alendronate, ibandronate)	Bone resorption inhibitors
Evista®	Generic raloxifene	Bone resorption inhibitors
Moviprep®, Plenvu®, Osmoprep®	One of the following: Suprep or Clenpiq or Suflave	Bowel prep agents
Golytely®, Nulytely®	PEG-3350 oral solution	Bowel prep agents
Uroxatral®, Cardura® [XL], Flomax®, Rapaflo®	2 generic alpha blockers (e.g., alfuzosin, doxazosin, tamsulosin, prazosin, terazosin)	BPH
Jalyn®, Avodart™	Generic equivalent of the requested brand	BPH
Entadfi™ ³	One of the following generics (alfuzosin, doxazosin, tamsulosin, terazosin, silodosin) AND ONE of the following: 5-alpha-reductase inhibitor (i.e., finasteride 5mg, dutasteride) OR Phosphodiesterase type 5 inhibitor (i.e., tadalafil 2.5mg, 5mg)	BPH
Caduet®	Generic amlodipine-atorvastatin	Calcium channel blocker and HMG CoA reductase inhibitor combination
Cardizem CD®, Levamlodipine, Conjugri®, Norvasc®, Cardizem LA®, Cardizem®, Verelan®	3 generic calcium channel blockers (e.g., amlodipine, diltiazem, nifedipine, verapamil, etc.)	Calcium channel blockers
Inpefa™	Minimum 3 months trial of Jardiance® and minimum 3 months trial of Farxiga®	Cardiovascular agents
Penicillamine [Cuprimine®], Trientine/Clovique [Syprine®/Cuvrior™]	Depen®	Chelating agents
Niaspan®	Generic niacin	Cholesterol lowering agents
Lovaza®	Omega-3-acid ethyl esters	Cholesterol lowering agents
Zetia®	generic ezetimibe	Cholesterol lowering agents

Uceris®, Entocort EC®	Generic oral budesonide	Corticosteroid
Prednisolone [Millipred®], Alkindi®	One generic oral corticosteroid (e.g., hydrocortisone, methylprednisolone)	Corticosteroid
Prednisone Delayed Release (Rayos®)	Three generic immediate-release oral corticosteroids (e.g., hydrocortisone, dexamethasone, prednisone, methylprednisolone, prednisolone, etc.)	Corticosteroid
Livtency™ ¹	Minimum 2 weeks duration or inability to tolerate One of the following: ganciclovir IV, oral valganciclovir, foscarnet IV, or cidofovir IV	Cytomegalovirus (CMV)
Valcyte®	Generic valganciclovir	Cytomegalovirus (CMV)
Eucrisa®, Opzelura®	One of the following: one generic topical steroid (e.g., triamcinolone, clobetasol, halobetasol, etc.) or one generic topical calcineurin inhibitor	Dermatological agents
Elidel®	One generic topical steroid (e.g., triamcinolone, clobetasol, halobetasol, etc.) or generic tacrolimus	Dermatological agents
Vtama®	Minimum 30-day supply (14-day supply for topical corticosteroids) of THREE of the following: medium or higher potency topical corticosteroid, generic topical calcineurin inhibitor (e.g., tacrolimus ointment), Eucrisa (crisaborole), Opzelura (Ruxolitinib), Zoryve (roflumilast) 0.15% cream	Dermatological agents
Zoryve® cream 0.15%	ALL of the following: generic topical steroid (e.g., triamcinolone, clobetasol, halobetasol, etc.), generic tacrolimus ointment/ Pimecrolimus cream, Eucrisa (crisaborole) ointment.	Dermatological agents

Protopic®	generic tacrolimus	Dermatological agents
Plaquenil®, Sovuna™	Generic hydroxychloroquine tablet	Disease-modifying Antirheumatic Agents
Pradaxa Pak	One of the following: Eliquis, Xarelto, generic dabigatran capsules	DOAC
Varenicline (Tyrvaya™), Vevye®	Both of the following: Restasis Multidose and Xiidra	Dry eye disease
Cequa®	Generic cyclosporine emulsion	Dry eye disease
Cialis®, Viagra®, vardenafil [Levitra®], vardenafil, avanafil [Stendra®]	One of the following: sildenafil or tadalafil AND no concurrent use of nitrate	Erectile dysfunction agent
Crinone 8%	Endometrin®	Fertility
Gonal-F®, Gonal-RFF®, Menopur®	Follistim AQ®	Fertility
Trilipix™	Generic fenofibrate	Fibric acid derivatives
Ursodiol [Reltone™], Urso® [Forte]	Generic ursodiol capsule	Gallstone agents
Canasa®	Generic equivalent of requested brand	Gastrointestinal agent
Carafate®	Generic sucralfate tablet or suspension	Gastrointestinal agent
Colazal®	Generic balsalazide	Gastrointestinal agent
Lialda®	Generic mesalamine delayed release tablet	Gastrointestinal agent
Librax®	Generic equivalent of requested brand	Gastrointestinal agent
Asacol HD®, Delzicol®	Generic equivalent of requested brand	Gastrointestinal agent
Lotronex®	Generic alosetron	Gastrointestinal agent
Gimoti™ ⁵	Generic oral metoclopramide	Gastrointestinal agent
Pentasa 500mg capsule	Generic mesalamine ER 500mg capsule	Gastrointestinal agent
Rectiv®	Generic nitroglycerin ointment	Gastrointestinal agent
Syndros®	Generic dronabinol	Gastrointestinal agent
Glucagen®, Gvoke®2, Glucagon® (Lilly)	ONE of the following: Glucagon® (Fresenius), Baqsimi®, Zegalogue®	Glucagon agents

Pepcid	Two of the generics: famotidine, nizatidine, cimetidine, ranitidine	H2- Antagonists
Lescol® XL, Lipitor®, Crestor®, Livalo®, Vytorin® Zypitamag®, Ezallor®, Zocor®, Ezetimibe/rosuvastatin [Roszet®], ezetimibe/atorvastatin, Altoprev®	3 generic HMG CoA reductase inhibitors (e.g., simvastatin, atorvastatin, rosuvastatin, pravastatin, etc.)	HMG Co A reductase inhibitors
Minivelle®, Vivelles-Dot®, Alora®	Generic estradiol patch	Hormone Replacement Therapy
Angeliq® tablet	One generic estrogen- progestin combination (e.g., estradiol-norethindrone acetate, Jinteli, Minvey)	Hormone Replacement Therapy
Femring®, Vagifem®, Estrace cream®	Generic estradiol vaginal cream or vaginal tablet	Hormone replacement therapy
Intrarosa®	Imvexxy™	Hormone replacement therapy
Depo-Estradiol®	Generic estradiol injection in oil formulation	Hormone replacement therapy
Inspra®, Carospir®	Both of the following: generic spironolactone, eplerenone	Hypertension
Vecamyl®	2 generic antihypertensives in different classes	Hypertension
Viberzi®	One antidiarrheal medication (e.g., loperamide) AND one antispasmodic (e.g., dicyclomine, etc.)	IBS
Amitiza®	BOTH of the following: Lactulose solution or lubiprostone and Linzess® or Symproic®	IBS
Trulance®, Zelnorm®, Ibsrela®	Both of the following: Linzess® and One of the following: lactulose solution or lubiprostone	IBS
Motegrity®	ALL of the following: Linzess®, generic lactulose solution, and generic prucalopride	IBS
Xepi™, Altabax®	mupirocin	Impetigo agents
Arava®	Generic leflunomide	Inflammatory conditions

Accrufer®	One of the following generics: ferrous sulfate, ferrous gluconate, ferrous fumarate	Iron preparations
lactulose packet [Kristalose® packet]	lactulose solution	Laxative
Singulair®	Generic montelukast	Leukotriene modifiers
Zileuton ER, Zyflo®	Both of the following generics: montelukast and zafirlukast	Leukotriene modifiers
Soaanz®	Two generic loop diuretics (e.g., torsemide, furosemide)	Loop diuretics
Extavia®, Rebif [Rebidose]®, Mavenclad®, Ponvory®, Tascenso ODT™	2 of the following: Avonex®, Betaseron®, glatiramer (Copaxone® 40mg, Glatopa®), Plegridy®, Vumerity®, Bafiertam®, dimethyl fumarate, Kesimpta® OR continuation of therapy with the requested agent	MS
Aubagio®	Generic teriflunomide	MS
Copaxone® 20mg	Generic glatiramer	MS
Gilenya® 0.5mg	Generic fingolimod	MS
Tecfidera®	Dimethyl fumarate AND one of the following: Vumerity® or Bafiertam®	MS
Conzip®, Tramadol solution [Qdolo®]	2 generic tramadol products	Narcotic analgesic
Butalbital/APAP 25/325mg tablet [Allzital®], Butalbital/APAP 50/300mg tabs/caps	Butalbital/APAP 50/325mg tabs	Non-Narcotic Analgesic
Zebutal®, Esgic®	Butalbital/APAP/Caffeine 50/325mg/40mg tabs OR caps	Non-Narcotic Analgesic
Anaprox DS®, Naprosyn®, EC- Naprosyn®, Cambia pack®, Celebrex®, Arthrotec®, Daypro®, Mobic®, Diclofenac capsule [Zipsor®], Fenoprofen, Fenortho™, Nalfon®, Relafen [DS®], indomethacin [Tivorbex®], Indocin®], Meloxicam [Vivlodex®], diclofenac [Zorvolex®], Ketoprofen [Kiprofen] caps, Cataflam®, ketorolac tromethamine nasal spray [Sprix®], Elyxyb™, meloxicam suspension, Naprelan®, oxaprozin [Coxanto™], Dolobid®	3 generic prescription strength NSAIDS (e.g., ibuprofen, naproxen, diclofenac, celecoxib, meloxicam caps/tabs, etc.)	NSAIDs

Bromsite®, Ilevro®, Nevanac®, Prolensa®	TWO of the following: generic Ketorolac op sol 0.5%, Flurbiprofen op sol 0.03%, diclofenac op sol 0.1%	Ophthalmic NSAIDs
Zioptan®, Vyzulta™, Xelpros®, Travatan Z®, Iyuzeh™	ONE of the following generics: latanoprost, bimatoprost, travoprost AND Lumigan®	Ophthalmic prostaglandins
Pred Forte® ophthalmic suspension, clobetasol ophthalmic suspension	One generic ophthalmic steroid suspension (e.g., Prednisolone ophthalmic suspension, fluorometholone ophthalmic suspension, dexamethasone ophthalmic suspension)	Ophthalmic steroids
Seglantis®	3 generic alternatives indicated for acute pain (e.g., hydrocodone/acetaminophen, tramadol, acetaminophen, oxycodone/acetaminophen, etc.)	Opioid analgesic
Oxycodone [Roxybond®]	Two generic opioid analgesics or documentation of a history of or a potential for drug abuse for individual or a member of the individual's household	Opioid analgesics
Dilaudid®, MS Contin®, Roxicodone®, Oxaydo®, Percocet®, Xodol®, Methadose®, Ultracet®, Ultram®, Fioricet® with codeine, Fioricet®	Generic equivalent of requested brand	Opioid analgesics
Benzhydrocodone/Acetaminophen (Apadaz®)	Generic Hydrocodone/Acetaminophen and generic oxycodone/acetaminophen	Opioid analgesics
Prolate®, Oxycodone/Acetaminophen 2.5-300mg, 5-300mg, 7.5-300mg, 10-300mg, Nalocet 2.5-300mg, Oxycodone/Acetaminophen solution 5/325mg	Generic oxycodone/acetaminophen tablet	Opioid analgesics
Oxycontin®, Oxycodone ER, Hysingla®	Xtampza® ER	Opioid analgesics
Relistor®	BOTH of the following: Symproic® and One of the following: lactulose solution or lubiprostone	Opioid induced constipation
Lofexidine [Lucemyra®]	Generic clonidine	Opioid withdrawal

Carbamazepine suspension, gabapentin solution, pregabalin solution, oxcarbazepine suspension, nortriptyline solution, fluoxetine solution, metformin solution, amlodipine (Katerzia, Norliqva), enalapril solution, lisinopril (Qbrelis) solution, valsartan solution, vancomycin solution, nitrofurantoin suspension, valganciclovir solution, indomethacin suspension, naproxen suspension, methotrexate (Xatmep) solution, pyridostigmine solution, Thyquidity solution, simvastatin (Flolipid) suspension, atorvastatin calcium (Atorvaliq) suspension	Oral solid dosage formulation (tablet or capsule) of the drug requested OR one of the following: drug will be administered via nasogastric or gastronomy tube; or member is unable to swallow an intact capsule or tablet	Oral liquid dosage formulations that have a tablet or capsule formulation available ⁶
Gelnique®, Oxytrol®, Ditropan XL®, Detrol®, Detrol LA®	2 generic alternatives (e.g., solifenacin, oxybutynin, tolterodine, etc.)	Overactive bladder agents
Toviaz®, Gemtesa®	Both of the following: Myrbetriq® AND 2 generic alternatives (e.g., solifenacin, oxybutynin tabs/tab ER/syrup, tolterodine, etc.)	Overactive bladder agents
Vesicare®, Vesicare LS®	Generic solifenacin	Overactive bladder agents
Pancreaze®, Pertzye®, Viokace®	Both of the following: Creon® and Zenpep®	Pancreatic enzymes
Mestinon®	Generic pyridostigmine	Parasympathomimetic
Dhivy	Carbidopa-levodopa IR and carbidopa-levodopa ODT	Parkinson's disease
Gocovri®	Generic amantadine	Parkinson's disease
Ongentys®	Generic entacapone	Parkinson's disease
Neupro®	Generic pramipexole and ropinirole	Parkinson's Disease, Restless leg syndrome
Xadago®	generic rasagiline and selegiline	Parkinson's disease
Rytary®, Crexont®	generic carbidopa/ levodopa	Parkinson's disease
Lanthanum [Fosrenol®]	Generic sevelamer	Phosphate removing agents
Phoslyra® solution	Generic calcium acetate	Phosphate binder agents
Xphozah®, Velphoro®	Minimum 30-day supply of two of the following: calcium	Phosphate removing agents

	carbonate, calcium acetate, lanthanum carbonate, sevelamer carbonate, sevelamer HCL, Auryxia	
Durlaza®	aspirin	Platelet inhibitors
DDAVP	generic desmopressin acetate nasal spray	Posterior pituitary hormones
Sorilux® (calcipotriene foam 0.005%)	3 prescription strength, generic topical corticosteroids	Psoriasis agents
Zoryve™ cream 0.3%	ONE of the following: generic topical corticosteroids, vitamin D analogs, tazarotene, calcineurin inhibitors, anthralin, coal tar, or combination topical therapy	Psoriasis agents
Airsupra™	Both of the following: one inhaled corticosteroid (ICS) with albuterol AND minimum 30-day supply of brand Symbicort	Pulmonary
Pulmicort® suspension	Generic budesonide inhalation suspension	Pulmonary
Xopenex® nebulizer solution	Generic levalbuterol nebulizer solution	Pulmonary
ProAir Digihaler®, Proventil® Ventolin®, Xopenex®	albuterol HFA	Pulmonary
Alvesco®, Asmanex®, Qvar®, Armonair®, Flovent Diskus/ HFA®, Fluticasone HFA, Fluticasone AER	Two of the following: Arnuity Ellipta® and Pulmicort Flexhaler®	Pulmonary
Dulera®, AirDuo®, Fluticasone/Salmeterol HFA, Advair® Diskus, Fluticasone/vilanterol inhaler, Breyndra AER	TWO of the following: Breo Ellipta®, Symbicort® or Advair® HFA	Pulmonary
Bevespi Aerosphere®, Duaklir®	ONE of the following: Anoro Ellipta®, Stiolto Respimat®	Pulmonary
Tudorza® Lonhala Magnair®, Seebri®, Yupelri™, Incruse® Ellipta, tiotropium brom cap	Spiriva®	Pulmonary
Budesonide-formoterol fumarate dihydrate aerosol	Six-month trial of brand Symbicort® within the previous 365 days	Pulmonary
Anusol®-HC, Hemmorex®-HC, Proctocort® suppositories, Anucort-HC	Generic hydrocortisone acetate suppositories	Rectal preparations

Pokonza™	Generic Potassium chloride (tablets, solution, capsules, packets, crystals, etc.)	Replacement preparations
Finacea®, Zilxi®, Epsolay®	Soolantra®	Rosacea
Rhofade®	Mirvaso®	Rosacea
Noritate®	Soolantra® or Mirvaso®	Rosacea
Evoxac®	Generic cevimeline	Sjogren's Syndrome agent
Metaxalone [Skelaxin®], Soma®, Zanaflex®, Cyclobenzaprine ER [Amrix ER®], Lorzone®, Orphenadrine w aspirin & Caffeine [Norgesic®, Norgesic Forte®, Orphengesic tab forte®]	2 generic skeletal muscle relaxants (e.g., carisoprodol, tizanidine, cyclobenzaprine, chlorzoxazone 500mg, etc.)	Skeletal muscle relaxants
Baclofen solution [Ozobax™], Baclofen solution [Ozobax™ DS], Baclofen suspension [Fleqsuvy™], Lyvispah™	Generic baclofen tablets	Skeletal muscle relaxants
Zoryve™ foam	Minimum duration of a 4-weeks of two of the following: (1) Corticosteroids (e.g., betamethasone, clobetasol); (2) Antifungals (e.g., ciclopirox, ketoconazole); (3) calcineurin inhibitors (e.g., tacrolimus)	Skin and mucous membrane agents
Rozerem™	Generic ramelteon	Sleep agents
Restoril®, Halcion®, Doral®	2 generic benzodiazepines indicated for sleep (e.g., temazepam, triazolam, quazepam, estazolam, etc.)	Sleep agents
Ambien® 5mg [CR 6.25mg], Lunesta® 1mg, 2mg, Zolpidem 7.5mg capsules	2 generic sleep aids (e.g., zolpidem tablets, zolpidem ER tablets, eszopiclone, zaleplon, etc.)	Sleep agents
Doxepin [Silenor®], Belsomra®, Dayvigo™	Two of the following: eszopiclone, zaleplon, zolpidem	Sleep agents
Quviviq™	Belsomra® AND Two of the following: eszopiclone, zaleplon, zolpidem	Sleep agents
Nuvigil®, Provigil®	generic modafinil or armodafinil	Sleep agents
Ortikos®	Generic budesonide cap 3mg DR (Entocort EC®)	Systemic glucocorticoid

Acticlate®, Avidoxy, Doryx DR®, Doryx MPC®, Minocin®, Minolira™ 4, Solodyn®4, Vibramycin®, doxycycline hyclate [Targadox®], Minocycline ER [Ximino®]4, Seysara™ 4; doxycycline hyclate 80mg ER, Lymepak, Monodoxyne XL, Monodoxyne NL, doxycycline monohydrate 75mg and 150mg capsule and tablet	2 generic alternatives (e.g., doxycycline, minocycline, tetracycline)	Tetracyclines
Tetracycline tablet	Generic tetracycline capsule	Tetracyclines
Levothyroxine [Tirosint®], Ermeza™	Generic levothyroxine	Thyroid replacement
Actiq®, fentanyl citrate (Fentora®)	Generic oral transmucosal fentanyl citrate	TIRF
Tazorac®, tazarotene [Fabior®]	Tazarotene	Topical acne agents
Differin®, Retin-A®, Retin-A micro®, Atralin®, Altreno™, Aklief®, Adapalene pad 0.1%, Arazlo®, Avita®	2 generic topical vitamin A derivative products	Topical acne agents
Amzeeq®, Cleocin T®, Evoclin foam®, Azelex® cream®, Clindagel®, Onexton™	2 generic, topical antibiotic or topical antibiotic combination products	Topical acne agents
Dapson (Aczone®) gel	3 of the following generics: adapalene cream/gel, adapalene/benzoyl peroxide, clindamycin gel/lotion/solution, clindamycin/tretinoin, erythromycin/benzoyl peroxide, tretinoin cream/gel	Topical acne agents
Acanya®, Benzamycin gel®, Benzamycinpak gel®, Clindamycin/benzoyl peroxide 1% / 5%, Veltin gel®, Ziana®, Twyneo®, Cabtreo™ gel	Epiduo® Forte	Topical acne agents
Winlevi®	One generic topical vitamin A derivative product AND one generic topical antibiotic/topical antibiotic combination product	Topical acne agents
Lidoderm® patches, Ztlido™, Tridacaine [II]	generic lidocaine patch	Topical anesthetics
Loprox®, Extina®, Oxistat®, Ecoza®, Xolegel®, luliconazole [Luzu®], mico-zn-petro [Vusion®], Ertaczo®, sulconazole [Exelderm®], oxiconazole	2 generic, prescription strength, topical antifungals (e.g., ketoconazole, ciclopirox, etc.)	Topical antifungal

Carac®	Fluorouracil 0.5% topical cream	Topical antineoplastics
Duobrii®	All of the following: (1) Generic tazarotene cream; and (2) one high potency topical corticosteroid (e.g., clobetasol, betamethasone, halobetasol, fluocinonide); and (3) one of the following: (a) Enstilar®; or (b) Wyzora®, or brand/generic Taclonex® (calcipotriene-betamethasone)	Topical steroid
Clobex®, Olux/ Olux E®, Ultravate®, Topicort®, Kenalog®, Luxiq®, clocortolone pivalate [Cloderm®], Desowen®, flurandrenolide [Cordran®], Nolix®, Derma-smoothe®, Synalar®, Locoid®, Locoid Lipocream®, Halog®, Verdeso®, Capex®, Pandel®, Sernivo®, Lexette®, Bryhali®; diflorasone diacetate [Apexicon E®], triamcinolone ointment 0.05% /Tritocin [Trianex®], Impeklo™, Pramosome®, hydrocortisone [Texacort™], Impoyz™, Ala Scalp®	3 prescription strength, generic topical steroids	Topical steroid
Anafranil™, Pamelor®	3 generic tricyclic antidepressants (e.g., nortriptyline, amitriptyline, imipramine, etc.)	Tricyclic antidepressants
Rayaldee®	generic calcitriol	Vitamin D analog
Brand prenatal vitamins	3 generic prenatal vitamins (various)	Vit

1. Livtency™ is approved for 56 days/180 days
2. Gvoke® does not require prior authorization for members under 6 years of age.
3. Entadfi is approved for maximum 182 days/365 days (authorization duration is 182 days)
4. Solodyn®, Minolira™, Seysara™, Ximino® are approved for maximum of 84 days/180 days (authorization duration is 84 days)
5. Gimoti™ is approved for maximum of 56 days/180 days (authorization duration is 56 days)
6. Oral liquid dosage formulations that have a tablet or capsule formulation available, prior authorization does not apply for members under 13 years of age.

P&T Approval Date: Mar-20-2025

Title: Propranolol oral solution (Hemangeol™)

Applicable Drugs:

Brand Name	Generic Name
Hemangeol	Propranolol hydrochloride

Policy:

Propranolol oral solution (Hemangeol™) is approved when all of the following are met:

1. Diagnosis of proliferating infantile hemangioma; and
2. Member is less than 1 year of age.

Authorization Duration: through member's age of 12 months

P&T Approval Date: Mar-20-2025

Title: Proton Pump Inhibitors and Other Acid Reducers

Applicable Drugs:

Brand Name	Generic Name
Aciphex® [Sprinkles]	rabeprazole
Dexilant®	dexlansoprazole
Prevacid® [Solutab]	lansoprazole
Nexium® [Suspension]	esomeprazole magnesium
Prilosec® [Suspension]	omeprazole
Protonix® [Suspension]	pantoprazole
Zegerid® Suspension	omeprazole/sodium bicarbonate
Konvomep™ Suspension	omeprazole/sodium bicarbonate
Voquezna	vonoprazan

Policy:

INITIAL CRITERIA Brand proton pump inhibitor capsules and tablets (e.g., Aciphex® tablets, Protonix® tablets, Dexilant® capsules, Prilosec® capsules), dexlansoprazole, generic esomeprazole or omeprazole-sodium bicarbonate (Konvomep™), vonoprazan (Voquezna®) is medically necessary when BOTH of the following are met:

1. An FDA or compendia approved indication; and
2. Inadequate response to a two-week trial of maximally tolerated dose or inability to tolerate THREE of the following generic proton pump inhibitors:
 1. Omeprazole
 2. Lansoprazole
 3. Pantoprazole
 4. Rabeprazole

Initial authorization duration: H. Pylori 14 days; all other indications 2 years

REAUTHORIZATION CRITERIA Brand proton pump inhibitor capsules and tablets (e.g., Aciphex[®] tablets, Protonix[®] tablets, Dexilant[®] capsules, Prilosec[®] capsules), dextansoprazole, generic esomeprazole or omeprazole-sodium bicarbonate (Konvomep[™]), vonoprazan (Voquezna[®]) is medically necessary when BOTH of the following are met:

1. Documentation of positive clinical response to therapy; and
2. Documentation of continued need for treatment beyond 2 years

Reauthorization duration: 2 years

INITIAL CRITERIA Formulations other than capsules or tablets (e.g., lansoprazole [Prevacid[®] solutab], rabeprazole (Aciphex[®]) Sprinkles, Zegerid[®] packet, Prilosec[®] granules for suspension, pantoprazole [Protonix[®] packets] and esomeprazole [Nexium[®]] packets) require prior authorization for members aged 12 years and older and are medically necessary when there is documentation of BOTH of the following:

1. An FDA approved indication or clinically accepted use; and
2. One of the following:
 - a. Drug will be administered via nasogastric or gastrostomy tube; or
 - b. Member is unable to swallow an intact capsule or tablet

Initial authorization duration: H. Pylori 14 days; all other indications 2 years

REAUTHORIZATION CRITERIA Formulations other than capsules or tablets (e.g. lansoprazole [Prevacid[®] solutab], rabeprazole [Aciphex[®]] Sprinkles, Zegerid[®] packet, Prilosec[®] granules for suspension, pantoprazole [Protonix[®] packets] and esomeprazole [Nexium[®]] packets) require prior authorization for members age 12 years and older and are medically necessary when BOTH of the following criteria are met:

1. Documentation of positive clinical response to therapy; and
2. Documentation of continued need for treatment beyond 2 years

Reauthorization duration: 2 years

P&T Approval Date: Dec-12-2024

Title: Pulmonary Hypertension agents

Applicable Drugs:

Brand Name	Generic Name
Adcirca [®] , Tadliq [®]	tadalafil
Adempas [®]	riociguat
Letaris [®]	ambrisentan
Liqrev [®]	sildenafil
Opsumit [®]	macitentan
Orenitram [®]	treprostinil
Revatio [®]	sildenafil
Tracleer [®]	bosentan
Tyvaso [®] , Tyvaso DPI [®]	treprostinil
Uptravi [®]	selexipag
Ventavis [®]	iloprost
Winrevair [™]	sotatercept
Opsynvi [®]	Macitentan-tadalafil

Policy:

INITIAL CRITERIA: Tadalafil (Adcirca[®], Tadliq[®]) is approved when all of the following are met:

1. Documentation of a diagnosis of pulmonary arterial hypertension (PAH) WHO Group I with New York Heart Association (NYHA) Functional Class II or III; and
2. Diagnosis confirmed by catheterization (right-heart or Swan-Ganz) or echocardiography;
or

3. Documentation of all of the following:
 - a. Mean pulmonary artery pressure (mPAP) > 20 mm Hg; and
 - b. Pulmonary artery wedge pressure (PAWP) ≤ 15 mmHg; and
 - c. Pulmonary vascular resistance (PVR) > 2 Wood units; and
4. No concurrent use of nitrates or other contraindicated medications for the drug requested, unless recommended by a cardiologist or pulmonologist; and
5. For brand Adcirca® and Tadliq® only, inadequate response or inability to tolerate generic tadalafil [Adcirca®, Tadliq®]; and
6. Prescribed by or in consultation with a cardiologist or pulmonologist; and
7. Member is 18 years of age or older

Initial authorization duration: 6 months

INITIAL CRITERIA: Sildenafil (Revatio®, Liquev®) is approved when all of the following are met:

1. One of the following:
 - a. Member is 18 years of age or older and all of the following:
 1. Documentation of a diagnosis of pulmonary arterial hypertension (PAH) WHO Group I with New York Heart Association (NYHA) Functional Class II or III; and
 2. Diagnosis confirmed by catheterization (right-heart or Swan-Ganz) or echocardiography; or
 3. Documentation of all of the following:
 1. Mean pulmonary artery pressure (mPAP) > 20 mm Hg; and
 2. Pulmonary artery wedge pressure (PAWP) ≤ 15 mmHg; and
 3. Pulmonary vascular resistance (PVR) > 2 Wood units; and
 - b. For sildenafil (Revatio®) only, member is 1 to 17 years of age with a diagnosis of pulmonary arterial hypertension (PAH) WHO Group I; and
2. Prescribed by or in consultation with a cardiologist or pulmonologist; and
3. For brand Revatio® and Liquev® only, inadequate response or inability to tolerate generic sildenafil [Revatio®]; and

4. No concurrent use of nitrates or other contraindicated medications for the drug requested, unless recommended by a cardiologist or pulmonologist

Initial authorization duration: 6 months

INITIAL CRITERIA: Bosentan (Tracleer®), Ambrisentan (Letairis®) and macitentan (Opsumit®) are approved when ALL of the following are met:

1. Diagnosis of pulmonary arterial hypertension (PAH) WHO Group I with New York Heart Association (NYHA) Functional Class II – IV; and
2. Diagnosis confirmed by catheterization (right-heart or Swan-Ganz) or echocardiography; or
3. Documentation of all of the following:
 - a. Mean pulmonary artery pressure (mPAP) > 20 mm Hg; and
 - b. Pulmonary artery wedge pressure (PAWP) ≤ 15 mmHg; and
 - c. Pulmonary vascular resistance (PVR) > 2 Wood units; and
4. For brand Letairis® only, inadequate response or inability to tolerate ambrisentan; and
5. For brand Tracleer® only, Inadequate response or inability to tolerate bosentan tablets; and
6. Prescribed by or in consultation with a cardiologist or pulmonologist; and
7. One of the following:
 - a. For bosentan (Tracleer®) only, member is 3 years of age or older; or
 - b. For ambrisentan (Letairis®) and macitentan (Opsumit®), member is 18 years of age or older

Initial authorization duration: 6 months

INITIAL CRITERIA: Treprostinil (Orenitram®) and iloprost (Ventavis®) are approved when ALL of the following are met:

1. Diagnosis of pulmonary arterial hypertension (PAH) WHO Group I with New York Heart Association (NYHA) Functional Class II – IV; and
2. Diagnosis confirmed by catheterization (right-heart or Swan-Ganz) or echocardiography;
or

3. Documentation of all of the following:
 - a. Mean pulmonary artery pressure (mPAP) > 20 mm Hg; and
 - b. Pulmonary artery wedge pressure (PAWP) ≤ 15 mmHg; and
 - c. Pulmonary vascular resistance (PVR) > 2 Wood units; and
4. Prescribed by or in consultation with a cardiologist or pulmonologist; and
5. One of the following:
 - a. For Treprostinil (Orenitram®) only, member is 18 years of age or older; or
 - b. For iloprost (Ventavis®) only, member is 4 months of age or older

Initial authorization duration: 6 months

INITIAL CRITERIA: Riociguat (Adempas®) is approved when ALL of the following are met:

1. Member has a diagnosis of ONE of the following:
 - a. Pulmonary arterial hypertension (PAH) WHO Group I with New York Heart Association (NYHA) Functional Class II – IV; or
 - b. Persistent/recurrent Chronic Thromboembolic Pulmonary Hypertension (CTEPH) (WHO Group 4) after surgical treatment or inoperable CTEPH; and
2. Diagnosis confirmed by catheterization (right-heart or Swan-Ganz) or echocardiography;
or
3. Documentation of all of the following:
 - a. Mean pulmonary artery pressure (mPAP) > 20 mm Hg; and
 - b. Pulmonary artery wedge pressure (PAWP) ≤ 15 mmHg; and
 - c. Pulmonary vascular resistance (PVR) > 2 Wood units; and
4. No concurrent use of specific (i.e. sildenafil) or non-specific (i.e. dipyridamole, theophylline) phosphodiesterase inhibitors; and
5. No concurrent use of nitrates or nitric oxide donors (i.e. amyl nitrite); and
6. Prescribed by or in consultation with a cardiologist or pulmonologist; and
7. Member is 18 years of age or older

Initial authorization duration: 6 months

INITIAL CRITERIA: Selexipag (Uptravi®) is approved when ALL of the following are met:

1. Diagnosis of pulmonary arterial hypertension (PAH) WHO Group I with New York Heart Association (NYHA) Functional Class II-IV; and
2. Diagnosis confirmed by catheterization (right-heart or Swan-Ganz) or echocardiography; or
3. Documentation of all of the following:
 - a. Mean pulmonary artery pressure (mPAP) > 20 mm Hg; and
 - b. Pulmonary artery wedge pressure (PAWP) ≤ 15 mmHg; and
 - c. Pulmonary vascular resistance (PVR) > 2 Wood units; and
4. Inadequate response or inability to tolerate TWO of the following:
 - a. Endothelin Receptor Antagonist (e.g., Letairis (ambrisentan), Opsumit (macitentan), Tracleer (bosentan)); or
 - b. Phosphodiesterase Type 5 Inhibitor (sildenafil if naïve to the class); or
 - c. Riociguat (Adempas®); and
5. Not taken in combination with a prostanoid/prostacyclin analogue (e.g. epoprostenol, iloprost, treprostinil); and
6. Prescribed by or in consultation with a cardiologist or pulmonologist; and
7. Member is 18 years of age or older

Initial authorization duration: 6 months

INITIAL CRITERIA Treprostinil (Tyvaso®, Tyvaso DPI®) is approved when ALL of the following are met:

1. One of the following:
 - a. Diagnosis of pulmonary arterial hypertension (PAH) WHO Group I with New York Heart Association (NYHA) Functional Class II – IV; or
 - b. Diagnosis of pulmonary hypertension associated with interstitial lung disease (WHO Group 3); and
2. Diagnosis of PAH confirmed by catheterization (right-heart or Swan-Ganz) or echocardiography; or

3. Documentation of all of the following:
 - a. Mean pulmonary artery pressure (mPAP) > 20 mm Hg; and
 - b. Pulmonary artery wedge pressure (PAWP) ≤ 15 mmHg; and
 - c. Pulmonary vascular resistance (PVR) > 2 Wood units; and
4. Prescribed by or in consultation with a cardiologist or pulmonologist; and
5. Member is 18 years of age or older

INITIAL CRITERIA: Sotatercept-csrk (Winrevair™) is medically necessary when ALL of the following are met:

1. Documentation of a diagnosis of pulmonary arterial hypertension (PAH) WHO Group I with New York Heart Association (NYHA) Functional Class II to III; and
2. Documentation of all of the following:
 1. Mean pulmonary artery pressure (mPAP) > 20 mm Hg; and
 2. Pulmonary artery wedge pressure (PAWP) ≤ 15 mm Hg; and
 3. Pulmonary vascular resistance (PVR) > 2 Wood units; and
3. Pulmonary arterial hypertension is symptomatic; and
4. One of the following:
 1. Diagnosis of pulmonary arterial hypertension was confirmed by right heart catheterization or echocardiography; or
 2. Member is currently on any therapy for the diagnosis of pulmonary arterial hypertension; and
5. Inadequate response or inability to tolerate two of the following:
 1. Endothelin Receptor Antagonist (bosentan, ambrisentan, macitentan)
 2. Phosphodiesterase 5 inhibitor (tadalafil, sildenafil); and
6. Member is 18 years of age or older; and
7. Prescribed by or in consultation with cardiologist or pulmonologist

Initial authorization duration: 6 months

INITIAL CRITERIA: Macitentan-tadalafil (Opsynvi®) is medically necessary when ALL of the following are met:

1. Diagnosis of pulmonary arterial hypertension (PAH) WHO Group I with New York Heart Association (NYHA) Functional Class II-IV; and
2. Documentation of all of the following:
 1. Mean pulmonary artery pressure (MPAP) > 20 mm Hg; and
 2. Pulmonary artery wedge pressure (PAWP) ≤ 15 mm Hg; and
 3. Pulmonary vascular resistance (PVR) > 2 Wood units; and
3. One of the following:
 1. Diagnosis has been confirmed by right heart catheterization or echocardiography; or
 2. Member is currently on any therapy for the diagnosis of pulmonary arterial hypertension; and
4. Member is 18 years of age or older; and
5. Prescribed by or in consultation with a cardiologist or pulmonologist

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Tadalafil (Adcirca[®], Tadliq[®]), sildenafil (Revatio[®]), sildenafil (Liqrev), bosentan (Tracleer[®]), ambrisentan (Letairis[®]), macitentan (Opsumit[®]), Treprostinil (Orenitram[®]), Treprostinil (Tyvaso[®], Tyvaso DPI[®]), iloprost (Ventavis[®]), riociguat (Adempas[®]) or selexipag (Uptravi[®]), or sotatercept-csrk (Winrevair[™]), macitentan-tadalafil (Opsynvi[®]) is re-approved when there is documentation of stabilization or improvement as evaluated by a cardiologist or pulmonologist

Reauthorization duration: 12 months

P&T Approval Date: Sep-12-2024

Title: Quantity Level Limits for Pharmaceuticals Covered under the Prescription Drug Benefit

Applicable Drugs:

Medication	Maximum Quantity per day	Quantity limit per rolling 30 days, unless otherwise specified (tablets, capsules, mL)	
ADHD Agents			
Atomoxetine HCL (Strattera®) 10mg, 18mg, 25mg, 40mg	2	60	
Atomoxetine HCL (Strattera®) 60mg, 80mg, 100mg	1	30	
Clonidine HCL (Kapvay®) 0.1mg	4	120	
Clonidine (Onyda XR™)	4	120	
Guanfacine HCL (Intuniv ER®) 1mg, 2mg, 3mg, 4mg tablet	1	30	
Viloxazine (Qelbree™) 100 mg	1	30	
Viloxazine (Qelbree™) 150 mg, 200 mg	2	60	
Antiemetics			
Aprepitant (Emend®) 80mg	NA	8	
Aprepitant (Emend®) 40mg	NA	2	
Aprepitant (Emend®) 125mg	NA	4	

Aprepitant (Emend®) trifold pack	NA	4 packs	
Antidepressant			
Fluoxetine (Prozac weekly®)	NA	4	
Zuranolone (Zurzuvae™) 20mg and 25mg	2	NA	14 days supply in 365 days
Zuranolone (Zurzuvae™) 30mg	1	NA	14 days supply in 365 days
Antipsychotics			
xanomeline & trospium chloride (Cobenfy™)	2	60	
Anti-Seizure Agents			
Diazepam (Valtoco®) nasal spray	NA	5 boxes (10 units)	
Diazepam (Libervant™) buccal film	NA	10	
Midazolam (Nayzilam®) nasal spray	NA	5 boxes (10 single dose spray units)	
Antivirals/Anti-infectives			
Acyclovir (Sitavig®)		2/30	
Baloxavir marboxil (Xofluza™) Therapy Packs 2 x 20mg (40mg dose) 2 x 40mg (80mg dose)	NA	2 tablets (1 box)/28 days	

Baloxavir marboxil (Xofluza™) therapy packs 1 x 40mg (40mg dose) 1 x 80mg (80mg dose)	NA	1 tablet/28 days	
Delafloxacin (Baxdela®) tablet 450mg	NA	28 tablets per 14 days	

Fidaxomicin (Difacid®) tablets	NA	20/10 days	
Fidaxomicin (Difacid®) suspension	NA	136 ml per 10 days	
Isavuconazonium (Cresemba®) capsule 186mg	NA	68	
Isavuconazonium (Cresemba®) capsule 74.5 mg	NA	170	
Ibrexafungerp (Brexafemme®)	NA	4/28 days	
Lefamulin (Xenleta™)	NA	10 tablets for 5 days	
Linezolid (Zyvox®) tablet 600mg	NA	56 tablets per 28 days	
Linezolid (Zyvox®) oral suspension 100mg/5ml	NA	1680 ml per 28 days	
Lotilaner (Xdemvy™) ophthalmic solution	NA	10ml per 42 days	
Mebendazole (Emverm®)	NA	6/21 days	
Minocycline ER (Solodyn®, Minolira™, Ximino®)	NA	84 days' supply per 180 days	

Nirmatrelvir 10 x 150mg /ritonavir 10 x 100mg pack (Paxlovid 150-100)	NA	20 tablets per course, 2 courses per year	
Nirmatrelvir 20 x 150mg /ritonavir 10 x 100mg pack (Paxlovid 300-100)	NA	30 tablets per course, 2 courses per year	

Nitazoxanide (Alinia®) tablet	NA	12 tablets per 6 days	
Nitazoxanide (Alinia®) suspension	NA	300ml per 6 days	
Omadacycline (Nuzyra®) tablet 150mg	2.15	30 tablets per 14 days	28 days per 180 days
Oseltamivir (Tamiflu®) 6mg/ml	NA	180mL (3 bottles) per Rx	
Oseltamivir (Tamiflu®) 30mg	NA	20 per Rx	
Oseltamivir (Tamiflu®) 45mg, 75mg	NA	10 per Rx	
Posaconazole (Noxafil®) 100mg tab	NA	93	
Posaconazole (Noxafil®) 40mg/1ml oral suspension	20 ml	NA	
Quinine sulfate (Qualaquin®)	NA	60 capsule per 10 days	
Rifamycin tablet delayed release 194 mg (Aemcolo™)	NA	12 tablets per 30 days	
Sarecycline (Seysara™)	NA	84 days' supply per 180 days	

Tedizolid phosphate (Sivextro®)	1	6 per 6 days	28 days per 180 days
Tenofovir 300mg (Viread®)	1	30	
Emtricitabine/tenofovir disoproxil fumarate (Truvada® 200mg/300mg)	1	30	
Penciclovir (Denavir®)	NA	5 grams	

Zanamivir (Relenza®)	NA	1 Diskhaler per Rx	
Rifaximin (Xifaxan® 200mg)	NA	9/ 90days	
Acyclovir cream (Zovirax®)	NA	5g	
Acyclovir ointment (Zovirax®)	NA	30g	
Doxycycline DR (Doryx DR®) 200mg	1	7 days' supply per 30 days	
Miltefosine (Impavido®)	NA	84 per 28 days	
Bowel Prep Kits			
Peg 3350-electrolyte (Nulytely, Golytely)	NA	2 kits/year (8000ml)	
Peg-prep kits	NA	2 kits/year	
Contraceptives			
Diaphragm	NA	1 per year	
Ethinyl estradiol/etonogestrel (Nuvaring®)	NA	1per 28 days	

Ethinyl estradiol/norelgestromine (Xulane patch®, Zafemy®)	NA	3	
Ethinyl estradiol/segesterone acetate (Annovera®)	NA	1 per 365 days	
Condoms	NA	15	
Levonorgestrel 1.5mg (My Way®, Next Choice®, One Dose®, Plan B one-step®)	NA	3	

Levonorgestrel-ethinyl estradiol TD patch weekly (Twirla®)	NA	3	
Medroxyprogesterone acetate (Depo-Provera®)	NA	1 per 90 days	
Ulipristal (Ella®)	NA	3	
Diabetic Supplies/Drugs			
Blood glucose monitor	NA	2 per year	
Diabetic test strips	NA	200	
Freestyle Libre® reader; Dexcom® receiver	NA	2 per year	
Dexcom® transmitters	NA	4 per year	
Guardian® transmitters, Minilink® transmitters, Eversense® transmitters	NA	2 per year	
Freestyle Libre® 14-day sensor, Freestyle Libre® 2 sensor, Freestyle Libre® kit 3 sensor	NA	2 per 28 days	

Freestyle Libre® 10-day sensor	NA	3 per 30 days	
Dexcom G4, G5, G6, G7 sensor	NA	4 per 28 days	
Eversense® sensor	NA	2 per year	
Eversense® E3 sensor/transmitters	NA	2 per year	
Guardian sensor, Enlite sensor	NA	5 per 30 days	

Insulin injecting device (e.g., Novopen®)	NA	2 per year	
Insulin syringes and pen needles	NA	200	
Lancets	NA	200	
Insulin products	2mL	60	
Erectile Dysfunction			
Alprostadil (Caverject®, IFE-PG20)	NA	8 per 30 days	
Alprostadil (Edex®, Muse®)	NA	8 per 30 days	
Avanafil (Stendra®)	NA	8 per 30 days	
Sildenafil (Viagra®)	NA	8 per 30 days	
Tadalafil (Cialis®) 2.5mg, 5mg	1	30	
Tadalafil (Cialis®) 10mg, 20mg	NA	8	
Vardenafil (Levitra®, Staxyn®)	NA	8	
GLP-1 (diabetic and obesity)			

Exenatide (Bydureon BCise)	0.15	4 syringes per 28 days	
Exenatide (Byetta®) 10 mcg/0.04ml	0.08	1 syringe	
Exenatide (Byetta®) 5 mcg/0.02ml	0.04	1 syringe	
Tirzepatide (Mounjaro™)	0.08	4 syringes per 28 days	
Semaglutide (Ozempic®) 2mg/1.5ml	0.06	1 syringe per 28 days	

Semaglutide (Ozempic®) 2mg/3ml, 4mg/3ml, 8mg/3ml	0.11	1 syringe per 28 days	
Semaglutide (Rybelsus®)	1	30	
Dulaglutide (Trulicity®)	0.08	4 syringes per 28 days	
Liraglutide (Victoza®)	0.3	3 syringes	
Liraglutide (Saxenda®)	0.5	5 syringes	
Semaglutide (Wegovy®) 0.25mg/0.5ml, 0.5mg/0.5ml, 1mg/0.5ml	0.08	4 syringes per 28 days	
Semaglutide (Wegovy®) 1.7mg/0.75ml, 2.4mg/0.75ml	0.11	4 syringes per 28 days	
Tirzepatide (Zepbound®)	0.08	4 per 28 days	
Injectable Fertility			
Follitropin Beta (Follistim AQ®) 75 unit vial	NA	60	

Follitropin Beta (Follistim AQ®) 150 unit vial	NA	30	
Follitropin Beta (Follistim AQ®) 300 unit cartridge	NA	15	
Follitropin Beta (Follistim AQ®) 600 unit cartridge	NA	8	
Follitropin Beta (Follistim AQ®) 900 unit cartridge	NA	5	

Follitropin Alfa (Gonal-F®) 450 units vial	NA	10	
Follitropin Alfa (Gonal-F®) 1050 units vial	NA	5	
Follitropin Alfa (Gonal-F RFF®) 300/0.5ml pen injector	NA	15	
Follitropin Alfa (Gonal-F RFF®) 450/0.75ml pen injector	NA	10	
Follitropin Alfa (Gonal-F RFF®) 900/1.5ml pen injector	NA	5	
Follitropin Alfa (Gonal-F RFF®) 75 unit vial	NA	60	
Menotropins (Menopur®) 75 units vial	NA	180	
Migraine Agents			
Atogepant (Qulipta™)	1	30	

Eletriptan (Relpax®) 20mg, 40mg	NA	12	
Butorphanol nasal spray	NA	10	
Dihydroergotamine (Migranal®)	NA	8	
Dihydroergotamine mesylate HFA (Trudhesa™)	NA	12/28 days	
Emgality 100mg/ml	NA	9 injections/ 180 days	
Frovatriptan (Frova®) 2.5mg	NA	18	

Lasmiditan (Reyvow™) 50mg	NA	4	
Lasmiditan (Reyvow™) 100mg	NA	8	
Naratriptan 1mg, 2.5mg	NA	9	
Rimegepant (Nurtec ODT®)	NA	18	
Rizatriptan 5mg and 10mg	NA	12	
Sumatriptan (Imitrex®) 4mg injections	NA	14 kits (28 injections)	
Sumatriptan (Imitrex®) 6mg injections	NA	9 kits (18 injections)	
Sumatriptan (Imitrex®) 5mg/actuation nasal spray	NA	36	
Sumatriptan (Imitrex®) 20mg/actuation nasal spray	NA	18	

Sumatriptan (Imitrex®) 6mg/0.5ml subcutaneous cartridge/pen injection	NA	9ml	
Sumatriptan (Imitrex®) 4mg/0.5ml subcutaneous cartridge/pen injection	NA	14ml	
Sumatriptan (Imitrex®) 25mg, 50mg, 100mg	NA	18	
Sumatriptan (Onzetra Xsail®) nasal	NA	16	
Sumatriptan (Tosymra®)	NA	12 single dose nasal sprays	

Sumatriptan/Naproxen (Treximet®) 85mg/500mg	NA	18	
Sumatriptan (Zembrace symtouch®) 3mg/0.5mL	NA	8	
Ubrogepant (Ubrelevy™)	NA	16	
Zavegepant (Zavzpret™)	0.27	8	
Zolmitriptan (Zomig®, Zomig ZMT®) 2.5mg, 5mg	NA	9	
Zolmitriptan (Zomig®) 2.5mg, 5mg nasal spray	NA	9	
Miscellaneous			
Adalimumab 10mg/0.1ml	0.08	2 injections per 28 days	

Adalimumab 20mg/0.2ml	0.08	2 injections per 28 days	
Adalimumab 40mg/0.8ml, 40mg/0.4ml	0.08	2 injections per 28 days	
Adalimumab 80mg/0.8ml	0.08	2 injections per 28 days	
Alpelisib (Vijoice®) 250mg	2	60	
Alpelisib (Vijoice®) 50mg, 125mg	1	30	
Baclofen suspension (Fleqsuvy®)	16 ml	480 ml	
Belumosudil (Rezurock™)	1	30	

Birch triterpenes (Filsuvez®)	NA	19 tubes per 30 days	
Bremelanotide (Vyleesi™)	NA	8	
Budesonide (Eohilia™)	20ml	600ml	
Budesonide (Tarpeyo™)	4	120	
Caplacizumab-yhdp (Cablivi®)	1 kit (11mg)	30 days' supply per 365 days	
Celecoxib (Elyxyb™)	4.8 ml	144 ml	
Cenegermine-BKBJ (Oxervate™)	2	60	
Cyclosporine (Restasis®, Cequa®)	2	60	
Cyclosporine (Verkazia®)	4	120	

Cyclosporine (Vevye®)	0.2	6	
Cysteamine (Cystaran®) 0.44% ophthalmic solution	NA	4 bottles/30 days	
Cysteamine (Cystadrops®)	NA	20/28 days	
Diclofenac (Flector®) patch	2	60	
Diclofenac (Licart®) patch	1	30	
Diclofenac potassium (Zipsor®)	4	120	
Doxepin 5% cream (Prudoxin®, Zonalon®)	NA	45g/ 90 days	
Epinephrine pens/auto-injectors (Epi-Pen®, Auvi-Q®, Symjepi™)	NA	3 twin packs (6 injections) per 180 days	

Eplontersen (Wainua™)	NA	0.8 ml per 28 days	
Fecal microbiota spores, live-brpk (Vowst™)	NA	24 capsules per 1 year (2 treatment courses)	
Sparsentan (Filspari™) 200mg, 400mg	1	30	
Gimoti®	NA	56 days' supply per 180 days	
Glycopyrrolate (Dartisla ODT™)	4	120	
Glycopyrronium (Qbrexza™)	1	30	

Icatibant (Firazyr®/Sajazir™) 30mg/3ml syringe	NA	27mL	
Ketorolac tromethamine (Sprix®)	NA	5	
Levacetylleucine (Aqneursa™)	4 packets	120 packets	
Levoketoconazole (Recorlev®)	8	240	
Lidocaine (Lidoderm®, Ztlido™, Tridacaine [II]) patch	3	90	
Lifitegrast (Xiidra®)	2	60	
Maribavir (Livtencity™)	4	224/56 days	
Mavacamten (Camzyos™)	1	30	
Mavorixafor (Xolremdi™)	4	120	
Mesalamine (Pentasa®) 250mg	4		

Migalastat (Galafold®)	NA	14 tablets per 28 days	
Nalmefene (Opvee®)	NA	6	
Naloxone (Zimhi®)	NA	3ml (6 units)	
Naloxone (Kloxxado™)	NA	6	
Naloxone (Rextovy™)	0.2	6	
Nedosiran (Rivfloza™) 80mg/0.5ml	NA	2 vials per 28 days	

Nedosiran (Rivfloza™) 128mg/0.8ml, 160mg/ml	NA	1 syringe per 28 days	
Oxandrolone 2.5mg	8	30 days/180 days	
Oxandrolone 10mg	2	30 days/180 days	
Osilodrostat (Isturisa®) 1mg	8	240	
Osilodrostat (Isturisa®) 5mg	2	60	
Osilodrostat (Isturisa®) 10mg	6	180	
Oteseconazole (Vivjoa™)	N/A	18 tablets per 180 days	
Perfluorohexyloctane (Miebo™)	0.4	12	
Pitolisant (Wakix®) 4.45mg	2	60	
Pitolisant (Wakix®) 17.8mg	2	NA	
Resmetirom (Rezdiffra™)	1	30	

Ruxolitinib (Opzelura™)	NA	240 grams/28 days	
Sacubitril/valsartan (Entresto®) tablets	2	60	
Sacubitril/valsartan (Entresto®) sprinkles	4	120	
Sodium oxybate (Lumryz™)	1 packet	NA	

Sodium oxybate (Xyrem®), calcium, magnesium, potassium and sodium oxybates (Xywav™)	18	540	
Lofexidine (Lucemyra™)	16	480	Two 14 days' supply in 365 days
Apomorphine (Kynmobi™)	5	NA	
Vericiguat (Verquvo®)	1	30	
Varenicline (Tyrvaya™)	NA	8.4ml (2 bottles)	
Voclosporin (Lupkynis™)	6	180	
Multiple sclerosis agents			
Dalfampridine (Ampyra®)	2	60	
Interferon beta-1a (Avonex®)	NA	4	
Interferon beta-1a (Rebif/Rebif Rebidose®)	NA	12	
Interferon beta-1b (Betaseron®)	NA	15	

Interferon beta-1b (Extavia®)	NA	15	
Glatiramer acetate (Copaxone® 20mg)	1	30	
Glatiramer acetate (Copaxone® 40mg)	NA	12	

Peginterferon beta-1a (Plegridy®)	NA	1mL per 28 days	
Oncology Agents			
Afatinib dimaleate (Gilotrif®) 20mg, 30mg, 40mg	1	30	
Asciminib (Scemblix®) 20 mg	2	60	
Asciminib (Scemblix®) 40mg	8	240	
Asciminib (Scemblix®) 100mg	4	120	
Avapritinib (Ayvakit™) 25mg, 50mg, 100mg, 200mg, 300mg	1	30	
Brigatinib (Alunbrig®) 90mg, 180mg and initiation pack	1	30	
Brigatinib (Alunbrig®) 30mg	4	120	
Enasidenib mesylate (Idhifa®) 50mg, 100mg	1	30	
Erlotinib (Tarceva®) 25mg	3	90	
Everolimus (Afinitor®, Torpenz®) tablet 2.5mg, 5mg, 7.5mg, 10mg	1	30	
Ibrutinib (Imbruvica®) 70mg capsule	1	30	
Ibrutinib (Imbruvica®) 140mg capsule	2	60	

Ibrutinib (Imbruvica®) 140mg, 280mg, 420mg tablet	1	30	
Momelotinib (Ojjaara) 100mg, 150mg, 200mg	1	30	
Niraparib tosylate (Zejula®) 100mg	1	30	
Niraparib/abiraterone (Akeega™) 50mg/500mg, 100mg/500mg	2	60	
Osimertinib mesylate (Tagrisso®) 40mg	1	30	
Pemigatinib (Pemazyre®) 4.5mg, 9mg, 13.5mg	1	30	
Pirtobrutinib (Jaypirca®) 50mg	1	30	
Ponatinib (Iclusig®) 10mg, 15mg	1	30	
Ruxolitinib (Jakafi®) 5mg, 10mg	2	60	
Talazoparib tosylate (Talzenna®) 0.25mg, 0.5mg	1	30	
Vandetanib (Caprelsa®) 100mg tablet	2	60	
Osteoporosis Agents			
Alendronate 70mg/75ml solution	NA	300mL per 28 days	
Alendronate (Fosamax® and Binosto®) 35mg, 70mg	NA	4 per 28 days	

Alendronate with Vitamin D (Fosamax plus D®) 70mg/2.8ml, 70mg/5.6ml	NA	4 per 28 days	
Ibandronate (Boniva®) 150mg	NA	1	
Risedronate sodium (Actonel® and Atelvia®) 35mg	NA	4 per 28 days	
Risedronate sodium (Actonel®) 150mg	NA	1 per 30 days	
Proton Pump Inhibitor/Acid Reducer			
Dexlansoprazole (Dexilant®)	2	60	
Esomeprazole magnesium (Nexium®) and strontium capsules	2	60	
Esomeprazole magnesium (Nexium®) packet	1	30	
Lansoprazole (Prevacid®)	2	60	
Lansoprazole (Prevacid®) solu-tab	1	30	
Omeprazole (Prilosec®)	2	60	
Omeprazole/sodium bicarbonate (Konvomep®)	20ml	600ml	
Omeprazole/sodium bicarbonate (Zegerid®) packets	1	30	
Prilosec 2.5mg pak	1	30	
Pantoprazole sodium (Protonix®)	2	60	

Pantoprazole sodium (Protonix®) packet	1	30	
Rabeprazole (Aciphex®)	2	60	
Rabeprazole (Aciphex®) sprinkle	1	30	
Vonoprazan (Voquezna®) 10 mg tablets	1	30	
Vonoprazan (Voquezna®) 20 mg tablets	2	30	
Sedative Hypnotics			
Daridorexant (Quviviq™)	1	30	
Estazolam	1	30	
Eszopiclone (Lunesta®) 1mg	2	60	
Eszopiclone (Lunesta®) 2mg, 3mg	1	30	
Flurazepam HCL	1	30	
Lemborexant (Dayvigo™)	1	30	
Quazepam	1	30	
Ramelteon (Rozerem®)	1	30	
Suvorexant (Belsomra®)	1	30	
Tasimelteon (Hetlioz®)	1	30	
Temazepam (Restoril®)	1	30	
Triazolam (Halcion®)	1	30	

Zaleplon	1	30	
Zolpidem (Zolpimist®)	NA	7.7ml (1 pump)	
Zolpidem tartrate (Ambien®, Ambien CR®, Edluar®, Intermezzo®)	1	30	
Smoking Cessation Products			
Bupropion HCL	2	60	180 cumulative days' supply per 365 days
Nicotine gum/inhaler/lozenges	10	300	
Nicotine nasal spray (Nicotrol® NS)	NA	80ml per 30 days	
Nicotine patches	1	30	
Varenicline (Chantix®, Apo-varenicline)	2	60	
Bronchodilator Products			
Albuterol sulfate (Proair HFA, Proair Respiclick, Proair Digihaler, Ventolin HFA, Proventil HFA)	NA	2 inhalers per 30 days	
Levalbuterol tartrate (Xopenex HFA)	NA	2 inhalers per 30 days	
Ensifentrine (Ohtuvayre™)	2 vials or 5 ml	60 vials or 150 ml	

Policy:

General quantity limit criteria

Quantity limit requests are approved when ONE of the following is met: (drug specific criteria below).

1. Requests that exceed the cumulative daily dose, dose frequency, or duration of therapy approved or recommended by the FDA or as stated in accepted compendia¹ are considered off-label and are reviewed per Off-Label Use policy, OR
2. Requests that do not exceed the cumulative daily dose, dose frequency or duration of therapy approved or recommended by the FDA or as stated in accepted compendia¹: A quantity limit exceeding those listed in the following table is approved when ONE of the following is met:
 1. Documentation of the inability to reach the requested dose with higher strengths of commercially available dosage forms due to member specific characteristics (i.e., inability to swallow larger pills, malabsorption, presence of a feeding tube, etc.); or
 2. The requested dose is not commercially available; or
 3. The requested dose is used for titration or loading-dose purposes (one-time authorization)

¹ Please refer to the Off-Label Use policy for definition of accepted compendia

Authorization duration: 2 years

Authorization duration for dose titration: 14 days

Drug specific quantity limit criteria:

Belumosudil (Rezurock™) specific criteria:

A quantity limit exceeding that listed is approved when BOTH of the following are met:

1. One of the following:
 - a. Member is taking a strong CYP3A4 inducer; or
 - b. Member is on a proton pump inhibitor; and
2. Quantity requested does not exceed 2 per day

Authorization duration: 2 years

Icatibant (Firazyr®, Sajazir®) specific criteria:

A quantity limit exceeding those listed is approved when BOTH of the following criteria are met:

1. The total dose does not exceed FDA approved maximum dose; and
2. ONE of the following:
 - a. For Hereditary Angioedema (HAE) Types I and II: documentation of an inadequate response or inability to tolerate C1 inhibitor replacement therapy (e.g., Cinryze®, Berinert®); or
 - b. For HAE non-Type I or II: documentation of medical necessity

Authorization duration: 2 years

Acute migraine Agents specific criteria:

An increased quantity of a migraine agent is approved when there is a diagnosis of acute treatment of migraine headache and all of the following inclusion criteria are met:

1. Trial of prophylactic treatment with one of the following: beta blocker, calcium channel blocker, tricyclic antidepressant, valproic acid, cyproheptadine calcitonin gene-related peptide receptor antagonist (CGRP) indicated for prophylaxis (e.g., Erenumab [Aimovig™], fremanezumab [Ajovy™] or galcanezumab [Emgality™] 120mg/ml) or topiramate; and
2. Requested quantity does not exceed the manufacturer-recommend maximum doses; and
3. The member has been examined by a neurologist within the past three years.

Authorization duration: 2 years

Proton pump inhibitor specific criteria:

Increased quantity limits of proton pump inhibitors are approved when ONE of the following is met:

1. Pathological hypersecretory condition including Zollinger-Ellison syndrome; or
2. Barrett's esophagus; or
3. Upper gastrointestinal bleed (gastric or duodenal); or

4. Inadequate response to once daily proton pump inhibitor therapy with ONE of the following:
 - a. Gastroesophageal reflux disease (GERD) with nocturnal symptoms; or
 - b. GERD or erosive esophagitis for member less than 11 years old; or
 - c. Laryngopharyngeal reflux; or
 - d. Treatment for the eradication of H pylori with triple therapy (duration of therapy will be limited to 14 days)

Authorization duration: 2 years

Doxycycline DR (Doryx DR®) 200mg specific criteria

A quantity limit exceeding those listed is approved when ONE of the following are met:

1. Diagnosis of acne and inadequate response or inability to tolerate 2 generic alternatives (e.g doxycycline, minocycline, tetracycline); or
2. Other diagnosis approved by the FDA or as stated in accepted compendia are considered off-label and are reviewed per Off-Label policy

Authorization duration: 2 years

Smoking Cessation Agents specific criteria:

Additional days' supply of bupropion (Zyban®), Varenicline (Chantix®, Apo-varenicline) and Nicotine Replacements (Nicotine gum, patches, inhalers, and spray) are approved when all the following are met:

1. One month has passed since last treatment failure with any product indicated for smoking cessation; and
2. Member is enrolled in a Smoking Cessation Program (in person or online); and
3. Member is currently a smoker

Authorization duration: 6 months

Epinephrine pens/ auto-injectors

A quantity limit exceeding those listed may be considered with documentation that a member needs an additional supply based on medical necessity (where additional doses or storage at additional locations are required).

Authorization duration: 6 months

Lofexidine (Lucemyra®)

Criteria for approving more than two 14-day supplies:

Lofexidine (Lucemyra®): An exception for increased days' supply is approved when there is documentation that lofexidine (Lucemyra®) will be used concurrently with comprehensive addiction care (this includes participation in nonpharmacological interventions such as drug abuse counseling, self-help programs, behavioral therapy, or other psychosocial services)

Authorization duration: 6 months

Caplacizumab-yhdp (Cablivi®)

Criteria for approving more than 30-day supply per 365 days:

Caplacizumab-yhdp (Cablivi®): Additional quantities will be approved when the total duration of therapy does not exceed 58 doses after the last plasma exchange.

Authorization duration: 30 days

Tedizolid phosphate (Sivextro®) specific criteria

Additional days' supply of Sivextro is approved when all of the following are met:

1. Prescribed by or in consultation with an infectious disease specialist; and
2. Submission of medical records (e.g., chart notes, susceptibility testing) supporting medical necessity for continuing treatment beyond 28 days

Authorization duration: 6 months

Omadacycline (Nuzyra®) specific criteria

Additional days' supply of Nuzyra is approved when all of the following are met:

1. Prescribed by or in consultation with an infectious disease specialist; and
2. Submission of medical records (e.g., chart notes, susceptibility testing) supporting medical necessity for continuing treatment beyond 28 days

Authorization duration: 6 months

Adalimumab specific criteria:

A quantity limit exceeding that listed is medically necessary when ONE of the following is met:

1. For 10mg/0.1ml request only, both of the following:
 1. Requested dose and frequency does not exceed maximum FDA recommendation per label; and
 2. Documentation of the inability to reach the target dose using 20mg/0.2ml or 40mg/0.8ml formulation; or
2. For 20mg/0.2ml request only, both of the following:
 1. Requested dose and frequency does not exceed maximum FDA recommendation per label; and
 2. Documentation of the inability to reach the target dose using 40mg/0.8ml formulation; or
3. For 40mg/0.8ml and 40mg/0.4ml request only, both of the following:
 1. Requested dose and frequency does not exceed maximum FDA recommendation per label; and
 2. The requested to achieve 80mg target dose for each injection; or
4. For 80mg/0.8ml request only, one of the following:
 1. Requested dose and frequency does not exceed maximum FDA recommendation per label; and
 2. The requested dose is used for loading dose purposes (one-time authorization); or

Authorization duration: 12 months

Authorization duration for loading dose: aligns with label

Black Box Warning as shown in the drug Prescribing Information:

Adalimumab products

SERIOUS INFECTIONS

- Patients treated with adalimumab products are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these

infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids.

- Discontinue drug if a patient develops a serious infection or sepsis.
- Reported infections include:
 - Active tuberculosis (TB), including reactivation of latent TB. Patients with TB have frequently presented with disseminated or extrapulmonary disease. Test patients for latent TB before adalimumab product use and during therapy. Initiate treatment for latent TB prior to adalimumab product use.
 - Invasive fungal infections, including histoplasmosis, coccidioidomycosis, candidiasis, aspergillosis, blastomycosis, and pneumocystosis. Patients with histoplasmosis or other invasive fungal infections may present with disseminated, rather than localized, disease. Antigen and antibody testing for histoplasmosis may be negative in some patients with active infection. Consider empiric anti-fungal therapy in patients at risk for invasive fungal infections who develop severe systemic illness.
 - Bacterial, viral and other infections due to opportunistic pathogens, including Legionella and Listeria.
 - Carefully consider the risks and benefits of treatment with adalimumab products prior to initiating therapy in patients with chronic or recurrent infection.
 - Monitor patients closely for the development of signs and symptoms of infection during and after treatment with adalimumab products, including the possible development of TB in patients who tested negative for latent TB infection prior to initiating therapy.

MALIGNANCY

Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers including adalimumab products. Post-marketing cases of hepatosplenic T-cell lymphoma (HSTCL), a rare type of T-cell lymphoma, have been reported in patients treated with TNF blockers including adalimumab products. These cases have had a very aggressive disease course and have been fatal. The majority of reported TNF blocker cases have occurred in patients with Crohn's disease or ulcerative colitis and the majority were in adolescent and young adult males. Almost all these patients had received treatment with azathioprine or 6-mercaptopurine (6-MP) concomitantly with a TNF blocker at or prior to diagnosis. It is uncertain whether the occurrence of HSTCL is related to use of a TNF blocker or a TNF blocker in combination with these other immunosuppressants.

Antivirals/Anti-infective

Truvada® (emtricitabine and tenofovir disoproxil fumarate), tenofovir, Viread® (tenofovir disoproxil fumarate)

Severe acute exacerbations of hepatitis B virus (HBV) have been reported in HBV-infected patients who have discontinued Truvada® and tenofovir. Hepatic function should be monitored closely in HBV-infected patients who discontinue Truvada® and tenofovir. If appropriate, initiation of anti-hepatitis B therapy may be warranted.

Truvada® (emtricitabine and tenofovir disoproxil fumarate)

TRUVADA used for HIV-1 PrEP must only be prescribed to individuals confirmed to be HIV-negative immediately prior to initiating and at least every 3 months during use. Drug resistant HIV-1 variants have been identified with the use of TRUVADA for HIV-1 PrEP following undetected acute HIV-1 infection. Do not initiate TRUVADA for HIV-1 PrEP if signs or symptoms of acute HIV infection are present unless negative infection status is confirmed.

Tenofovir

Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs, including VIREAD, in combination with other antiretrovirals. A majority of these cases have been in women. Obesity and prolonged nucleoside exposure may be risk factors. Particular caution should be exercised when administering nucleoside analogs to any patient with known risk factors for liver disease; however, cases have also been reported in patients with no known risk factors. Treatment with VIREAD should be suspended in any patient who develops clinical or laboratory findings suggestive of lactic acidosis or pronounced hepatotoxicity (which may include hepatomegaly and steatosis even in the absence of marked transaminase elevations).

Strattera®

Suicidal ideation in children and adolescents: increases the risk of suicidal ideation in short-term studies in children and adolescents with ADHD. Anyone considering the use in a child or adolescent must balance this risk with the clinical need. Co-morbidities occurring with ADHD may be associated with an increase in the risk of suicidal ideation and/or behavior. Patients who are started on therapy should be monitored closely for suicidality (suicidal thinking and behavior), clinical worsening, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. Strattera® is approved for ADHD in pediatric and adult patients. Strattera® is not approved for major depressive disorder. Pooled analyses of short-term (6 to 18 weeks) placebo-controlled trials in children and adolescents (a total of 12 trials involving over 2200 patients, including 11 trials in ADHD and 1 trial in enuresis) have revealed a greater risk of suicidal ideation early during treatment in those receiving Strattera® compared to placebo. The average risk of suicidal ideation in patients receiving Strattera® was 0.4% (5/1357 patients), compared to none in placebo-treated patients (851 patients). No suicides occurred in these trials.

Impavido®

Impavido® may cause fetal harm. Fetal death and teratogenicity occurred in animals administered Impavido® at doses lower than the recommended human dose. Do not administer Impavido® to pregnant women. Obtain a serum or urine pregnancy test in females of reproductive potential prior to prescribing Impavido®.

Females of reproductive potential should be advised to use effective contraception during Impavido® therapy and for 5 months after therapy.

Fluoroquinolones (Baxdela®)

Fluoroquinolones have been associated with disabling and potentially irreversible serious adverse reactions that have occurred together including:

- Tendinitis and tendon rupture
- Peripheral neuropathy
- Central nervous system effects

Discontinue immediately and avoid the use of fluoroquinolones in patients who experience any of these serious adverse reactions.

Fluoroquinolones may exacerbate muscle weakness in patients with myasthenia gravis. Avoid fluoroquinolones in patients with known history of myasthenia gravis.

Quinine sulfate (Qualaquin®)

QUALAQUIN use for the treatment or prevention of nocturnal leg cramps may result in serious and life-threatening hematologic reactions, including thrombocytopenia and hemolytic uremic syndrome/thrombotic thrombocytopenic purpura (HUS/TTP). Chronic renal impairment associated with the development of TTP has been reported. The risk associated with QUALAQUIN use in the absence of evidence of its effectiveness in the treatment or prevention of nocturnal leg cramps outweighs any potential benefit.

Levoketoconazole (Recorlev®)

Cases of hepatotoxicity with fatal outcome or requiring liver transplantation have been reported with oral ketoconazole. Some patients had no obvious risk factors for liver disease. RECORLEV is associated with serious hepatotoxicity. Evaluate liver enzymes prior to and during treatment. RECORLEV is associated with dose-related QT interval prolongation. QT interval prolongation may result in life-threatening ventricular dysrhythmias such as torsades de pointes. Perform ECG prior to and during treatment.

Paxlovid (nirmatrelvir tablets; ritonavir tablets)**WARNING: SIGNIFICANT DRUG INTERACTIONS WITH PAXLOVID**

PAXLOVID includes ritonavir, a strong CYP3A inhibitor, which may lead to greater exposure of certain concomitant medications, resulting in potentially severe, life-threatening, or fatal events.

Prior to prescribing PAXLOVID: 1) Review all medications taken by the patient to assess potential drug-drug interactions with a strong CYP3A inhibitor like PAXLOVID and 2) Determine if concomitant medications require a dose adjustment, interruption, and/or additional monitoring.

Consider the benefit of PAXLOVID treatment in reducing hospitalization and death, and whether the risk of potential drug-drug interactions for an individual patient can be appropriately managed.

Antidepressants**Prozac® Weekly™**

Suicidal thoughts and behaviors: antidepressants increased the risk of suicidal thoughts and behavior in children, adolescents, and young adults in short-term studies. These studies did not show an increased. These studies did not show an increase in the risk of suicidal thoughts and behavior with antidepressant use in patients over age 24; there was a reduction in risk with antidepressant use in patients aged 65 and older.

In patients of all ages who are started in antidepressant therapy, monitor closely for worsening and for emergence of suicidal thoughts and behaviors. Advise families and caregivers of the need for close observation and communication with the prescriber.

Not approved for use in children less than 7 years of age.

Zuruvae (zuranolone)

WARNING: IMPAIRED ABILITY TO DRIVE OR ENGAGE IN OTHER POTENTIALLY HAZARDOUS ACTIVITIES See full prescribing information for complete boxed warning. ZURZUVAE causes driving impairment due to central nervous system (CNS) depressant effects. Advise patients not to drive or engage in other potentially hazardous activities until at least 12 hours after administration. Patients may not be able to assess their own driving competence or the degree of impairment caused by ZURZUVAE

Attention Deficit Hyperactivity Disorder (ADHD)**Qelbree™**

In clinical trials, higher rates of suicidal thoughts and behavior were reported in pediatric patients treated with Qelbree than in patients treated with placebo. Closely monitor for worsening and emergence of suicidal thoughts and behaviors.

Contraceptives

NuvaRing®, Xulane®, Annovera®, Twirla®

Cigarette smoking and serious cardiovascular events: cigarette smoking increases the risk of serious cardiovascular events from combination hormonal contraceptive (CHC) use. This risk increases with age, particularly in women over 35 years of age and with the number of cigarettes smoked. For this reason, CHCs should not be used by women who are over 35 years of age and smoke.

Xulane®

Risk of venous thromboembolism: the risk of VTE among women aged 15-44 who used the patch compared to women who used several different oral contraceptives was assessed in five U.S. epidemiologic studies using electronic healthcare claims data. The relative risk estimates ranged from 1.2 to 2.2; one of the studies found a statistically significant increased relative risk of VTE for current users.

Pharmacokinetic profile of ethinyl estradiol: the PK profile for the patch is different from the PK profile for oral contraceptives in that it has a higher steady state concentration and a lower peak concentration. Area under the time-concentration curve (AUC) and average concentration at steady state (C_{ss}) for EE are approximately 60% higher in women than compared with women using an oral contraceptive containing 35 mcg of EE. In contrast, the peak concentration (C_{max}) for EE is approximately 25% lower in women using the patch. It is not known whether there are changes in the risk of serious adverse events based on the differences in PK profiles of EE in women using norelgestromin and ethinyl estradiol transdermal system compared with women using oral contraceptives containing 30–35 mcg of EE. Increased estrogen exposure may increase the risk of adverse events, including VTE.

Depo-Provera®

Loss of bone mineral density: women may lose significant bone mineral density. Bone loss is greater with increasing duration of use and may not be completely reversible. It unknown if use during adolescence or early adulthood, a critical period of bone accretion, will reduce peak bone mass and increase the risk for osteoporotic fracture in later life. It should not be used as a long-term birth control method (i.e., longer than 2 years) unless other birth control methods are considered inadequate.

GLP-1 (Diabetic and obesity)

Exenatide (Bydureon®/Bydureon BCise®), tirzepatide (Mounjaro™), semaglutide (Ozempic®), semaglutide (Rybelsus®), dulaglutide (Trulicity®), liraglutide (Victoza®), liraglutide (Saxenda®), semaglutide (Wegovy®), tirzepatide (Zepbound)

RISK OF THYROID C-CELL TUMORS

Both Liraglutide and semaglutide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures in both genders of rats and mice. It is unknown whether these drugs causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as the human relevance of liraglutide-induced or semaglutide-induced rodent thyroid C-cell tumors has not been determined.

Liraglutide and semaglutide are contraindicated in patients with a personal or family history of MTC and in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Counsel patients regarding the potential risk of MTC with use of either liraglutide or semaglutide and inform them of symptoms of thyroid tumors (e.g., a mass in the neck, dysphagia, dyspnea, persistent hoarseness). Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with liraglutide or semaglutide.

In rats, tirzepatide causes thyroid C-cell tumors. It is unknown whether tirzepatide causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans as the human relevance of tirzepatide-induced rodent thyroid C-cell tumors has not been determined. Tirzepatide is contraindicated in patients with a personal or family history of MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Counsel patients regarding the potential risk of MTC and symptoms of thyroid tumors.

Migraine Agents

Butorphanol tartrate NS

- Exposes patients and others to the risks of opioid addiction, abuse, and misuse, which can lead to overdose and death. Assess each patient's risk prior to prescribing and monitor all patients regularly for the development of these behaviors and conditions.
- Serious, life-threatening, or fatal respiratory depression may occur with use. Monitor for respiratory depression, especially during initiation or following a dose increase.
- Accidental exposure, especially by children, can result in fatal overdose.
- Prolonged use during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated, and requires management according to protocols developed by neonatology experts.
- Interactions with drugs affecting cytochrome P450 isoenzymes: the concomitant use of butorphanol tartrate NS with all cytochrome P450 3A4 inhibitors may result in an increase in butorphanol plasma concentrations, which could increase or prolong adverse reactions and potentially fatal respiratory depression. Discontinuation of a concomitantly used cytochrome P450 3A4 inducer may result in an increase in butorphanol concentration. The effects of concomitant use or discontinuation of

cytochrome P450 3A4 inducers, 3A4 inhibitors, or 2D6 inhibitors with tramadol or codeine are complex and requires careful consideration of the effects on the parent drug and the active metabolite.

- Concomitant use of opioids with benzodiazepines or other CNS depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death.

Migranal®, Trudhesa™

Serious and/or life-threatening peripheral ischemia has been associated with the co-administration of dihydroergotamine with potent CYP 3A4 inhibitors including protease inhibitors and macrolide antibiotics. Because CYP 3A4 inhibition elevates the serum levels of dihydroergotamine, the risk for vasospasm leading to cerebral ischemia and/or ischemia of the extremities is increased. Hence, concomitant use of these medications is contraindicated.

Treximet® (sumatriptan/naproxen)

May cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk.

TREXIMET® is contraindicated in the setting of coronary artery bypass graft.

NSAID containing products cause an increased risk of serious gastrointestinal adverse events including bleeding, ulceration, and perforation of the stomach or intestines which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients are at greater risk for serious gastrointestinal events

Miscellaneous agents

Flector® patch, Zipsor®, Sprix®, Licart™, Elyxyb™

Cardiovascular thrombotic events: NSAIDs cause an increased risk of serious cardiovascular thrombotic events, including myocardial infarction and stroke, which can be fatal. This risk may occur early in treatment and may increase with duration of use. It is contraindicated in the setting of coronary artery bypass graft surgery.

Gastrointestinal bleeding, ulceration, and perforation: NSAIDs cause an increased risk of serious gastrointestinal (GI) adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients and patients with a prior history of peptic ulcer disease and/or GI bleeding are at greater risk for serious GI events.

Entresto™

Fetal toxicity: when pregnancy is detected, discontinue as soon as possible. Drugs that act directly on the renin-angiotensin system can cause injury and death to the developing fetus.

Oxandrin®

Peliosis hepatis, a condition in which liver and sometimes splenic tissue is replaced with blood-filled cysts, has been reported in patients receiving androgenic anabolic steroid therapy. These cysts are sometimes present with minimal hepatic dysfunction, but at other times they have been associated with liver failure. They are often not recognized until life-threatening liver failure or intra-abdominal hemorrhage develops. Withdrawal of drug usually results in complete disappearance of lesions. Liver cell tumors are also reported. Most often these tumors are benign and androgen-dependent, but fatal malignant tumors have been reported. Withdrawal of drug often results in regression or cessation of progression of the tumor. However, hepatic tumors associated with androgens or anabolic steroids are much more vascular than other hepatic tumors and may be silent until life-threatening intra-abdominal hemorrhage develops. Blood lipid changes that are known to be associated with increased risk of atherosclerosis are seen in patients treated with androgens or anabolic steroids. These changes include decreased high-density lipoproteins and sometimes increased low-density lipoproteins. The changes may be very marked and could have a serious impact on the risk of atherosclerosis and coronary artery disease.

Xyrem®, Xywav™

Central nervous system depression: Xyrem and Xywav are CNS depressants. Clinically significant respiratory depression and obtundation may occur in patients treated with Xyrem and Xywav at recommended doses. Many patients who received Xyrem and Xywav during clinical trials in narcolepsy were receiving central nervous system stimulants.

Misuse and abuse: Xyrem and Xywav are sodium salt of gamma hydroxybutyrate (GHB). Abuse of GHB, either alone or in combination with other CNS depressants, is associated with CNS adverse reactions, including seizure, respiratory depression, decreases in the level of consciousness, coma, and death. Because of the risks of CNS depression, abuse, and misuse, it is available only through a restricted distribution program called the Xyrem and Xywav REMS Program, using the central pharmacy that is specially certified. Prescribers must enroll in the program.

Verquvo® (vericiguat)

Embryo-fetal toxicity

Do not administer Verquvo® to a pregnant female because it may cause fetal harm.

Females of reproductive potential: Exclude pregnancy before the start of treatment. To prevent pregnancy, females of reproductive potential must use effective forms of contraception during treatment and for one month after stopping treatment.

Lupkynis™ (voclosporin)

Malignancies and serious infections

Increased risk for developing serious infections and malignancies with Lupkynis or other immunosuppressants that may lead to hospitalization or death.

Opzelura™ (ruxolitinib)

Serious infections leading to hospitalization or death, including tuberculosis and bacterial, invasive fungal, viral, and other opportunistic infections, have occurred in patients receiving Janus kinase inhibitors for inflammatory conditions. Higher rate of all-cause mortality, including sudden cardiovascular death have been observed in patients treated with Janus kinase inhibitors for inflammatory conditions. Lymphoma and other malignancies have been observed in patients treated with Janus kinase inhibitors for inflammatory conditions. Higher rate of MACE (including cardiovascular death, myocardial infarction, and stroke) has been observed in patients treated with Janus kinase inhibitors for inflammatory conditions. Thrombosis, including deep venous thrombosis, pulmonary embolism, and arterial thrombosis, some fatal, have occurred in patients treated with Janus kinase inhibitors for inflammatory conditions.

Sedative Hypnotics

Estazolam, Flurazepam HCL, quazepam, Restoril®, Halcion®, Nayzilam®, Valtoco®

Concomitant use of benzodiazepines and opioids: may result in profound sedation, respiratory depression, coma, and death. Reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate. Limit dosages and duration to the minimum required. Follow patients for signs and symptoms of respiratory depression and sedation.

Nayzilam®, Valtoco®, Libervant

Concomitant use of benzodiazepines and opioids may result in profound sedation, respiratory depression, coma, and death.

The unapproved use of benzodiazepines exposes users to risks of abuse, misuse, and addiction, which can lead to overdose or death. Before prescribing and throughout treatment, assess each patient's risk for abuse, misuse, and addiction.

Although benzodiazepine is indicated only for intermittent use if used more frequently than recommended, abrupt discontinuation or rapid dosage reduction of benzodiazepine may precipitate acute withdrawal reactions, which can be life-threatening. For patients using benzodiazepine more frequently than recommended, to reduce the risk of withdrawal reactions, use a gradual taper to discontinue.

Zolpidem, Ambien®, Ambien CR®, Zolpimist®, Intermezzo®, Edluar®, (eszopiclone) Lunesta®, (zaleplon) Sonata®

Complex Sleep Behaviors: Complex sleep behaviors including sleepwalking, sleep driving, and engaging in other activities while not fully awake have been reported following use of the above

agents. Some of these events have resulted in serious injuries, including death. Discontinue use immediately if a patient experiences a complex sleep behavior.

Camzyos (mavacamten)

CAMZYOS can cause heart failure due to systolic dysfunction.

Echocardiogram assessments of left ventricular ejection fraction (LVEF) required before and during CAMZYOS use.

Initiation in patients with LVEF <55% not recommended. Interrupt if LVEF <50% or if worsening clinical status.

Certain CYP450 inhibitors and inducers are contraindicated in patients taking CAMZYOS because of an increased risk of heart failure.

CAMZYOS is available only through a restricted program called the CAMZYOS REMS Program.

Smoking Cessation Products

Bupropion hydrochloride (oral tablet/extended release tablet)

Suicidality and antidepressant drugs: although it is not indicated for the treatment of depression, it contains the same active ingredient as the antidepressant medication Wellbutrin®. Antidepressants increased the risk of suicidal thoughts and behavior in children, adolescents, and young adults in short-term trials. These trials did not show an increase in the risk of suicidal thoughts and behavior with antidepressant use in subjects over age 24; there was a reduction in risk with antidepressant use in subjects aged 65 and older. In patients of all ages who are started on antidepressant therapy, monitor closely for worsening, and for emergence of suicidal thoughts and behaviors. Advise families and caregivers of the need for close observation and communication with the prescriber.

Miscellaneous

Gimoti™

Tardive Dyskinesia: Metoclopramide can cause tardive dyskinesia (TD), a serious movement disorder that is often irreversible. The risk of developing TD increases with duration of treatment and total cumulative dosage. Discontinue Gimoti in patients who develop signs or symptoms of TD. Avoid treatment with metoclopramide (all dosage forms and routes of administration) for longer than 12 weeks because of the risk of developing TD with longer-term use.

Filspari™

HEPATOTOXICITY and EMBRYO-FETAL TOXICITY

- FILSPARI is only available through a restricted distribution program called the FILSPARI Risk Evaluation and Mitigation Strategies (REMS) because of these risks

- Some endothelin receptor antagonists have caused elevations of aminotransferases, hepatotoxicity, and liver failure
- Measure liver aminotransferases and total bilirubin prior to initiation of treatment and ALT and AST monthly for 12 months, then every 3 months during treatment
- Interrupt treatment and closely monitor patients developing aminotransferase elevations more than 3x Upper Limit of Normal (ULN)
- Based on animal data, FILSPARI can cause major birth defects if used during pregnancy
- Pregnancy testing is required before, during, and after treatment
- Patients who can become pregnant must use effective contraception prior to initiation of treatment, during treatment, and for one month after

Oncology Agents

Enasidenib mesylate (Idhifa)

WARNING: DIFFERENTIATION SYNDROME

Patients treated with IDHIFA have experienced symptoms of differentiation syndrome, which can be fatal if not treated. Symptoms may include fever, dyspnea, acute respiratory distress, pulmonary infiltrates, pleural or pericardial effusions, rapid weight gain or peripheral edema, lymphadenopathy, bone pain, and hepatic, renal, or multi-organ dysfunction. If differentiation syndrome is suspected, initiate corticosteroid therapy and hemodynamic monitoring until symptom resolution.

Ponatinib (Iclusig)

WARNING: ARTERIAL OCCLUSIVE EVENTS, VENOUS THROMBOEMBOLIC EVENTS, HEART FAILURE, AND HEPATOTOXICITY

Arterial occlusive events (AOEs), including fatalities, have occurred in ICLUSIG-treated patients. AOEs included fatal myocardial infarction, stroke, stenosis of large arterial vessels of the brain, severe peripheral vascular disease, and the need for urgent revascularization procedures.

Patients with and without cardiovascular risk factors, including patients age 50 years or younger, experienced these events. Monitor for evidence of AOEs. Interrupt or discontinue ICLUSIG based on severity. Consider benefit-risk to guide a decision to restart ICLUSIG.

Venous thromboembolic events (VTEs) have occurred in ICLUSIG-treated patients. Monitor for evidence of VTEs. Interrupt or discontinue ICLUSIG based on severity.

Heart failure, including fatalities, occurred in ICLUSIG-treated patients. Monitor for heart failure and manage patients as clinically indicated. Interrupt or discontinue ICLUSIG for new or worsening heart failure.

Hepatotoxicity, liver failure and death have occurred in ICLUSIG-treated patients. Monitor liver

function tests. Interrupt or discontinue ICLUSIG based on severity.

Vandetanib (Caprelsa)

WARNING: QT PROLONGATION, TORSADES DE POINTES, AND SUDDEN DEATH

CAPRELSA can prolong the QT interval. Torsades de pointes and sudden death have occurred in patients receiving CAPRELSA. Do not use CAPRELSA in patients with hypocalcemia, hypokalemia, hypomagnesemia, or long QT syndrome. Correct hypocalcemia, hypokalemia and/or hypomagnesemia prior to CAPRELSA administration. Monitor electrolytes periodically. Avoid drugs known to prolong the QT interval. Only prescribers and pharmacies certified with the restricted distribution program are able to prescribe and dispense CAPRELSA

P&T Approval Date: Mar-20-2025

Title: Resmetirom (Rezdiffra)

Applicable Drugs:

Brand Name	Generic Name
Rezdiffra	Resmetirom

Policy:

INITIAL CRITERIA: Resmetirom (Rezdiffra™) is medically necessary when ALL of the following are met:

1. Diagnosis of metabolic dysfunction-associated steatohepatitis (MASH), formerly known as nonalcoholic steatohepatitis (NASH); and
2. Member does not have cirrhosis (e.g., decompensated cirrhosis); and
3. Member is 18 years of age or older; and
4. Submission of medical records (e.g., chart notes) confirming diagnosis has been confirmed by one of the following:
 1. FibroScan-aspartate aminotransferase (FAST); or
 2. MRI-aspartate aminotransferase (MAST); or
 3. Liver biopsy; and
5. Submission of medical records (e.g., chart notes) confirming disease is fibrosis stage F2 or F3 as confirmed by one of the following:
 1. FibroScan; or
 2. Fibrosis-4 index (FIB-4); or
 3. Magnetic Resonance Elastography (MRE); and
6. Presence of greater than or equal to 3 metabolic risk factors (e.g., Type 2 diabetes, hypertension, obesity); and
7. Submission of medical records (e.g., chart notes) confirming drug is used as adjunct to lifestyle modifications (e.g., dietary or caloric restriction, exercise, behavioral support, community-based program); and
8. Prescribed by or in consultation with one of the following:
 1. Gastroenterologist

2. Hepatologist

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Resmetirom (Rezdiffra™) is medically necessary when ALL of the following are met:

1. Member demonstrates positive clinical response to therapy (e.g., NASH resolution, fibrosis stage improvement, etc.); and
2. Submission of medical records (e.g., chart notes) confirming drug will continue to be used as an adjunct to lifestyle modification (e.g., dietary or caloric restriction, exercise, behavioral support, community-based program); and
3. Member has not progressed to cirrhosis

Reauthorization duration: 12 months

P&T Approval Date: Dec-12-2024

Title: Rifaximin (Xifaxan)

Applicable Drugs:

Brand Name	Generic Name
Xifaxan®	Rifaximin

Policy:

Hepatic disease with risk of hepatic encephalopathy

INITIAL CRITERIA: Rifaximin (Xifaxan®) 550 mg is approved when BOTH of the following are met:

1. Diagnosis of hepatic disease with risk for hepatic encephalopathy (i.e., previous episode of hepatic encephalopathy, advanced liver disease, hepatocellular carcinoma); and
2. Member is 18 years of age or older; and
3. Inadequate response or inability to tolerate lactulose

Initial authorization duration: 2 years (Maximum daily dose 2/day)

REAUTHORIZATION CRITERIA Rifaximin (Xifaxan®) 550mg is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years (Maximum daily dose 2/day)

Irritable Bowel Syndrome with Diarrhea

INITIAL CRITERIA: Rifaximin (Xifaxan®) 550mg is approved when All of the following are met:

1. Diagnosis of irritable bowel syndrome- diarrhea; and
2. Inadequate response or inability to tolerate an antispasmodic; and
3. Member is 18 years of age or older; and
4. Member does not exceed 3 courses (42 days) of therapy

Initial authorization duration: 3 months (max of 14 days/84 days; Maximum daily dose 3/day)

REAUTHORIZATION CRITERIA: Rifaximin (Xifaxan®) 550mg is re-approved when ALL of the following are met:

1. Diagnosis of irritable bowel syndrome – diarrhea; and
2. Symptoms of Irritable Bowel Syndrome continue to persist; and
3. Member demonstrates positive clinical response to therapy as evidenced by both of the following:
 - a. Improvement in abdominal pain; and
 - b. Reduction in the Bristol Stool Scale; and
4. Inadequate response or inability to tolerate an antispasmodic; and
5. BOTH of the following:
 - a. Member does not exceed 3 courses (42 days) of therapy; and
 - b. No documentation of rifaximin (Xifaxan®) treatment within the last 10 weeks.

Reauthorization duration: 3 months (max of 14 days/84 days; Maximum daily dose 3/day)

Small Bowel Bacterial Overgrowth (SBBO)/Small Intestinal Bacterial Overgrowth (SIBO)

INITIAL CRITERIA: Rifaximin (Xifaxan®) 550mg is approved when ALL of the following are met:

1. Diagnosis of Small Bowel Overgrowth (SBBO)/Small Intestinal Bacterial Overgrowth (SIBO); and
2. Inadequate response or inability to tolerate two of the following antibiotics:
 - a. Neomycin; or
 - b. Amoxicillin/clavulanic acid (Augmentin); or
 - c. Ciprofloxacin (Cipro); or
 - d. Trimethoprim-sulfamethoxazole (Bactrim); or
 - e. Doxycycline (Vibramycin) or minocycline (Minocin) or tetracycline; or
 - f. Metronidazole (Flagyl); or
 - g. Cephalexin (Keflex)

Initial authorization duration: 3 months (Maximum daily dose 3/day)

REAUTHORIZATION CRITERIA: Rifaximin (Xifaxan®) 550mg is re-approved when all of the following are met:

1. Diagnosis of Small Bowel Overgrowth (SBBO)/Small Intestinal Bacterial Overgrowth (SIBO); and
2. Member demonstrates positive clinical response to therapy (e.g., resolution of symptoms); and
3. Member experiences relapse with Xifaxan discontinuation

Reauthorization duration: 3 months (Maximum daily dose 3/day)

P&T Approval Date: Jul-01-2024

Title: Risdiplam (Evrysdi™)

Applicable Drugs:

Brand Name	Generic Name
Evrysdi™	Risdiplam

Policy:

INITIAL CRITERIA: Risdiplam (Evrysdi™) is approved when ALL of the following are met:

1. Diagnosis of spinal muscular atrophy (SMA) type 1, 2 or 3; and
2. BOTH of the following:
 1. The mutation or deletion of genes in chromosome 5q resulting in one of the following:
 1. Homozygous gene deletion or mutation (e.g., homozygous deletion of exon 7 at locus 5q13); or
 2. Compound heterozygous mutation (e.g., deletion of SMN1 exon 7 [allele 1] and mutation of SMN1 [allele 2]); and
 2. Member has at least 2 copies of SMN2; and
3. Prescribed by or in consultation with a neurologist or a psychiatrist with subspecialty certification in neuromuscular medicine; and
4. Member is not to receive concomitant chronic survival motor neuron (SMN) modifying therapy for the treatment of SMA (e.g., Spinraza)

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Risdiplam (Evrysdi™) is re-approved when ALL of the following are met:

1. Documentation of positive clinical response to therapy from pretreatment baseline status; and
2. Prescribed by or in consultation with a neurologist or a psychiatrist with subspecialty certification in neuromuscular medicine; and
3. Member is not to receive concomitant chronic survivor motor neuron (SMN) modifying therapy for the treatment of SMA (e.g., Spinraza)

Reauthorization duration: 2 years

P&T Approval Date: Mar-20-2025

Title: Sacrosidase (Sucraid)

Applicable Drugs:

Brand Name	Generic Name
Sucraid®	sacrosidase

Policy:

INITIAL CRITERIA: Sacrosidase (Sucraid®) is medically necessary when all of the following are met:

1. Diagnosis of sucrase deficiency (which is part of congenital sucrose-isomaltase deficiency [CSID]); and
2. Prescribed by or in consultation with gastroenterologist or geneticist

Initial Authorization duration: 2 years

REAUTHORIZATION CRITERIA: Sacrosidase (Sucraid®) is medically necessary when there is positive clinical response to therapy (e.g., decrease in symptoms of abdominal pain, cramps, bloating or gas; decrease in number and frequency of stools per day).

Reauthorization duration: 2 years

P&T Approval Date: Dec-12-2024

Title: Sapropterin dihydrochloride (Kuvan®, Javygtor®)

Applicable Drugs:

Brand Name	Generic Name
Kuvan, Javygtor®	Sapropterin dihydrochloride

Policy:

INITIAL CRITERIA: Sapropterin dihydrochloride (Kuvan®, Javygtor®) is medically necessary when ALL the following are met:

1. Diagnosis of phenylketonuria (PKU); and
2. Used in conjunction with phenylalanine (Phe)-restricted diet; and
3. Prescribed by or in consultation with a specialist with expertise in diagnosis and management of phenylketonuria; and
4. For Brand Kuvan® and Javygtor® only: inadequate response or inability to tolerate generic sapropterin dihydrochloride; and
5. Member will have Phe blood levels measured after 1 week of therapy (new starts to therapy only) and periodically for up to a month of therapy to determine response.

Initial authorization duration: 6 months

CONTINUATION CRITERIA: Sapropterin dihydrochloride (Kuvan®, Javygtor®) is medically necessary when ALL the following are met:

1. Member has had a positive clinical response to therapy (i.e. there is a reduction of phenylalanine (Phe) blood levels from baseline); and
2. Used in conjunction with phenylalanine (Phe)-restricted diet

Reauthorization duration: 2 years

P&T Approval Date: Sep-12-2024

Title: Satralizumab-mwge (Enspryng®)

Applicable Drugs:

Brand Name	Generic Name
Enspryng™	Satralizumab-mwge

Policy:

INITIAL CRITERIA: Satralizumab-mwge (Enspryng™) is approved when ALL of the following are met:

1. Diagnosis of neuromyelitis optica spectrum disorder (NMOSD); and
2. Member is anti-aquaporin-4 (AQP4) antibody positive; and
3. Prescribed by or in consultation with a neurologist or ophthalmologist; and
4. Member is 18 years of age or older

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA: Satralizumab-mwge (Enspryng™) is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

P&T Approval Date: Mar-20-2025

Title: Seizure Disorder Agents

Applicable Drugs:

Brand Name	Generic Name
Epidiolex®	Cannabidiol
Diacomit®	Stiripentol
Onfi®, Sympazan®	Clobazam
Banzel®	Rufinamide
Fintepla®	Fenfluramine
Sabril®/Vigafyde	Vigabatrin

Policy:

Dravet Syndrome

INITIAL CRITERIA: Cannabidiol (Epidiolex) is approved when ALL of the following are met:

1. Member is 1 years of age or older; and
2. Baseline CBC, serum transaminases and total bilirubin obtained prior to initiating therapy; and
3. Diagnosis of Dravet syndrome; and
4. Inadequate response or inability to tolerate ONE of the following:
 1. Clobazam*; or
 2. Valproic acid; or
 3. Levetiracetam; o
 4. Topiramate; and
5. Documentation of concurrent use with additional anti-epileptic(s); and
6. Prescribed by or in consultation with a neurologist

INITIAL CRITERIA: Stiripentol (Diacomit®) is approved when ALL of the following are met:

1. Diagnosis of seizures associated with Dravet syndrome; and
2. Member is 6 months of age or older and weighing 7kg or more; and
3. Used in combination with clobazam*; and
4. Prescribed by or in consultation with a neurologist

INITIAL CRITERIA: Clobazam (Onfi®, Sympazan®) tablets, films, or oral suspension is approved when ALL of the following are met:

1. Member is 6 months of age or older and weighs greater than or equal to 7 kg; and
2. Diagnosis of seizures associated with Dravet Syndrome (DS); and
3. Used in combination with Diacomit (Stiripentol); and
4. Prescribed by or in consultation with a neurologist; and
5. For brand Onfi® and brand Sympazan® only, inadequate response or inability to tolerate generic clobazam tablets or oral suspension

INITIAL CRITERIA: Fenfluramine (Fintepla®) is approved when ALL of the following are met:

1. Diagnosis of Dravet Syndrome; and
2. Member is 2 years of age or older; and
3. Inadequate response or inability to tolerate ONE of the following:
 1. Clobazam*; or
 2. Valproic acid; or
 3. Divalproex sodium; or
 4. Topiramate; or
 5. Levetiracetam; and
4. Prescribed by or in consultation with a neurologist

Initial authorization duration: 2 years

CONTINUATION CRITERIA: Cannabidiol (Epidiolex®), Stiripentol (Diacomit®), clobazam (Onfi®, Sympazan®), or fenfluramine (Fintepla®) is re-approved when ALL of the following are met:

1. Documentation of reduction in seizure activity or intensity; and

2. Stiripentol (Diacomit®) only, used in combination with clobazam*; and
3. Prescribed by or in consultation with a neurologist

Continuation authorization duration: 2 years

Lennox-Gastaut Syndrome (LGS)

INITIAL CRITERIA: Cannabidiol (Epidiolex®) is approved when ALL of the following are met:

1. Member is 1 years of age or older; and
2. Baseline CBC, serum transaminases and total bilirubin obtained prior to initiating therapy; and
3. Diagnosis of Lennox-Gastaut syndrome (LGS); and
4. Inadequate response or inability to tolerate ONE of the following:
 1. Valproic acid; or
 2. Lamotrigine; or
 3. Topiramate; or
 4. Felbamate; or
 5. Rufinamide*; or
6. Clobazam*; and
5. Documentation of concurrent use with additional anti-epileptic(s); and
6. Prescribed by or in consultation with a neurologist

INITIAL CRITERIA: Rufinamide (Banzel®) tablet or suspension is approved when ALL of the following are met:

1. Diagnosis of seizures associated with Lennox-Gastaut Syndrome (LGS); and
2. Used as adjunctive therapy; and
3. Member is 1 year of age or older; and
4. Inadequate response or inability to tolerate ONE of the following generics:
 1. Valproic acid; or
 2. Lamotrigine; or

3. Topiramate; or
4. Felbamate; or
5. Clobazam*; and
5. Prescribed by or in consultation with a neurologist; and
6. For rufinamide (Banzel®) suspension only; ONE of the following:
 1. Drug will be administered via nasogastric or gastrostomy tube; or
 2. Member is unable to swallow an intact capsule or tablet

INITIAL CRITERIA: Fenfluramine (Fintepla®) is approved when ALL of the following are met:

1. Diagnosis of seizures associated with Lennox-Gastaut Syndrome (LGS); and
2. Member is 2 years of age or older; and
3. Inadequate response or inability to tolerate ONE of the following generics:
 1. Valproic acid; or
 2. Lamotrigine; or
 3. Topiramate; or
 4. Felbamate; or
 5. Clobazam; and
4. Prescribed by or in consultation with a neurologist

Initial authorization duration: 2 years

INITIAL CRITERIA: Clobazam (Onfi®, Sympazan®) tablets, films or oral suspension is approved when ALL of the following are met:

1. Member is 2 years of age and older; and
2. Diagnosis of seizure associated with Lennox-Gastaut Syndrome; and
3. Used as adjunctive therapy; and
4. Prescribed by or in consultation with a neurologist; and
5. For Brand Onfi® and brand Sympazan® only, inadequate response or inability to tolerate generic clobazam tablets or oral suspension

Initial authorization duration: 2 years

CONTINUATION CRITERIA: Cannabidiol (Epidiolex®), clobazam (Onfi®, Sympazan®), rufinamide (Banzel®), or fenfluramine (Fintepla®) is re-approved when there is documentation of reduction in seizure activity or intensity.

Continuation authorization duration: 2 years

Seizures associated with tuberous sclerosis complex

INITIAL CRITERIA: Cannabidiol (Epidiolex®) is approved when ALL of the following are met:

1. Member is 1 years of age or older; and
2. Baseline CBC, serum transaminases and total bilirubin obtained prior to initiating therapy; and
3. Diagnosis of seizures associated with tuberous sclerosis complex; and
4. Inadequate response or inability to tolerate ONE of the following:
 1. Vigabatrin*; or
 2. Carbamazepine; or
 3. Oxcarbazepine; and
5. Documentation of concurrent use with additional anti-epileptic(s); and
6. Prescribed by or in consultation with a neurologist

Initial authorization duration: 2 years

CONTINUATION CRITERIA: Cannabidiol (Epidiolex®) is re-approved when there is documentation of reduction in seizure activity or intensity.

Continuation authorization duration: 2 years

Refractory complex partial seizure or infantile spasms

INITIAL CRITERIA: Vigabatrin (Sabril®, Vigafyde™), is approved when ALL of the following are met:

1. One of the following:
 1. ALL of the following:
 1. Diagnosis of refractory complex partial seizures as adjunctive therapy; and

2. Member is 2 years of age or older; and
3. Used as adjunctive therapy; or
2. BOTH of the following:
 1. Diagnosis of infantile spasms; and
 2. Member is 1 month to 2 years of age; and
2. For brand Sabril® only, inadequate response or inability to tolerate generic vigabatrin or vigadrone; and
3. Prescribed by or in consultation with a neurologist

Initial authorization duration: 2 years

CONTINUATION CRITERIA: Vigabatrin (Sabril®, Vigafyde™) is re-approved when there is documentation of reduction in seizure activity of intensity.

Continuation authorization duration: 2 years

P&T Approval Date: Mar-20-2025

Title: Setmelanotide (Imcivree) Policy

Applicable Drugs:

Brand Name	Generic Name
Imcivree	Setmelanotide

Policy:

INITIAL CRITERIA: Setmelanotide (Imcivree™) is medically necessary when ALL of the following are met:

1. One of the following:
 - a. Submission of medical records (e.g., chart notes, lab values) confirming a diagnosis of proopiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), leptin receptor (LEPR) deficiency by genetic testing demonstrating variants in POMC, PCSK1, or LEPR genes that are interpreted as pathogenic, or of uncertain significance (VUS); or
 - b. Diagnosis of Bardet-Biedl syndrome; and
2. Other causes or types of obesity have been ruled out (e.g., obesity due to suspected POMC, PCSK1 or LEPR deficiency with POMC, PCSK1 or LEPR variants classified as benign or likely benign; obesity associated with other genetic syndromes; polygenic obesity; obesity due to Bardet-Biedl syndrome); and
3. Member is obese as defined by BMI of $\geq 30 \text{ kg/m}^2$ in adults or ≥ 95 th percentile in pediatric patients using growth chart assessments; and
4. Prescribed by or in consultation with ONE of the following:
 - a. Endocrinologist; or
 - b. Medical geneticist; or
 - c. Specialist in the diagnosis and treatment of obesity; and
5. Member is 6 years of age or older

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Setmelanotide (Imcivree™) is medically necessary with documentation of positive clinical response to therapy (e.g. 5% weight loss based on baseline body weight or BMI)

Reauthorization duration: 12 months

P&T Approval Date: Mar-20-2025

Title: Sickle Cell Disease Agents

Applicable Drugs:

Brand Name	Generic Name
Endari®	L-glutamine
Oxbryta®	Voxelotor

Policy:

INITIAL CRITERIA L-glutamine (Endari®) is medically necessary when ALL of the following are met:

1. Diagnosis of sickle cell disease; and
2. Member is 5 years of age or older; and
3. Member has had 2 or more painful sickle cell crises within the past 12 months; and
4. Prescribed by or in consultation with a hematologist/oncologist or specialist with expertise in the diagnosis and management of sickle cell disease, and
5. Documentation of ONE of the following:
 - a. Concurrent hydroxyurea therapy; or
 - b. Inadequate response or inability to tolerate hydroxyurea

Initial authorization duration: 12 months

CONTINUATION CRITERIA L-glutamine (Endari®) is medically necessary when there is documentation of positive clinical response to therapy from baseline (e.g., reduction in the number of sickle cell crises, fewer hospitalizations due to sickle cell pain, etc.).

Continuation authorization duration: 2 years

INITIAL CRITERIA Voxelotor (Oxbryta®) is medically necessary when ALL of the following are met:

1. Diagnosis of sickle cell disease; and
2. No concurrent therapy with crizanlizumab-tmca (Adakveo®); and
3. Member is 4 years of age or older; and

4. Member had at least one vaso-occlusive crisis (VOC) event within the past 12 months (e.g., acute painful crisis, acute chest syndrome); and
5. Hemoglobin level that is between 5.5g/dL and 10.5g/dL prior to therapy initiation; and
6. Inadequate response or inability to tolerate hydroxyurea (i.e. Siklos, Droxia); and
7. Prescribed by or in consultation with a hematologist/oncologist or specialist with expertise in the diagnosis and management of sickle cell disease.

Initial authorization duration: 12 months

CONTINUATION CRITERIA Voxelotor (Oxbryta®) is medically necessary when both of the following are met:

1. Documentation of positive clinical response to Oxbryta® therapy (e.g., an increase in hemoglobin level of greater than or equal to 1 g/dL from baseline, decreased annualized incidence rate of VOCs); and
2. Member demonstrates hemoglobin level that does not exceed 10.5 g/dL

Continuation authorization duration: 2 years

P&T Approval Date: Sep-12-2024

Title: Sinecatechins (Veregen®)

Applicable Drugs:

Brand Name	Generic Name
Veregen®	Sinecatechins

Policy:

Sinecatechins (Veregen®) is approved when all of the following are met:

1. Diagnosis of Condylomata acuminata (external genital and perianal warts); and
2. Member is immunocompetent; and
3. Member is 18 years of age or older; and
4. Inadequate response or inability to tolerate imiquimod (generic Aldara®)

Authorization duration: 4 months

Total duration of treatment is limited to 16 weeks per lifetime

P&T Approval Date: Mar-20-2025

Title: Sirolimus topical gel (Hyftor™)

Applicable Drugs:

Brand Name	Generic Name
Hyftor™	sirolimus

Policy:

INITIAL CRITERIA: Sirolimus (Hyftor™) is approved when ALL of the following are met:

1. Diagnosis of facial angiofibroma associated with tuberous sclerosis complex; and
2. Member is 6 years of age or older; and
3. Member is not a candidate for laser therapy or surgical treatments; and
4. Prescribed by or in consultation with a dermatologist, neurologist, or geneticist

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Sirolimus (Hyftor™) is re-approved with documentation of positive clinical response to therapy (e.g., improvement in size or redness of facial angiofibroma)

Reauthorization duration: 2 years

P&T Approval Date: Mar-20-2025

Title: Sleep Agents

Applicable Drugs:

Brand Name	Generic Name
Ambien® [CR]	zolpidem tartrate immediate and extended release (PA applies to generic 10mg IR and 12.5mg CR)
Edluar®	zolpidem sublingual tablets
Zolpimist®	zolpidem
Intermezzo®	zolpidem
Lunesta®	eszopiclone
Hetlioz®/Hetlioz LQ®	tasimelton

Policy:

Insomnia

INITIAL CRITERIA: Edluar® 5mg, Zolpimist® are approved when ALL of the following are met:

1. Diagnosis of insomnia; and
2. Member is 18 years of age or older; and
3. One of the following:
 1. Inadequate response or inability to tolerate TWO of the following:
 1. Eszopiclone
 2. Zaleplon
 3. Zolpidem; OR
 2. Inability to swallow capsules/tablets (i.e., dysphagia, gastrointestinal [GI] tubes)

INITIAL CRITERIA: Any of the following high dose products (brand and generic): zolpidem tartrate (Ambien®) 10mg, zolpidem tartrate ER (Ambien® CR) 12.5mg, eszopiclone (Lunesta®) 3mg or Edluar® 10mg is approved when ALL of the following are met:

1. Diagnosis of insomnia; and
2. Member is 18 years of age or older; and
3. Patient has been counseled on practices associated with good sleep hygiene (e.g., avoiding stimulants such as caffeine, nicotine, alcohol close to bedtime, etc.); and
4. Inadequate response to a two-week trial of the lower dose; and

5. For brand products with generic equivalents only, inadequate response or inability to tolerate a generic equivalent

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA: Edluar® 5mg, Zolpimist®, zolpidem tartrate (Ambien®) 10mg, zolpidem tartrate ER (Ambien® CR) 12.5mg, eszopiclone (Lunesta®) 3mg, or Edluar® 10mg is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

Non-24 hour Sleep-Wake Disorder

INITIAL CRITERIA Tasimelteon (Hetlioz®) is approved when ALL of the following are met:

1. Prescribed by or in consultation with a sleep specialist or neurologist; and
2. Diagnosis of Non-24-hour Sleep-Wake Disorder (also known as free-running disorder, free-running or non-entrained type circadian rhythm sleep disorder, or hypernycthemeral syndrome); and
3. Member is 18 years of age or older; and
4. Member is totally blind (has no light perception); and
5. Member has circadian period greater than 24 hours; and
6. For brand Hetlioz only, inadequate response or inability to tolerate generic tasimelteon

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA: Hetlioz® is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

Smith-Magenis Syndrome

INITIAL CRITERIA Tasimelteon (Hetlioz®/Hetlioz LQ®) is approved when ALL of the following are met:

1. Prescribed by or in consultation with a sleep specialist or neurologist; and
2. Diagnosis of Smith-Magenis Syndrome; and
3. Member experiences nighttime sleep disturbances (i.e., difficulty falling asleep, frequent nighttime waking and early waking); and
4. One of the following:
 1. For Hetlioz only, member is 16 years of age or older; or

2. For Hetlio^z LQ only, member is 3 to 15 years of age; and
5. For brand Hetlio^z capsules only, inadequate response or inability to tolerate generic tasimelteon

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA: Hetlio^z®/Hetlio^z LQ® is re-approved when there is documentation of positive clinical response to therapy (i.e., improvement in nighttime total sleep time, improvement in nighttime sleep quality)

Reauthorization duration: 2 years

P&T Approval Date: Mar-20-2025

Title: Sodium oxybate (Xyrem®/Lumryz™)/calcium, magnesium, potassium and sodium oxybates (Xywav™)

Applicable Drugs:

Drug name	Generic name
Xyrem®	sodium oxybate solution
Xywav™	calcium, magnesium, potassium and sodium oxybates
Lumryz™	sodium oxybate extended-release oral suspension

Policy:

Cataplexy with narcolepsy (Type 1)

INITIAL CRITERIA: Sodium oxybate (Xyrem®) solution or calcium, magnesium, potassium and sodium oxybates (Xywav™) is approved when ALL of the following are met:

1. Diagnosis of Cataplexy with narcolepsy (Type 1); and
2. Member is 7 years of age or older; and
3. Diagnosis was confirmed by ONE of the following tests:
 1. Polysomnography (PSG); or
 2. Multiple sleep latency test (MSLT); and
4. Prescribed by or in consultation with a neurologist, psychiatrist, or sleep specialist; and
5. No concurrent use of sedative hypnotics and alcohol; and
6. Symptoms of cataplexy are present; and
7. Symptoms of excessive daytime sleepiness (e.g., irrepressible need to sleep or daytime lapses into sleep) are present; and
8. For Xyrem® solution only, inadequate response or inability to tolerate sodium oxybate solution (by Hikma)

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Sodium oxybate (Xyrem®) solution or calcium, magnesium, potassium and sodium oxybate (Xywav™) is re-approved when ALL of the following are met:

1. Documentation to support the efficacy associated with the current regimen (including but not limited to reduction in the frequency of cataplexy attacks or an improvement in the Epworth sleepiness scale); and
2. There is no claim history of a sedative hypnotic agents within one year of the request; and
3. For Xyrem® solution only, inadequate response or inability to tolerate sodium oxybate solution (by Hikma); and
4. Yearly evaluation by a neurologist, psychiatrist, or sleep specialist

Reauthorization duration: 12 months

INITIAL CRITERIA: Sodium oxybate suspension extended-release (Lumryz™) is medically necessary when ALL of the following are met:

1. Diagnosis of Cataplexy with narcolepsy (Type 1); and
2. Member is 7 years of age or older; and
3. Diagnosis was confirmed by ONE of the following tests:
 1. Polysomnography (PSG); or
 2. Multiple sleep latency test (MSLT); and
4. Prescribed by or in consultation with a neurologist, psychiatrist, or sleep specialist; and
5. Symptoms of cataplexy are present; and
6. Symptoms of excessive daytime sleepiness (e.g., irrepressible need to sleep or daytime lapses into sleep) are present; and
7. No concurrent use of sedative hypnotics and alcohol

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Sodium oxybate suspension extended-release (Lumryz™) is re-approved when ALL of the following are met:

1. Documentation to support the efficacy associated with the current regimen (including but not limited to reduction in the frequency of cataplexy attacks or an improvement in the Epworth sleepiness scale); and
2. There is no claim history of a sedative hypnotic agents within one year of the request; and
3. Yearly evaluation by a neurologist, psychiatrist, or sleep specialist

Reauthorization duration: 12 month

Excessive daytime sleepiness in narcolepsy (Type 2)

INITIAL CRITERIA: Sodium oxybate (Xyrem®) solution or calcium, magnesium, potassium and sodium oxybates (Xywav™) is approved when ALL of the following are met:

1. Diagnosis of Excessive daytime sleepiness in narcolepsy (Type 2); and
2. Member is 7 years of age or older; and
3. Diagnosis was confirmed by ONE of the following tests:
 1. Polysomnography (PSG); or
 2. Multiple sleep latency test (MSLT); and
4. Inadequate response or inability to tolerate ALL of the following:
 1. Modafinil or armodafinil; and
 2. One of the following:
 1. One stimulant product (e.g., amphetamine, methylphenidate); or
 2. History of or potential for a substance use disorder; and
 3. Sunosi®; and

5. Prescribed by or in consultation with a neurologist, psychiatrist, or sleep specialist; and
6. No concurrent use of sedative hypnotics and alcohol; and
7. Symptoms of cataplexy are absent; and
8. Symptoms of excessive daytime sleepiness (e.g., irrepressible need to sleep or daytime lapses into sleep) are present; and
9. For Xyrem® solution only, inadequate response or inability to tolerate sodium oxybate solution (by Hikma)

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Sodium oxybate (Xyrem®) solution or calcium, magnesium, potassium and sodium oxybates (Xywav™) is re-approved when ALL of the following are met:

1. Documentation to support the efficacy associated with the current regimen (including but not limited to reduction in the frequency of cataplexy attacks or an improvement in the Epworth sleepiness scale); and
2. There is no claim history of a sedative hypnotic agents within one year of the request; and
3. For Xyrem® solution only, inadequate response or inability to tolerate sodium oxybate solution (by Hikma); and
4. Yearly evaluation by a neurologist, psychiatrist, or sleep specialist

Reauthorization duration: 12 months

INITIAL CRITERIA: Sodium oxybate suspension extended-release (Lumryz™) is approved when ALL of the following are met:

1. Diagnosis of Excessive daytime sleepiness in narcolepsy (Type 2); and
2. Member is 7 years of age or older; and
3. Diagnosis was confirmed by ONE of the following tests:
 1. Polysomnography (PSG); or
 2. Multiple sleep latency test (MSLT); and

4. Inadequate response or inability to tolerate ALL of the following:
 1. Modafinil or armodafinil; and
 2. One of the following:
 1. One stimulant product (e.g., amphetamine, methylphenidate); or
 2. history of or potential for a substance use disorder; and
 3. Sunosi®; and
5. Prescribed by or in consultation with a neurologist, psychiatrist, or sleep specialist; and
6. Symptoms of cataplexy are absent; and
7. Symptoms of excessive daytime sleepiness (e.g., irrepressible need to sleep or daytime lapses into sleep) are present; and
8. No concurrent use of sedative hypnotics and alcohol

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Sodium oxybate suspension extended-release (Lumryz™) is re-approved when ALL of the following are met:

1. Documentation to support the efficacy associated with the current regimen (including but not limited to reduction in the frequency of cataplexy attacks or an improvement in the Epworth sleepiness scale); and
2. There is no claim history of a sedative hypnotic agents within one year of the request; and
3. Yearly evaluation by a neurologist, psychiatrist, or sleep specialist

Reauthorization duration: 12 months

Idiopathic Hypersomnia (IH)

INITIAL CRITERIA: Calcium, magnesium, potassium and sodium oxybates (Xywav™) is approved when ALL of the following are met:

1. Diagnosis of idiopathic hypersomnia; and
2. Member is 18 years of age or older; and

3. Diagnosis was confirmed by ONE of the following tests:
 1. Polysomnography (PSG); or
 2. Multiple sleep latency test (MSLT); and
4. Symptoms of excessive daytime sleepiness (e.g., nap duration of longer than 60 minutes) are present; and
5. Prescribed by or in consultation with a neurologist, psychiatrist, or sleep specialist; and
6. No concurrent use of sedative hypnotics and alcohol

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Calcium, magnesium, potassium and sodium oxybates (Xywav™) is re-approved when ALL of the following are met:

1. Documentation demonstrating a reduction in symptoms of excessive daytime sleepiness associated with therapy; and
2. There is no claim history of a sedative hypnotic agents within one year of the request; and
3. Yearly evaluation by a neurologist, psychiatrist, or sleep specialist

Reauthorization duration: 12 months

P&T Approval Date: Mar-20-2025

Title: Sodium phenylbutyrate and Taurursodiol (Relyvrio™)

Applicable Drugs:

Brand Name	Generic Name
Relyvrio™	Sodium phenylbutyrate and Taurursodiol

Policy:

INITIAL CRITERIA Sodium phenylbutyrate and taurursodiol (Relyvrio™) is approved when ALL of the following are met:

1. Diagnosis of amyotrophic lateral sclerosis (ALS); and
2. Diagnosis of ALS is further supported by neurogenic changes in electromyography (EMG); and
3. Baseline functional ability has been conducted prior to initiating treatment (e.g., speech, walking, climbing stairs, etc.); and
4. Other differential diagnoses (e.g., multifocal motor neuropathy, cervical radiculomyelopathy, inflammatory myopathies, spinobulbar muscular atrophy, myasthenia gravis, etc.) have been ruled out); and
5. Member has a percent (%) forced vital capacity (%FVC) or slow vital capacity (%SVC) greater than or equal to 60% at the start of treatment; and
6. Member does not require permanent noninvasive ventilation or invasive ventilation; and
7. Member has had ALS symptoms for less than or equal to 18 months; and
8. Member is 18 years of age or older; and
9. Prescribed by or in consultation with a neurologist with expertise in the diagnosis of ALS

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA Sodium phenylbutyrate and taurursodiol (Relyvrio™) is re-approved when BOTH of the following are met:

1. Documentation of slowed disease progression from baseline; and
2. Prescribed by or in consultation with a neurologist with expertise in the diagnosis of ALS

Reauthorization duration: 6 months

P&T Approval Date: Mar-20-2025

Title: Sparsentan (Filspari™)

Applicable Drugs:

Brand Name	Generic Name
Filspari™	Sparsentan

Policy:

INITIAL CRITERIA: Sparsentan (Filspari) is medically necessary when all of the following are met:

1. Diagnosis of primary immunoglobulin A nephropathy (IgAN) as confirmed by a kidney biopsy; and
2. Documentation is provided that member is at risk of rapid disease progression [e.g., generally a urine protein-to-creatinine ratio (UPCR) greater than or equal to 1.5 g/g, or by other criteria such as clinical risk scoring using the International IgAN Prediction tool]; and
3. Medication will be used to reduce proteinuria; and
4. Member has an estimated glomerular filtration rate (eGFR) of greater than or equal to 30 mL/min/1.73m²; and
5. Member had an inadequate response or inability to tolerate a minimum 90-day trial of a maximally tolerated dose of one of the following:
 - a. Angiotensin-receptor blockers (ARB) (e.g., losartan, valsartan); or
 - b. Angiotensin-converting enzyme (ACE) inhibitor (e.g., benazepril, lisinopril); and
6. Medication will not be used in combination with any of the following:
 - a. Angiotensin receptor blockers or angiotensin receptor-neprilysin inhibitor; or
 - b. Endothelin receptor antagonists (ERAs) (e.g., ambrisentan, bosentan, Opsumit); or
 - c. Aliskiren; and
7. Member is 18 years or age or older; and
8. Prescribed by or in consultation with a nephrologist

Initial authorization duration: 1 year

CONTINUATION CRITERIA: Sparsentan (Filspari) is approved when BOTH of the following are met:

1. Documentation of positive clinical response to therapy from baseline as demonstrated by a decrease in urine protein-to-creatinine ratio (UPCR); and
2. Prescribed by or in consultation with a nephrologist; and
3. Medication is not taken in combination with any of the following:
 - a. Angiotensin receptor blocker or angiotensin receptor-neprilysin inhibitor
 - b. Endothelin receptor antagonists (ERAs) (e.g, ambrisentan, bosentan, Opsumit)
 - c. Aliskiren

Continuation authorization duration: 1 year

P&T Approval Date: Mar-20-2025

Title: Spesolimab-sbzo (Spevigo®) SQ

Applicable Drugs:

Brand Name	Generic Name
Spevigo® SQ	Spesolimab-sbzo

Policy:

INITIAL CRITERIA: Spesolimab-sbzo (Spevigo®) is medically necessary when ALL of the following are met:

1. Diagnosis of generalized pustular psoriasis (GPP) as defined by both of the following:
 1. Primary, sterile, macroscopically visible pustules on non-acral skin (excluding cases where pustulation is restricted to psoriatic plaques); and
 2. Disease is relapsing (>1 episode) or persistent (>3 months); and
2. Subcutaneous formulation will not be used to treat GPP flare; and
3. Both of the following:
 1. Member is 12 years of age or older; and
 2. Member weighs at least 40 kg; and
4. Prescribed by or in consultation with a dermatologist

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Spesolimab-sbzo (Spevigo®) is re-approved with documentation of positive clinical response to therapy (e.g., reduction in the number of flares)

Reauthorization duration: 12 months

P&T Approval Date: Sep-12-2024

Title: Stimulants

Applicable Drugs:

Brand Name	Generic Name
Adderall® [IR/XR]	Amphetamine/Dextroamphetamine
Mydayis®	Amphetamine/Dextroamphetamine
Adzenys® [XR ODT/ER]	Amphetamine
Dyanavel® XR	Amphetamine
Evekeo® [ODT]	Amphetamine
Dexedrine® [IR/SA]	Dextroamphetamine sulfate
ProCentra®	Dextroamphetamine sulfate
Zenzedi®	Dextroamphetamine
Xelstrym®	Dextroamphetamine
Focalin® [IR/XR]	Dexmethylphenidate HCL
Vvyanse®	Lisdexamfetamine dimesylate
Adhansia XR™	Methylphenidate HCL
Aptensio® XR	Methylphenidate HCL
Concerta®	Methylphenidate HCL
Daytrana®	Methylphenidate HCL
Jornay PM™	Methylphenidate HCL
Metadate® [ER/CD]	Methylphenidate HCL

Methylin®	Methylphenidate HCL
Ritalin® [IR/LA]	Methylphenidate HCL
Quillichew® ER	Methylphenidate HCL
Quillivant® XR	Methylphenidate HCL
Cotempla®	Methylphenidate ER
Relexxii®	Methylphenidate ER
Desoxyn®	Methamphetamine HCL
Azstarys™	Serdexmethylphenidate/Dexmethylphenidate

Policy:

Doses above the high cumulative dose are medically necessary when ALL of the following are met:

1. Inadequate response or inability to tolerate an alternative active ingredient within the CNS stimulant drug class prior to increasing the dose beyond the cumulative high dose limit; and
2. Member has been assessed for, and counseled by prescriber on ALL of the following:
 1. The risk for substance abuse; and
 2. The risk for cardiac related adverse events (i.e., hypertension); and
 3. The risk for new or worsening psychosis (i.e., maniac behavior); and
3. Requests that exceed the cumulative daily dose for the total daily dose of the drug, dose frequency, or duration of therapy approved or recommended by the FDA or as stated in accepted compendia are considered off-label and are reviewed per Off-Label Use policy

Authorization duration: 12 months

INITIAL CRITERIA: Amphetamine (Evekeo®) is medically necessary when ONE of the following is met:

1. Diagnosis of narcolepsy and ALL of the following:
 1. Prescribed by or in consultation with a neurologist or sleep specialist; and

2. Inadequate response or inability to tolerate generic modafinil or armodafinil; and

3. Diagnosis confirmed by ONE of the following tests:

1. Polysomnography (PSG); or

2. Multiple sleep latency test (MSLT); or

2. Attention Deficit Disorder with Hyperactivity (ADHD) and all of the following:

1. Member is 3 to 17 years of age; and

2. Inadequate response or inability to tolerate TWO of the following generic stimulant agents for

ADHD:

1. Methylphenidate

2. Mixed amphetamine salts

3. Dextroamphetamine

4. Methamphetamine hydrochloride

5. Dexmethylphenidate; or

3. Exogenous Obesity:

1. If member has weight loss rider please refer to Weight Loss Agents policy for approval criteria and duration; or

2. If member does not have a weight loss agents rider; deny as benefit exclusion*

*Drugs that are used for weight loss are covered only with weight loss rider.

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA: Amphetamine (Evekeo®) is re-approved when there is documentation of positive clinical response.

Reauthorization duration: 2 years

Quantity limit requests are approved when ONE of the following is met: (drug specific criteria below).

1. Requests that exceed the cumulative daily dose, dose frequency, or duration of therapy approved or recommended by the FDA or as stated in accepted compendia¹ are considered off-label and are reviewed per Off-Label Use policy, or
2. Requests that do not exceed the cumulative daily dose, dose frequency or duration of therapy approved or recommended by the FDA or as stated in accepted compendia¹: A quantity limit exceeding those listed in the following table is approved when ONE of the following is met:

1. Documentation of the inability to reach the requested dose with higher strengths of commercially available dosage forms due to member specific characteristics (i.e., inability to swallow larger pills, malabsorption, presence of a feeding tube, etc.); or
2. The requested dose is not commercially available; or
3. The requested dose is used for titration or loading-dose purposes (one-time authorization)

¹ Please refer to the Off-Label Use policy for definition of accepted compendia

Authorization duration: 2 years

Authorization duration for dose titration: 14 days

Medication	Maximum Quantity per day	Quantity limit per rolling 30 days, unless otherwise specified (tablets, capsules, mL)
Amphetamine (Adzenys XR [®])	1	30
Amphetamine (Adzenys ER [®]) 1.25mg/ml susp	15 ml	450
Dextroamphetamine/Amphetamine (Adderall [®]) 5mg, 7.5mg, 10mg, 12.5mg, 15mg and 20mg	3	90
Dextroamphetamine/Amphetamine (Adderall [®]) 30mg	2	60
Amphetamine/Dextroamphetamine ER (Mydayis [™])	1	30
Dextroamphetamine/Amphetamine (Adderall XR [®]) 5mg, 10mg, 15mg, 20mg, 25mg, 30mg	1	30
Amphetamine (Dyanavel XR [®]) 2.5mg/ml Susp	8mL	240

Amphetamine (Dyanavel XR®) 5mg, 10mg, 15mg, 20mg tablets	1	30
Dextroamphetamine sulfate (Dexedrine®) 5mg cap SA	3	90
Dextroamphetamine sulfate (Dexedrine®) 10mg cap SA	6	180
Dextroamphetamine sulfate (Dexedrine®) 15mg cap SA	4	120
Dextroamphetamine sulfate 5mg tablet	3	90
Dextroamphetamine sulfate 10mg tablet	3	90
Dexmethylphenidate HCL (Focalin®) 2.5mg, 5mg, 10mg	2	60
Dexmethylphenidate HCL (Focalin XR®) 5mg, 10mg, 15mg, 20mg, 25mg, 30mg, 35mg, 40mg	1	30
Dextroamphetamine sulfate (Procentra®) 5mg/5ml solution	60	1800
Dextroamphetamine (Xelstry™) 13.5 MG/9HR, 18 MG/9HR, 4.5 MG/9HR, 9 MG/9HR	1	30
Dextroamphetamine (Zenzedi®) 2.5mg, 5mg, 7.5mg, 10mg, 15mg, 20mg tablet	3	90
Dextroamphetamine (Zenzedi®) 30mg tablet	2	60
Amphetamine (Evekeo®) 5mg	3	90
Amphetamine (Evekeo®) 10mg	4	120
Amphetamine (Evekeo® ODT)	3	90

Lisdexamfetamine dimesylate (Vyvanse®) 20mg, 30mg, 40mg, 50mg, 60mg, 70mg	1	30
Methylphenidate HCL ER 24HR (Adhansia™ XR) 25mg, 35mg, 45mg, 55mg, 70mg, 85mg	1	30
Methylphenidate (Aptensio XR®)	1	30
Methylphenidate HCL (Concerta®) 18mg, 27mg, 54mg	1	30
Methylphenidate HCL (Concerta®) 36mg tablet ER	2	60
Methylphenidate HCL ER 72mg osmotic release tab	1	30
Methylphenidate (Relexxii®) tab ER osmotic release 45mg, 63mg	1	30
Methylphenidate (Daytrana patch®) 10mg/9hr, 15mg/9hr, 20mg/9hr, 30mg/9hr	1	30
Methamphetamine HCL (Desoxyn®) 5mg tablet	5	150
Methylphenidate HCL ER capsule (Jornay™ PM) 20mg, 40mg, 60mg, 80mg, 100mg	1	30
Methylphenidate HCL (Metadate CD®) 10mg, 20mg, 30mg, 40mg, 50mg, 60mg	1	30
Methylphenidate HCL (Metadate ER®) 10mg, 20mg tablet SA	3	90
Methylphenidate HCL (Methylin®) 2.5mg, 10mg chewable tablet	6	180
Methylphenidate HCL (Methylin®) 5mg chewable tablet	3	90

Methylphenidate HCL (Methylin®) 10mg/5ml	30	900
Methylphenidate HCL (Methylin®) 5mg/5ml	60	1800
Methylphenidate HCL (Ritalin®) 5mg, 10mg, 20mg	3	90
Methylphenidate HCL (Ritalin LA®) 10mg, 40mg capsule	1	30
Methylphenidate HCL (Ritalin LA®) 20mg capsule	3	90
Methylphenidate HCL (Ritalin LA®) 30mg capsule	2	60
Methylphenidate (Quillichew ER®) 20mg, 30mg	2	60
Methylphenidate (Quillichew ER®) 40mg	1	30
Methylphenidate (Quillivant XR®) 5mg/mL	12mL	360
Methylphenidate ER disintegrating tabs (Cotempla®) 8.6mg, 17.3mg, 25.9mg	1	30
Serdexmethylphenidate-dexmethylphenidate (Azstarys™)	1	30

P&T Approval Date: Mar-20-2025

Title: Teduglutide (Gattex)

Applicable Drugs:

Brand Name	Generic Name
Gattex®	teduglutide

Policy:

INITIAL CRITERIA: Teduglutide (Gattex®) is medically necessary when ALL of the following are met:

1. Diagnosis of Short Bowel Syndrome (SBS) (defined as a member left with <200 cm of functional small bowel); and
2. Currently receiving parenteral nutrition/intravenous (PN/IV) support for at least 12 consecutive months; and
3. Prescribed by or in consultation with a gastroenterologist; and
4. Member is 1 year of age or older

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Teduglutide (Gattex®) is medically necessary when BOTH of the following are met:

1. Documentation of reduction in parenteral nutrition/intravenous (PN/IV) support from baseline (prior to initiation of teduglutide therapy) while on Gattex therapy; and
2. Prescribed by or in consultation with a gastroenterologist

Reauthorization duration: 2 years

P&T Approval Date: Dec-12-2024

Title: Telotristat ethyl (Xermelo)

Applicable Drugs:

Brand Name	Generic Name
Xermelo®	telotristat

Policy:

INITIAL CRITERIA: Telotristat (Xermelo®) is medically necessary when ALL of the following are met:

1. Diagnosis of carcinoid syndrome diarrhea; and
2. Member is 18 years of age or older; and
3. Diarrhea is inadequately controlled by a stable dose of somatostatin analog (SSA) therapy (e.g., octreotide [Sandostatin, Sandostatin LAR], lanreotide [Somatuline Depot]) for at least 3 months; and
4. Used in combination with SSA therapy; and
5. Prescribed by or in consultation with one of the following:
 1. Oncologist
 2. Endocrinologist
 3. Gastroenterologist

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Telotristat (Xermelo®) is medically necessary when BOTH of the following are met:

1. Documentation of positive clinical response to Xermelo® therapy; and
2. Xermelo® will continue to be used in combination with SSA therapy (e.g., octreotide [Sandostatin, Sandostatin LAR], lanreotide [Somatuline Depot])

Reauthorization duration: 2 years

P&T Approval Date: Dec-12-2024

Title: Tezepelumab-ekko (Tezspire®)

Applicable Drugs:

Brand Name	Generic Name
Tezspire®	Tezepelumab-ekko

Policy:

INITIAL CRITERIA: Tezepelumab-ekko (Tezspire) solution is medically necessary when ALL of the following are met:

1. Submission of documentation (e.g., chart notes) confirming a diagnosis of severe asthma; and
2. Member is 12 years of age or older; and
3. One of the following:
 1. Member has had two or more asthma exacerbations requiring systemic corticosteroids (e.g., prednisone) within the past 12 months
 2. Prior asthma-related hospitalization within the past 12 months; and
4. Paid claims or submission of documentation (e.g., chart notes) confirming member is currently being treated with ONE of the following or is unable to tolerate these medications:
 1. Medium to high dose inhaled corticosteroid (e.g., greater than or equal to 500 mcg fluticasone propionate equivalent/day); and ONE additional controller medication; or
 2. One maximally dosed combination ICS/LABA products (e.g., Advair (fluticasone propionate/salmeterol), Dulera (mometasone/formoterol), Symbicort (budesonide/formoterol); and
5. Prescribed by or in consultation with a pulmonologist or allergy/immunology specialist; and
6. No concurrent therapy with any other biologic agents; and
7. Dosing and frequency does not exceed maximum FDA recommendation per indication requested

Initial authorization duration: 12 months

CONTINUATION CRITERIA: Tezepelumab-ekko (Tezspire) solution is medically necessary when ALL of the following are met:

1. Submission of documentation (e.g., chart note) of positive clinical response to therapy (e.g., reduction in exacerbations, improvement in FEV1, decreased use of rescue medications; and
2. Paid claims or submission of documentation (e.g., chart notes) confirming member is currently being treated with ONE of the following or is unable to tolerate these medications:
 1. Medium to high dose inhaled corticosteroid (e.g., greater than or equal to 500 mcg fluticasone propionate equivalent/day); and ONE additional controller medication; or
 2. One maximally dosed combination ICS/LABA products (e.g., Advair (fluticasone propionate/salmeterol), Breo Ellipta (fluticasone furoate/vilanterol), Symbicort (budesonide/formoterol); and
3. Prescribed by or in consultation with a pulmonologist or allergy/immunology specialist; and
4. No concurrent therapy with any other biologic agents; and
5. ONE of the following:
 1. Dosing and frequency does not exceed maximum FDA recommendation per indication requested; or
 2. Member is continuing on the established dose and frequency previously approved

Continuation approval duration: 12 months

P&T Approval Date: Mar-20-2025

Title: Tolvaptan (Samsca®, Jynarque®)

Applicable Drugs:

Brand Name	Generic Name
Samsca®	Tolvaptan
Jynarque®	Tolvaptan

Policy:

Hyponatremia

INITIAL CRITERIA Tolvaptan (Samsca®) is medically necessary when ALL of the following are met:

1. Member is 18 years of age or older; and
2. Clinically significant hypervolemic or euvolemic hyponatremia and ONE of the following:
 - a. Serum sodium less than 125meq/L; or
 - b. Serum sodium 125-134meq/L with symptoms (i.e., nausea, vomiting, headache, lethargy, confusion, etc.); and
3. Inadequate response or inability to tolerate therapies to control hyponatremia (i.e., fluid restriction, diuretics, demeclocycline, etc.); and
4. Prescribed by or in consultation with a cardiologist, nephrologist, or endocrinologist; and
5. Brand Samsca only, inadequate response or inability to tolerate generic tolvaptan; and
6. Treatment has been initiated or re-initiated in a hospital setting prior to discharge within the past 30 days

Initial authorization duration: 30 days

REAUTHORIZATION CRITERIA Tolvaptan (Samsca®) is medically necessary when ALL of the following are met:

1. Documentation of positive clinical response; and
2. Liver function is monitored and there are no signs or symptoms of liver injury; and
3. Prescriber is aware of the risk of liver injury with use beyond 30 days

Reauthorization duration: 12 months

Autosomal dominant polycystic kidney disease

INITIAL CRITERIA Tolvaptan (Jynarque®) is medically necessary when ALL of the following are met:

1. Member is 18 years of age or older; and
2. Diagnosis of autosomal dominant polycystic kidney disease with risk of rapidly progressing kidney disease; and
3. Baseline serum transaminases and bilirubin obtained prior to initiation of therapy; and
4. Prescribed by or in consultation with nephrologist or kidney transplant specialist

Initial authorization duration: 3 months

REAUTHORIZATION CRITERIA Tolvaptan (Jynarque®) is medically necessary when ALL of the following are met:

1. ONE of the following
 - a. Decline in kidney function has slowed; or
 - b. Kidney pain has improved; and
2. Serum transaminase less than 3 times the upper limit of normal; and
3. Bilirubin less than 2 times upper limit of normal

Reauthorization duration: 12 months

P&T Approval Date: Sep-12-2024

Title: Topical Hyperhidrosis Agents

Applicable Drugs:

Brand Name	Generic Name
Qbrexza™	Glycopyrronium
Sofdra™	Sofpironium

Policy:

INITIAL CRITERIA: glycopyrronium (Qbrexza®), sofpironium (Sofdra™) is medically necessary when ALL of the following are met:

1. Diagnosis of primary axillary hyperhidrosis for at least 6 months; and
2. Member is 9 years of age or greater; and
3. Prescribed by or in consultation with a dermatologist; and
4. Hyperhidrosis Disease Severity Scale grade 3 or 4; and
5. Documentation of an inadequate response (minimum 6 weeks trial), or inability to tolerate aluminum chloride (e.g. Drysol)

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA: glycopyrronium (Qbrexza®), sofpironium (Sofdra™) is medically necessary when there is positive clinical response to therapy.

Reauthorization duration: 2 years

P&T Approval Date: Mar-20-2025

Title: Transthyretin Amyloidosis Agents

Applicable Drugs:

Brand Name	Generic Name
Tegsedi™	Inotersen
Vyndamax®, Vyndaqel®	Tafamidis meglumine
Wainua™	eplontersen
Attruby™	acoramidis

Policy:

INITIAL CRITERIA Tegsedi™ (inotersen) is approved when ALL of the following are met:

1. Diagnosis of polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis with transthyretin mutation (e.g., V30M) confirmed by molecular genetic testing; and
2. Documentation of ONE of the following baseline ambulation parameters in either the Familial Amyloid Polyneuropathy (FAP) Stage or Polyneuropathy Disability (PND) Score
 - a. Stage 1 (unimpaired ambulation) or 2 (assisted ambulation) on the Familial Amyloid Polyneuropathy (FAP) staging tool; or
 - b. Score I, II, IIIa, or IIIb on the Polyneuropathy Disability (PND) scoring tool; AND
3. Documented presence of cardiac or renal manifestations, or motor, sensory, or autonomic neuropathy related to the hATTR amyloidosis with polyneuropathy (e.g., neuropathic pain, muscle weakness that affects daily living, orthostatic hypotension, diarrhea, nausea, vomiting, heart failure, arrhythmias, proteinuria, renal failure; vision disorders, such as vitreous opacity, dry eyes, glaucoma, or pupils with an irregular or scalloped appearance; and
4. Documentation confirming the member has not had a liver transplant; and
5. Prescribed by or in consultation with a neurologist, geneticist, or professional provider specializing in the treatment of amyloidosis; and
6. Member is 18 years of age or older; and
7. No concurrent use with another TTR silencer (e.g., patisiran (Onpattro), vutrisiran (Amvuttra), eplontersen (Wainua)) or with a TTR stabilizer (e.g., Vyndaqel, Vyndamax)

Initial authorization duration: 16 months

CONTINUATION CRITERIA Tegsedi™ (inotersen) is re-approved when BOTH of the following are met:

1. Documentation of one of the following
 - a. Stage 1 (unimpaired ambulation) or 2 (assisted ambulation) on the Familial Amyloid Polyneuropathy (FAP) staging tool; or
 - b. Score I, II, IIIa, or IIIb on the Polyneuropathy Disability (PND) scoring tool; and
2. Documented improvement or stability in the signs and symptoms hATTR amyloidosis with polyneuropathy (e.g., neuropathic pain, muscle weakness that affects daily living, orthostatic hypotension, diarrhea, nausea, vomiting, heart failure, arrhythmias, proteinuria, renal failure; vision disorders, such as vitreous opacity, dry eyes, glaucoma, or pupils with an irregular or scalloped appearance), based on objective or standard evaluation scales; and
3. No concurrent use with another TTR silencer (e.g., patisiran (Onpattro), vutrisiran (Amyvuttra), eplontersen (Wainua)) or with a TTR stabilizer (e.g., Vyndaqel, Vyndamax)

Continuation authorization duration: 2 years

INITIAL CRITERIA Tafamidis meglumine (Vyndamax®, Vyndaqel®) is approved when ALL of the following are met:

1. Member is 18 years of age or older; and
2. Diagnosis of transthyretin-mediated amyloidosis with cardiomyopathy (ATTR-CM) confirmed by ONE of the following:
 - a. Member has a transthyretin (TTR) mutation (e.g., V122I), or
 - b. Cardiac or noncardiac tissue biopsy demonstrating histologic confirmation of TTR amyloid deposits, or
 - c. All of the following: echocardiogram or cardiac magnetic resonance image suggestive of amyloidosis, scintigraphy scan suggestive of cardiac TTR amyloidosis, and absence of light-chain amyloidosis; and
3. Prescribed by or in consultation with a cardiologist; and
4. One of the following:
 - a. History of heart failure (HF), with at least one prior hospitalization for HF, or

- b. Presence of clinical signs and symptoms of HF (e.g., dyspnea, edema); or
- 5. Member has New York Heart Association (NYHA) Functional Class I, II, or III heart failure; and
- 6. No concurrent use with a TTR silencer (e.g., patisiran (Onpattro), vutrisiran (Amvuttra), eplontersen (Wainua), inotersen (Tegsedi))

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Tafamidis meglumine (Vyndamax®, Vyndaqel®) is re-approved when ALL of the following are met:

- 1. Positive clinical response to therapy; and
- 2. Member continues to have NYHA Functional Class I, II, or III heart failure; and
- 3. Prescribed by or in consultation with a cardiologist; and
- 4. No concurrent use with a TTR silencer (e.g., patisiran (Onpattro), vutrisiran (Amvuttra), eplontersen (Wainua), inotersen (Tegsedi))

Reauthorization duration: 12 months

INITIAL CRITERIA: Eplontersen (Wainua™) is approved when ALL of the following are met:

- 1. Diagnosis of hereditary transthyretin-mediated amyloidosis (hATTR amyloidosis) with polyneuropathy; and
- 2. Member is 18 years of age or older; and
- 3. Member has a transthyretin (TTR) mutation (e.g., V30M); and
- 4. One of the following:
 - 1. Member has a baseline familial amyloidotic polyneuropathy (FAP) stage of 1 or 2; or
 - 2. Member has a baseline neuropathy impairment score (NIS) greater than or equal to 10 and less than or equal to 130; or
 - 3. Member has a baseline Karnofsky Performance Status score greater than 50%; and
- 5. Presence of clinical signs and symptoms of the disease (e.g., neuropathy); and
- 6. Member has not had a liver transplant; and

7. Prescribed by or in consultation with a neurologist; and
8. No concurrent use with another TTR silencer (e.g., patisiran (Onpattro), vutrisiran (Amyvuttra), inotersen (Tegsedi)) or with a TTR stabilizer (e.g., Vyndaqel, Vyndamax)

Initial authorization duration: 12 months

CONTINUATION CRITERIA: Eplontersen (Wainua™) is re-approved when ALL of the following are met:

1. Member demonstrates positive clinical response to therapy as evidenced by an improvement in clinical signs and symptoms from baseline (e.g., neuropathy, quality of life, lower serum TTR level); and
2. One of the following:
 1. Member continues to have a familial amyloidotic polyneuropathy (FAP) stage of 1 or 2; or
 2. Member continues to have a neuropathy impairment score (NIS) greater than or equal to 10 and less than or equal to 130; or
 3. Member continues to have a Karnofsky Performance Status score greater than 50%; and
3. Member has not had a liver transplant; and
4. Prescribed by or in consultation with a neurologist; and
5. No concurrent use with another TTR silencer (e.g., patisiran (Onpattro), vutrisiran (Amyvuttra), inotersen (Tegsedi)) or with a TTR stabilizer (e.g., Vyndaqel, Vyndamax)

Continuation approval duration: 12 months

INITIAL CRITERIA: acoramidis (Attruby™) is medically necessary when ALL of the following are met:

1. Diagnosis of transthyretin-mediated amyloidosis with cardiomyopathy (ATTR-CM); and
2. One of the following:
 1. Presence of a transthyretin (TTR) mutation (e.g., V122I) as detected by an FDA-approved test or a test performed at a facility approved by Clinical Laboratory Improvement Amendments (CLIA); or
 2. Cardiac or noncardiac tissue biopsy demonstrating histologic confirmation of TTR amyloid deposits; or
 3. Both of the following:
 1. Cardiac magnetic resonance imaging or scintigraphy scan suggestive of amyloidosis; and
 2. Absence of light-chain amyloidosis; and
3. Member has a history of heart failure evidenced by at least one of the following:
 1. At least one prior hospitalization for heart failure; or
 2. Presence of clinical signs and symptoms of heart failure (e.g., dyspnea, edema); and
4. Member has New York Heart Association (NYHA) Functional Class I, II, or III heart failure; and
5. Requested drug is not used in combination with a TTR silencer (e.g., Amyvuttra) or a TTR stabilizer (e.g., Vyndamax/Vyndaqel); and
6. Prescribed by or in consultation with a cardiologist

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: acoramidis (Attruby™) is medically necessary when ALL of the following are met:

1. Member demonstrates positive clinical response to therapy (e.g., reduced cardiovascular-related hospitalizations); and
2. Member continues to have New York Heart Association (NYHA) Functional Class I, II, or III heart failure; and
3. Requested drug is not used in combination with a TTR silencer (e.g., Amvuttra) or a TTR stabilizer (e.g., Vyndamax/Vyndaqel); and
4. Prescribed by or in consultation with a cardiologist

Reauthorization duration: 12 months

P&T Approval Date: Mar-20-2025

Title: Triheptanoin (Dojolvi)

Applicable Drugs:

Brand Name	Generic Name
Dojolvi™	triheptanoin

Policy:

INITIAL CRITERIA: Triheptanoin (Dojolvi) is medically necessary when ALL of the following are met:

1. Diagnosis of molecularly confirmed long-chain fatty acid oxidation disorders (LC-FAOD); and
2. Will be used as a source of calories and fatty acids; and
3. Not used with any other medium-chain triglyceride (MCT) product; and
4. Prescribed by or in consultation with a clinical specialist knowledgeable in appropriate disease-related dietary management (e.g., geneticist, cardiologist, gastroenterologist, etc.)

Initial Authorization duration: 2 years

REAUTHORIZATION CRITERIA: Triheptanoin (Dojolvi) is medically necessary when ALL of the following are met:

1. Prescriber attests to continued need of therapy; and
2. Not used with any other medium-chain triglyceride (MCT) product; and
3. Prescribed by or in consultation with a clinical specialist knowledgeable in appropriate disease-related dietary management (e.g., geneticist, cardiologist, gastroenterologist, etc.)

Reauthorization duration: 2 years

P&T Approval Date: Dec-12-2024

Title: Trofinetide (Daybue)

Applicable Drugs:

Brand Name	Generic Name
Daybue™	trofinetide

Policy:

INITIAL CRITERIA: Trofinetide (Daybue™) is medically necessary when all of the following are met:

1. Diagnosis of Rett syndrome; and
2. One of the following:
 1. Presence of ALL of the following clinical signs and symptoms:
 1. A pattern of development, regression, then recovery or stabilization; and
 2. Partial or complete loss of purposeful hand skills such as grasping with fingers, reaching for things, or touching things on purpose; and
 3. Partial or complete loss of spoken language; and
 4. Repetitive hand movements, such as wringing the hands, washing, squeezing, clapping, or rubbing; and
 5. Gait abnormalities, including walking on toes or with an unsteady, wide-based, stiff-legged gait; or
 2. Molecular genetic testing confirms mutations in the MECP2 gene; and
3. Member is 2 years of age or older; and
4. Prescribed by or in consultation with one of the following:
 1. Geneticist; or
 2. Pediatrician knowledgeable in diagnosing and treating Rett Syndrome; or
 3. neurologist

Initial authorization duration: 1 year

REAUTHORIZATION CRITERIA: Trofinetide (Daybue™) is medically necessary when BOTH of the following are met:

1. Documentation of positive clinical response to therapy as evidenced by an improvement in clinical signs and symptoms from baseline (e.g., hand behavior, walking/standing, speech, quality of life);
2. Prescribed by or in consultation with one of the following:
 1. Geneticist; or
 2. Pediatrician knowledgeable in diagnosing and treating Rett Syndrome; or
 3. neurologist

Reauthorization duration: 1 year

P&T Approval Date: Dec-12-2024

Title: Urea Cycle Disorder

Applicable Drugs:

Brand Name	Generic Name
Ravicti®	Glycerol Phenylbutrate
Pheburane®	sodium phenylbutyrate oral pellets
Buphenyl®	sodium phenylbutyrate tablet/powder
Olpruva™	sodium phenylbutyrate oral suspension

Policy:

INITIAL CRITERIA Brand Buphenyl® tablet and powder, sodium phenylbutyrate oral suspension (Olpruva™), Pheburane®, glycerol phenylbutyrate (Ravicti®), generic sodium phenylbutyrate tablet and powder are medically necessary when ALL of the following are met:

1. Diagnosis of Urea Cycle Metabolism Disorder; and
2. Member has one of the following deficiencies:
 - a. Carbamylphosphate synthetase (CPS), or
 - b. Ornithine transcarbamylase (OTC), or
 - c. Argininosuccinic acid synthetase (AS); and
3. Molecular genetic testing confirms mutations in the CPS1, OTC, or ASS1 gene; and
4. Member cannot be managed by dietary protein restriction and/or amino acid supplementation alone; and
5. For brand Buphenyl tablet and powder, Olpruva, Ravicti only, ONE of the following:
 - a. For members 18 years of age or older, inadequate response or inability to tolerate Pheburane and generic sodium phenylbutyrate tablet or powder; or
 - b. For members less than 18 years of age, inadequate response or inability to tolerate Pheburane or generic sodium phenylbutyrate tablet or powder; and
6. Will be used concomitantly with dietary protein restriction and, in some cases, dietary supplements (e.g., essential amino acids, protein-free calorie supplements, arginine, etc.); and

7. Prescribed by or in consultation with a specialist experienced with the treatment of metabolic disorders

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA Brand Buphenyl® tablet and powder, generic sodium phenylbutyrate tablet and powder, Pheburane®, Glycerol phenylbutyrate (Ravicti®) and sodium phenylbutyrate oral suspension (Olpruva™) is medically necessary when BOTH of the following are met:

1. Documentation of positive clinical response to therapy; and
2. Will be used concomitantly with dietary protein restriction and, in some cases, dietary supplements (e.g., essential amino acids, protein-free calorie supplements, arginine, etc.)

Reauthorization duration: 2 years

P&T Approval Date: Sep-12-2024

Title: VMAT2 Inhibitors

Applicable Drugs:

Brand Name	Generic Name
Xenazine®	Tetrabenazine
Austedo® [XR]	Deutetrabenazine
Ingrezza®	Valbenazine

Policy:

Chorea associated with Huntington's disease

INITIAL CRITERIA: Tetrabenazine (Xenazine®), Valbenazine (Ingrezza®) or deutetrabenazine (Austedo® [XR]) is approved when ALL of the following are met:

1. Used for the treatment of chorea associated with Huntington's disease; and
2. Member is 18 years of age or older; and
3. Prescribed by or in consultation with a neurologist; and
4. For brand Xenazine® only, inadequate response or inability to tolerate a minimum 30-day supply of generic tetrabenazine

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA: Tetrabenazine (Xenazine®), Valbenazine (Ingrezza®) or deutetrabenazine (Austedo® [XR]) is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

Tardive Dyskinesia

INITIAL CRITERIA: Valbenazine (Ingrezza®) or deutetrabenazine (Austedo® [XR]) is approved when ALL of the following are met:

1. Diagnosis of moderate to severe tardive dyskinesia; and
2. Member is 18 years of age or older; and
3. One of the following:
 1. Persistent symptoms of tardive dyskinesia despite a trial of dose reduction, tapering, or discontinuation of the offending medication; or
 2. Member is not a candidate for a trial of dose reduction, tapering, or discontinuation of the offending medication; and
4. Prescribed by or in consultation with one of the following:
 1. Neurologist; or
 2. Psychiatrist

Initial Authorization duration: 3 months

REAUTHORIZATION CRITERIA: Valbenazine (Ingrezza®) or deutetrabenazine (Austedo® [XR]) is re-approved with documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

Tourette's syndrome

INITIAL CRITERIA: Tetrabenazine (Xenazine®) is approved when ALL of the following are met:

1. Diagnosis of Tourette's Syndrome; and
2. Member has tics associated with Tourette's syndrome; and
3. Inadequate response or inability to tolerate haloperidol or risperidone; and

4. Prescribed by or on consultation with a neurologist or a psychiatrist; and
5. For brand Xenazine® only, inadequate response or inability to tolerate a minimum 30-day supply of generic tetrabenazine

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA: Tetrabenazine (Xenazine®) is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

P&T Approval Date: Mar-20-2025

Title: Vosoritide (Voxzogo)

Applicable Drugs:

Brand Name	Generic Name
Voxzogo™	vosoritide

Policy:

INITIAL CRITERIA Vosoritide (Voxzogo™) is medically necessary when ALL of the following are met:

1. Diagnosis of achondroplasia as confirmed by ONE of the following:
 1. BOTH of the following:
 1. Member has clinical manifestations characteristic of achondroplasia (e.g., macrocephaly, frontal bossing, midface retrusion, disproportionate short stature with rhizomelic shortening of the arms and the legs, brachydactyly, trident configuration of the hands, thoracolumbar kyphosis, and accentuated lumbar lordosis); and
 2. Member has radiographic findings characteristic of achondroplasia (e.g., large calvaria and narrowing of the foramen magnum region, undertubulated, shortened long bones with metaphyseal abnormalities, narrowing of the interpedicular distance of the caudal spine, square ilia and horizontal acetabula, small sacrosclatic notches, proximal scooping of the femoral metaphyses, and short and narrow chest); or
 2. Molecular genetic testing confirmed c.1138G>A or c.1138G>C variant (i.e., p.Gly380Arg mutation) in the fibroblast growth factor receptor-3 (FGFR3) gene; and
2. Member has open epiphyses; and
3. Member did not have limb-lengthening surgery in the previous 18 months and does not plan on having limb-lengthening surgery while on Voxzogo therapy; and
4. Prescribed by or in consultation with one of the following:
 1. Clinical geneticist; or
 2. Endocrinologist; or
 3. A provider who has specialized expertise in the management of achondroplasia

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA Vosoritide (Voxzogo™) is medically necessary when ALL of the following are met:

1. Member continues to have open epiphyses; and
2. Documentation of positive clinical response to therapy [e.g., improvement in annualized growth velocity (AGV) compared to baseline, or an improvement in height Z-score compared to baseline]; and
3. Prescribed by or in consultation with one of the following:
 1. Clinical geneticist; or
 2. Endocrinologist; or
 3. A provider who has specialized expertise in the management of achondroplasia

Reauthorization duration: 12 months

P&T Approval Date: Dec-12-2024

Title: Wakefulness Promoting Agents

Applicable Drugs:

Generic name	Brand name
Pitolisant	Wakix®
Solriamfetol	Sunosi™

Policy:

Excessive daytime sleepiness in narcolepsy (Type 2)

INITIAL CRITERIA: Solriamfetol (Sunosi™) is approved when ALL of the following are met:

1. Diagnosis of excessive daytime sleepiness in narcolepsy (Type 2); and
2. Prescribed by or in consultation with a neurologist, psychiatrist, or sleep specialist; and
3. Diagnosis was confirmed by one of the following tests:
 1. Polysomnography (PSG); or
 2. Multiple sleep latency test (MSLT); and
4. Member is 18 years of age or older; and
5. Inadequate response or inability to tolerate BOTH of the following:
 1. Modafinil or armodafinil; and
 2. One of the following:
 1. One stimulant product (e.g., amphetamine, methylphenidate); or
 2. History of or potential for a substance use disorder

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA: Solriamfetol (Sunosi™) is re-approved when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

INITIAL CRITERIA: Pitolisant (Wakix®) is approved when ALL of the following are met:

1. Diagnosis of excessive daytime sleepiness in narcolepsy (Type 2); and
2. Member is 6 years of age or older; and
3. Diagnosis was confirmed by ONE of the following tests:
 1. Polysomnography (PSG); or
 2. Multiple sleep latency test (MSLT); and
4. Prescribed by or in consultation with a neurologist, psychiatrist, or sleep specialist; and
5. Symptoms of cataplexy are absent; and
6. Symptoms of excessive daytime sleepiness (e.g., irrepressible need to sleep or daytime lapses into sleep) are present; and
7. Inadequate response or inability to tolerate ALL of the following:
 1. Modafinil or armodafinil; and
 2. One of the following:
 1. One stimulant product (e.g., amphetamine, methylphenidate); or
 2. History of or potential for a substance use disorder; and
 3. Sunosi®

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Pitolisant (Wakix®) is re-approved when ALL of the following are met:

1. Documentation to support the efficacy associated with the current regimen; and
2. Yearly evaluation by a neurologist, psychiatrist, or sleep specialist

Reauthorization duration: 12 months

Cataplexy with narcolepsy (Type 1)

INITIAL CRITERIA: Pitolisant (Wakix®) is approved when ALL of the following are met:

1. Diagnosis of cataplexy with narcolepsy (Type 1); and
2. Member is 18 years of age or older; and
3. Symptoms of cataplexy are present; and
4. Symptoms of excessive daytime sleepiness (e.g., irrepressible need to sleep or daytime lapses into sleep) are present; and
5. Diagnosis was confirmed by ONE of the following tests:
 1. Polysomnography (PSG); or
 2. Multiple sleep latency test (MSLT); and
6. Prescribed by or in consultation with a neurologist, psychiatrist, or sleep specialist

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Pitolisant (Wakix®) is re-approved when ALL of the following are met:

1. Documentation to support the efficacy associated with the current regimen (including but not limited to reduction in the frequency of cataplexy attacks or an improvement in the Epworth sleepiness scale); and
2. Yearly evaluation by a neurologist, psychiatrist, or sleep specialist

Reauthorization duration: 12 months

Obstructive sleep apnea/hypopnea syndrome (OSAHS)

INITIAL CRITERIA: Solriamfetol (Sunosi™) is medically necessary when ALL of the following are met:

1. Diagnosis of obstructive sleep apnea (OSA) defined by one of the following:
 1. Member has 15 or more obstructive respiratory events per hour of sleep confirmed by a sleep study, unless the prescriber provides justification confirming that a sleep study would not be feasible; or
 2. Both of the following:
 1. Member has 5 or more obstructive respiratory events per hour of sleep confirmed by a sleep study (unless the prescriber provides justification confirming that a sleep study would not be feasible); and
 2. Member has symptoms of OSA (e.g., daytime sleepiness, fatigue); and
2. Member is 18 years of age or older; and
3. Prescribed by or in consultation with a sleep specialist; and
4. Used as adjunct to standard therapy; and
5. Inadequate response or inability to tolerate ONE of the following:
 - a. Modafinil or armodafinil; and
 - b. One of the following:
 1. One stimulant product (e.g., amphetamine, methylphenidate); or
 2. History of or potential for a substance use disorder

Initial authorization duration: 2 years

REAUTHORIZATION CRITERIA: Solriamfetol (Sunosi™) is medically necessary when there is documentation of positive clinical response to therapy.

Reauthorization duration: 2 years

P&T Approval Date: Mar-20-2025

Title: Wegovy for Major Adverse Cardiovascular Events Risk Reduction

Applicable Drugs:

Brand Name	Generic Name
Wegovy®	Semaglutide

Policy:

Major Adverse Cardiovascular Events Risk Reduction

INITIAL CRITERIA: Semaglutide (Wegovy) is medically necessary for cardiovascular events risk reduction when all of the following are met:

1. Member is 45 years of age or older; and
2. Member does not have a diagnosis of type 1 or type 2 diabetes mellitus; and
3. Submission of documentation (e.g., chart note) confirming all of the following:
 1. BMI $\geq$ 27 kg/m²; and
 2. Member has a history of cardiovascular disease, as evidenced by at least one of the following:
 1. Prior myocardial infarction; or
 2. Prior stroke (ischemic and hemorrhagic stroke); or
 3. Symptomatic peripheral arterial disease, as evidenced by one of the following:
 1. intermittent claudication with ankle-brachial index $<$ 0.85, or
 2. peripheral arterial revascularization procedure, or
 3. amputation due to atherosclerotic disease; and
 4. Submission of documentation (e.g., chart note) showing member is on guideline therapy management for multiple risk factors (e.g., dyslipidemia, hypertension) associated with cardiovascular disease as evidenced by the presence of all of the following:
 1. One of the following:

1. Platelet aggregation inhibitor (e.g., acetylsalicylic acid, P2Y12 receptor inhibitors) or antithrombotic medication (e.g., vitamin K antagonists, direct oral anticoagulants); or
 2. Member has inability to tolerate Platelet aggregation inhibitor or anti-thrombotic medication; and
2. One of the following:
 1. Lipid-lowering medications (e.g., statins, ezetimibe, fibrates, PCSK-9 inhibitors); or
 2. Member has inability to tolerate lipid-lowering medications; and
3. One of the following:
 1. Other cardiac medications including beta blocker, angiotensin-converting-enzyme inhibitor, angiotensin-receptor blocker, and calcium channel blocker; or
 2. Member has inability to tolerate cardiac medications including beta blocker, angiotensin converting enzyme inhibitor, angiotensin-receptor blocker, and calcium channel blocker; and
5. No concurrent use of any other GLP-1 receptor agonist (e.g., Adlyxin®, Byetta®, Bydureon®, Mounjaro™, Ozempic®, Rybelsus®, Saxenda®, Trulicity®, Victoza®)

Initial authorization duration: 1 year

REAUTHORIZATION CRITERIA: Semaglutide (Wegovy) is medically necessary for cardiovascular events risk reduction when all of the following are met:

1. Submission of documentation (e.g., chart note) showing member is on guideline therapy management for multiple risk factors (e.g., dyslipidemia, hypertension) associated with cardiovascular disease as evidenced by the presence of all of the following:
 1. One of the following:
 1. Platelet aggregation inhibitor (e.g., acetylsalicylic acid, P2Y12 receptor inhibitors) or antithrombotic medication (e.g., vitamin K antagonists, direct oral anticoagulants); or

2. Member has inability to tolerate platelet aggregation inhibitor or anti-thrombotic medication; and
2. One of the following:
 1. Lipid-lowering medications (e.g., statins, ezetimibe, fibrates, PCSK-9 inhibitors); or
 2. Member has inability to tolerate lipid-lowering medications; and
3. One of the following:
 1. Other cardiac medications including beta blocker, angiotensin-converting-enzyme inhibitor, angiotensin-receptor blocker, and calcium channel blocker; or
 2. Member has inability to tolerate cardiac medications including beta blocker, angiotensin converting enzyme inhibitor, angiotensin-receptor blocker, and calcium channel blocker; and
2. Documentation is provided confirming one of the following:
 1. Member has not experienced a cardiovascular event since starting treatment (i.e., nonfatal myocardial infarction, nonfatal stroke); and
 2. Member has experienced a non-fatal myocardial infarction or nonfatal stroke since starting treatment, but the prescriber attests the benefit outweighs risk for member to continue treatment with semaglutide (Wegovy); and
3. No concurrent use of any other GLP-1 receptor agonist (e.g., Adlyxin®, Byetta®, Bydureon®, Mounjaro™, Ozempic®, Rybelsus®, Saxenda®, Trulicity®, Victoza®)

Reauthorization duration: 1 year

P&T Approval Date: Mar-20-2025

Title: Weight Loss Medications for Obesity and Related Health Conditions

Policy: Coverage is subject to the terms, conditions, and limitations of the member's contract.

Weight loss medications are not covered under the pharmacy benefit except for members whose benefit does not exclude weight loss drugs.

This Claim Payment Policy is available to those groups that do not exclude weight loss drugs.

Major Adverse Cardiovascular Events Risk Reduction

INITIAL CRITERIA: Semaglutide (Wegovy) is approved for major adverse cardiovascular events risk reduction when ALL of the following are met:

1. Treatment is being requested to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke); and
2. Member is 18 years of age or older; and
3. Member has established cardiovascular disease defined as CAD, ACS, those with history of MI, stable or unstable angina or coronary or other arterial revascularization, prior percutaneous coronary intervention/coronary bypass surgery, stroke, TIA, carotid or other arterial stenosis, or PAD including aortic aneurysm, all of atherosclerotic origin; and
4. Drug will be used as an adjunct to lifestyle modification (e.g., dietary or caloric restriction, exercise, behavioral support, community-based program); and
5. BMI prior to treatment is greater than or equal to 27kg/m²; and
6. Drug is not being co-administered with tirzepatide-containing products (e.g., Mounjaro, Zepbound) or GLP-1 receptor agonists (e.g., Ozempic, Rybelsus, Trulicity, Saxenda)

Initial authorization duration: 1 year

REAUTHORIZATION CRITERIA: Semaglutide (Wegovy) is re-approved for major adverse cardiovascular events risk reduction when ALL of the following are met:

1. Member is currently on a maintenance dose of 1.7mg or 2.4mg once weekly; and
2. Drug will be used as an adjunct to lifestyle modification (e.g., dietary or caloric restriction, exercise, behavioral support, community-based program); and

3. Drug is not being co-administered with tirzepatide-containing products (e.g., Mounjaro, Zepbound) or GLP-1 receptor agonists (e.g., Ozempic, Rybelsus, Trulicity, Saxenda)

Reauthorization duration: 1 year

Obstructive Sleep Apnea

INITIAL CRITERIA: Tirzepatide (Zepbound) is medically necessary for the treatment of moderate to severe obstructive sleep apnea (OSA) in obesity when all of the following are met:

1. Diagnosis of obstructive sleep apnea; and
2. Submission of medical records (e.g., chart notes) confirming disease is moderate to severe as defined by 15 or more obstructive respiratory events per hour of sleep confirmed by a sleep study; and
3. Member is 18 years of age or older; and
4. Submission of medical records (e.g., chart notes) confirming Body Mass Index (BMI) of greater than or equal to 30kg/m²; and
5. Submission of medical records (e.g., chart notes) confirming one of the following:
 1. Member has been evaluated and counseled on continuous positive airway pressure CPAP therapy as the preferred treatment of choice; or
 2. Member is not a candidate for CPAP therapy (e.g., upper airway anatomic abnormalities, etc.); and
6. Submission of medical records (e.g., chart notes) confirming medication will be used as an adjunct to lifestyle modification (e.g., dietary or caloric restriction, exercise, behavioral support, community-based program); and
7. Submission of medical records (e.g., chart notes) or absence of paid claims confirming medication is not being co-administered with tirzepatide-containing products (e.g., Mounjaro) or GLP-1 receptor agonists (e.g., Ozempic, Rybelsus, Trulicity, Saxenda)

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Tirzepatide (Zepbound) is medically necessary for the treatment of moderate to severe obstructive sleep apnea (OSA) in obesity when all of the following are met:

1. Paid claims or submission of medical records (e.g., chart notes) confirming member is currently on a maintenance dose of 10mg, 12.5mg, or 15mg once weekly; and
2. Submission of medical records (e.g., chart notes) confirming one of the following:
 1. Member has been receiving Zepbound therapy for up to 6 months and has had a weight loss of greater than or equal to 5% of baseline body weight; or
 2. Member has been receiving Zepbound therapy for greater than 6 months and is continuing to experience or maintain weight loss; and
3. Submission of medical records (e.g., chart notes) confirming medication will be used as an adjunct to lifestyle modification (e.g., dietary or caloric restriction, exercise, behavioral support, community-based program); and
4. Submission of medical records (e.g., chart notes) or absence of paid claims confirming medication is not being co-administered with tirzepatide-containing products (e.g., Mounjaro) or GLP-1 receptor agonists (e.g., Ozempic, Rybelsus, Trulicity, Saxenda)

Reauthorization duration: 6 months

Short Term Weight Management

INITIAL CRITERIA: Amphetamine (Evekeo®), diethylpropion, diethylpropion ER, benzphetamine, phendimetrazine tablet, phendimetrazine ER capsule is approved when ALL of the following are met:

1. Treatment is being requested for appetite suppression or weight loss; and
2. One of the following:
 1. For diethylpropion, diethylpropion ER, phendimetrazine ER capsule only, member is 17 years of age or older; or

2. For phendimetrazine and benzphetamine only, member is 18 years of age or older; and
3. Drug will be used as adjunct to lifestyle modification (e.g., dietary or caloric restriction, exercise, behavioral support, community-based program); and
4. One of the following:
 1. Diagnosis of obesity defined as baseline BMI ≥ 30 kg/m²* prior to initiation treatment; or
 2. Both of the following:
 1. Baseline BMI ≥ 27 kg/m² prior to initiating treatment; and
 2. Member has one or more comorbidities (e.g., hypertension, coronary artery disease, type 2 diabetes mellitus, dyslipidemia, or obstructive sleep apnea); and
5. For brand Evekeo only, inadequate response or inability to tolerate generic amphetamine

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Amphetamine (Evekeo®), diethylpropion, diethylpropion ER, benzphetamine, phendimetrazine tablet, phendimetrazine ER capsule is re-approved when ALL of the following are met:

1. Weight loss of greater than or equal to 5% of baseline body weight; and
2. Drug will be used as adjunct to lifestyle modification (e.g., dietary or caloric restriction, exercise, behavior support, community-based program)

Reauthorization duration: 6 months

Chronic Weight Management

INITIAL CRITERIA: Liraglutide (Saxenda) is approved when ALL of the following are met:

1. Treatment is being requested for appetite suppression or weight loss; and
2. ONE of the following:

1. BOTH of the following:
 1. Member is 18 years of age or older; and
 2. Baseline BMI greater than or equal to 30kg/m² prior to initiating Saxenda therapy; or
2. ALL of the following:
 1. Member is 18 years of age or older; and
 2. Baseline BMI greater than or equal to 27kg/m² prior to initiating Saxenda therapy; and
 3. Member has a weigh-related comorbidity (e.g., hypertension, coronary artery disease, type 2 diabetes, dyslipidemia, or obstructive sleep apnea); or
3. ALL of the following:
 1. Member is between 12 and 17 years of age; and
 2. Baseline body weight above 60kg prior to initiating Saxenda therapy; and
 3. Baseline BMI corresponding to greater than or equal to 30kg/m² for adults (obese) by international cut-offs (e.g., Cole Criteria) prior to initiating Saxenda therapy; and
3. ONE of the following:
 1. Member is new to Saxenda therapy or has been on Saxenda therapy for less than 16 weeks; or
 2. Member is continuing Saxenda therapy and one of the following:
 1. Both of the following:
 1. Member is 18 years of age or older; and
 2. Member has been on therapy for at least 16 weeks and has had a weight loss of greater than or equal to 4% of baseline body weight; or
 2. Both of the following:
 1. Member is between 12 to 17 years of age; and
 2. Member has been on therapy for at least 16 weeks and has had a weight loss of greater than or equal to 1% of baseline body weight; and

4. Drug will be used as an adjunct to lifestyle modification (e.g., dietary or caloric restriction, exercise, behavioral support, community-based program); and
5. Drug is not being co-administered with tirzepatide-containing products (e.g., Mounjaro, Zepbound) or GLP-1 receptor agonists (e.g., Ozempic, Rybelsus, Trulicity, Wegovy)

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Liraglutide (Saxenda) is approved when ALL of the following are met:

1. One of the following:
 1. BOTH of the following:
 1. Member is 18 years of age and older; and
 2. ONE of the following:
 1. Member has been receiving Saxenda therapy for up to 6 months and has had a weight loss of greater than or equal to 4% of baseline body weight; or
 2. Member has been receiving Saxenda therapy for greater than 6 months and is continuing to experience or maintain weight loss; or
 2. BOTH of the following:
 1. Member is between 12 and 17 years of age; and
 2. ONE of the following:
 1. Member has been receiving Saxenda therapy for up to 6 months and has had a weight loss of at least 1% from baseline body weight or BMI; or
 2. Member has been receiving Saxenda therapy for greater than 6 months and is continuing to experience or maintain weight loss; and
2. Drug will be used as an adjunct to lifestyle modification (e.g., dietary or caloric restriction, exercise, behavioral support, community-based program); and
3. Drug is not being co-administered with tirzepatide-containing products (e.g., Mounjaro, Zepbound) or GLP-1 receptor agonists (e.g., Ozempic, Rybelsus, Trulicity, Wegovy); and

4. BOTH of the following:

1. Member has been adherent to 3 consecutive months of treatment; and
2. Member is currently on a maintenance dose of 3mg once daily.

Reauthorization duration: 6 months

INITIAL CRITERIA: Semaglutide (Wegovy) is approved when ALL of the following are met:

1. Treatment is being requested for appetite suppression or weight loss; and

2. ONE of the following:

1. BOTH of the following:

1. Member is 18 years of age or older; and
2. Baseline BMI greater than or equal to 30kg/m² prior to initiating Wegovy therapy; or

2. ALL of the following:

1. Member is 18 years of age or older; and
2. Baseline BMI greater than or equal to 27kg/m² prior to initiating Wegovy therapy; and
3. Member has a weigh-related comorbidity (e.g., hypertension, coronary artery disease, type 2 diabetes, dyslipidemia, or obstructive sleep apnea); or

3. BOTH of the following:

1. Member is between 12 and 17 years of age; and
2. Baseline BMI is in the 95th percentile or greater standardize for age and sex prior to initiating Wegovy therapy; and

3. ONE of the following:

1. Member is new to Wegovy therapy or has been on Wegovy therapy for less than 7 months; or
2. Member has been on therapy for at least 7 months and has had a weight loss of greater than or equal to 5% of baseline body weight; and

4. Drug will be used as an adjunct to lifestyle modification (e.g., dietary or caloric restriction, exercise, behavioral support, community-based program); and
5. Drug is not being co-administered with tirzepatide-containing products (e.g., Mounjaro, Zepbound) or GLP-1 receptor agonists (e.g., Ozempic, Rybelsus, Trulicity, Saxenda)

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Semaglutide (Wegovy) is approved when ALL of the following are met:

1. ONE of the following:
 1. Member has been receiving Wegovy therapy for up to 7 months and has had a weight loss of greater than or equal to 5% of baseline body weight; or
 2. Member has been receiving Wegovy therapy for greater than 7 months and is continuing to experience or maintain weight loss; and
2. Drug will be used as an adjunct to lifestyle modification (e.g., dietary or caloric restriction, exercise, behavioral support, community-based program); and
3. Drug is not being co-administered with tirzepatide-containing products (e.g., Mounjaro, Zepbound) or GLP-1 receptor agonists (e.g., Ozempic, Rybelsus, Trulicity, Saxenda); and
4. BOTH of the following:
 1. Member has been adherent to 4 consecutive months of treatment; and
 2. ONE of the following:
 1. Member is currently on a maintenance dose of 1.7mg or 2.4mg once weekly; or
 2. Member has received less than 7 months of treatment with Wegovy and is continuing to titrate to target dose of 1.7mg or 2.4mg once weekly.

Reauthorization duration: 6 months

INITIAL CRITERIA: Tirzepatide (Zepbound) is approved when ALL of the following are met:

1. Treatment is being requested for appetite suppression or weight loss; and

2. ONE of the following:
 1. BOTH of the following:
 1. Member is 18 years of age or older; and
 2. Baseline BMI greater than or equal to 30kg/m² prior to initiating Zepbound therapy; or
 2. ALL of the following:
 1. Member is 18 years of age or older; and
 2. Baseline BMI greater than or equal to 27kg/m² prior to initiating Zepbound therapy; and
 3. Member has a weight-related comorbidity (e.g., hypertension, coronary artery disease, type 2 diabetes, dyslipidemia, or obstructive sleep apnea); and
3. ONE of the following:
 1. Member is new to Zepbound therapy or has been on Zepbound therapy for less than 6 months; or
 2. Member has been on therapy for at least 6 months and has had a weight loss of greater than or equal to 5% of baseline body weight; and
 4. Drug will be used as an adjunct to lifestyle modification (e.g., dietary or caloric restriction, exercise, behavioral support, community-based program); and
 5. Drug is not being co-administered with tirzepatide-containing products (e.g., Mounjaro) or GLP-1 receptor agonists (e.g., Ozempic, Rybelsus, Trulicity, Saxenda, Wegovy)

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Tirzepatide (Zepbound) is approved when ALL of the following are met:

1. ONE of the following:
 1. Member has been receiving Zepbound therapy for up to 6 months and has had a weight loss of greater than or equal to 5% of baseline body weight; or

2. Member has been receiving Zepbound therapy for greater than 6 months and is continuing to experience or maintain weight loss; and
2. Drug will be used as an adjunct to lifestyle modification (e.g., dietary or caloric restriction, exercise, behavioral support, community-based program); and
3. Drug is not being co-administered with tirzepatide-containing products (e.g., Mounjaro) or GLP-1 receptor agonists (e.g., Ozempic, Rybelsus, Trulicity, Saxenda, Wegovy); and
4. BOTH of the following:
 1. Member has been adherent to 1 month of treatment; and
 2. Member is currently on a dose of 5mg, 7.5mg, 10mg, 12.5mg, or 15mg once weekly.

Reauthorization duration: 6 months

INITIAL CRITERIA: Phentermine/topiramate (Qsymia) is approved when ALL of the following are met:

1. Treatment is being requested for appetite suppression or weight loss; and
2. ONE of the following:
 1. BOTH of the following:
 1. Member is 18 years of age or older; and
 2. Baseline BMI greater than or equal to 30kg/m² prior to initiating Qsymia therapy; or
 2. ALL of the following:
 1. Member is 18 years of age or older; and
 2. Baseline BMI greater than or equal to 27kg/m² prior to initiating Qsymia therapy; and
 3. Member has a weight-related comorbidity (e.g., hypertension, coronary artery disease, type 2 diabetes, dyslipidemia, or obstructive sleep apnea); or
 3. BOTH of the following:
 1. Member is between 12 and 17 years of age; and

2. Baseline BMI is in the 95th percentile or greater standardized for age and sex prior to initiating Qsymia therapy; and
3. Drug will be used as an adjunct to lifestyle modification (e.g., dietary or caloric restriction, exercise, behavioral support, community-based program)

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Phentermine/topiramate (Qsymia) is approved when ALL of the following are met:

1. Weight loss of greater than or equal to 5% of baseline body weight; and
2. Drug will be used as an adjunct to lifestyle modification (e.g., dietary or caloric restriction, exercise, behavioral support, community-based program)

Reauthorization duration: 6 months

INITIAL CRITERIA: Naltrexone/bupropion (Contrave) is approved when ALL of the following are met:

1. Treatment is being requested for appetite suppression or weight loss; and
2. ONE of the following:
 1. BOTH of the following:
 1. Member is 18 years of age or older; and
 2. Baseline BMI greater than or equal to 30kg/m² prior to initiating Contrave therapy; or
 2. ALL of the following:
 1. Member is 18 years of age or older; and
 2. Baseline BMI greater than or equal to 27kg/m² prior to initiating Contrave therapy; and
 3. Member has a weigh-related comorbidity (e.g., hypertension, coronary artery disease, type 2 diabetes, dyslipidemia, or obstructive sleep apnea); and

3. Drug will be used as an adjunct to lifestyle modification (e.g., dietary or caloric restriction, exercise, behavioral support, community-based program)

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Naltrexone/bupropion (Contrave) is approved when ALL of the following are met:

1. Weight loss of greater than or equal to 5% of baseline body weight; and
2. Drug will be used as an adjunct to lifestyle modification (e.g., dietary or caloric restriction, exercise, behavioral support, community-based program)

Reauthorization duration: 6 months

INITIAL CRITERIA: Orlistat (Xenical) is approved when ALL of the following are met:

1. Treatment is being requested for appetite suppression or weight loss; and
2. Member is greater than or equal to 12 years of age; and
3. Drug will be used as an adjunct to lifestyle modification (e.g., dietary or caloric restriction, exercise, behavioral support, community-based program); and
4. ONE of the following:
 1. Baseline BMI greater than or equal to 30kg/m² prior to initiating orlistat (Xenical) therapy; or
 2. BOTH of the following:
 1. Baseline BMI greater than or equal to 27kg/m² prior to initiating orlistat (Xenical) therapy; and
 2. Member has a weight-related comorbidity (e.g., hypertension, coronary artery disease, type 2 diabetes, dyslipidemia, or obstructive sleep apnea)

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA: Xenical or Orlistat is approved when ALL of the following are met:

1. Weight loss of greater than or equal to 5% of baseline body weight; and
2. Drug will be used as an adjunct to lifestyle modification (e.g., dietary or caloric restriction, exercise, behavioral support, community-based program)

Reauthorization duration: 6 months

NOTES: *For member's 12 to 17 years of age, use the Cole criteria for the corresponding BMI for member's age and sex. International Obesity Task Force BMI Cut-offs for Obesity by Sex and Age for Pediatric Patients Aged 12 Years and Older (Cole Criteria)

Age (years)	Body Mass Index 30kg/m ²	
	Males	Females
12	26.02	26.67
12.5	26.43	27.24
13	26.84	27.76
13.5	27.25	28.2
14	27.63	28.57
14.5	27.98	28.87
15	28.3	29.11
15.5	28.6	29.29
16	28.88	29.43
16.5	29.14	29.56
17	29.41	29.69
17.5	29.7	29.84

P&T Approval Date: Mar-20-2025

Title: Xdemvy®

Applicable Drugs:

Brand	Generic
Xdemvy®	Lotilaner

Policy:

Lotilaner (Xdemvy®) is approved when ALL of the following are met:

1. Diagnosis of Demodex blepharitis; and
2. Member exhibits one of the following signs of Demodex infestation:
 1. Collarettes; or
 2. Eyelid margin erythema; or
 3. Eyelash anomalies (e.g., eyelash misdirection); and
3. Member is experiencing symptoms of architectural changes associated with Demodex infestation (e.g., burning, tearing, itching, foreign body sensation, eyelashes missing, eyelashes growing inward); and
4. Inadequate response or inability to tolerate tea tree-oil; and
5. Prescribed by or in consultation with one of the following:
 1. Ophthalmologist; or
 2. Optometrist

Authorization duration: 2 months

P&T Approval Date: Jul-01-2024

Title: Zilucoplan (Zilbrysq®)

Applicable Drugs:

Brand Name	Generic Name
Zilbrysq®	Zilucoplan

Policy:

INITIAL CRITERIA: Zilucoplan (Zilbrysq®) is approved when ALL of the following are met:

1. Diagnosis of generalized myasthenia gravis (gMG); and
2. Member is 18 years of age or older; and
3. Member is anti-acetylcholine receptor (AChR) antibody positive; and
4. One of the following:
 1. Inadequate response or inability to tolerate two immunosuppressive therapies (e.g., glucocorticoids, azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, tacrolimus); or
 2. Both of the following:
 1. Inadequate response or inability to tolerate one immunosuppressive therapy (e.g., glucocorticoids, azathioprine, cyclosporine, mycophenolate mofetil, methotrexate, tacrolimus); and
 2. Inadequate response or inability to tolerate one of the following:
 1. Chronic plasmapheresis or plasma exchange (PE); or
 2. Intravenous Immunoglobulin (IVIG); and
5. Prescribed by or in consultation with a neurologist; and
6. No concurrent use with rozanolixizumab-noli (Rystiggo), eculizumab (Soliris), ravulizumab-cwvz (Ultomiris) or efgartigimod alfa-fcab (Vyvgart, Vyvgart Hytrulo)

Initial authorization duration: 12 months

REAUTHORIZATION CRITERIA: Zilucoplan (Zilbrysq®) is re-approved when ALL of the following are met:

1. Documentation of positive clinical response to therapy; and
2. Prescribed by or in consultation with a neurologist; and
3. No concurrent use with rozanolixizumab-noli (Rystiggo), eculizumab (Soliris), ravulizumab-cwvz (Ultomiris) or efgartigimod alfa-fcab (Vyvgart, Vyvgart Hytrulo)

Reauthorization duration: 12 months

P&T Approval Date: Mar-20-2025

Title: Intravitreal Injection of Vascular Endothelial Growth Factor (VEGF) Antagonists, VEGF Biosimilars, and Combination VEGF/Angiopoietin-2 (Ang-2) Inhibitors

MEDICALLY NECESSARY:

COMPANY-DESIGNATED PREFERRED PRODUCTS

Although there are many brands of vascular endothelial growth factor (VEGF) antagonists and VEGF/Angiopoietin-2 (Ang-2) inhibitors on the market for the treatment of vascular diseases of the eye, there is no reliable evidence of the superiority of any one brand of VEGF antagonists compared with other brands. The company has designated the following as its preferred product for members who are treatment-naïve:

- First line:
 - Any bevacizumab product
- Second line:
 - Ranibizumab (Lucentis®)
 - Ranibizumab-nuna (Byooviz™)
 - Ranibizumab-eqrn (Cimerli®)

These products are less costly and at least as likely to produce equivalent therapeutic results as the non-preferred products, which include, but are not limited to, Beovu®, Eylea®, Eylea® High Dose (HD), Susvimo®, Vabysmo®, and related biosimilars.

According to the US Food and Drug Administration (FDA), “a biosimilar is a biological product that has no clinically meaningful differences from the existing FDA-approved reference product. All biosimilar products meet the FDA’s rigorous standards for approval for the indications described in the product labeling. Once a biosimilar has been approved by the FDA, the safety and effectiveness of these products have been established, just as they have been for the reference product.” Coverage of a biosimilar product as an alternate to a reference product is not considered a form of step therapy by the Company.

NON-PREFERRED PRODUCTS*

For individuals who meet the medical necessity criteria below, use of non-preferred products (which include Beovu, Eylea, Eylea HD, Susvimo, Vabysmo, and any biosimilars to non-preferred products) is considered medically necessary and, therefore, covered when the individual has a documented contraindication, or documented nonresponse, to any bevacizumab product and at least one other preferred product.

*The use of non-preferred products that do not meet either of these instances are considered not medically necessary and, therefore, not covered.

NOTE: Use of non-preferred product samples administered by the professional provider will not meet coverage criteria for the exception. Additional clinical information demonstrating medical necessity of the desired medication must be submitted by the requesting provider for review.

Initial Therapy

AFLIBERCEPT (EYLEA) AND RELATED BIOSIMILARS

The intravitreal injection of VEGF antagonist aflibercept (Eylea) and related biosimilars are considered medically necessary and, therefore, covered for individuals who have the following conditions and meet the requirements listed in the COMPANY-DESIGNATED PREFERRED PRODUCTS and NON-PREFERRED PRODUCTS sections above:

- Neovascular (wet or exudative) age-related macular degeneration (AMD)
- Macular edema following retinal vein occlusion (RVO)
- Diabetic macular edema (DME)
- Diabetic retinopathy (DR)
- Retinopathy of prematurity (ROP)

AFLIBERCEPT HD (EYLEA HD) AND RELATED BIOSIMILARS

The intravitreal injection of VEGF antagonist aflibercept HD (Eylea HD) and related biosimilars are considered medically necessary and, therefore, covered for individuals who have the following conditions and meet the requirements listed in the COMPANY-DESIGNATED PREFERRED PRODUCTS and NON-PREFERRED PRODUCTS sections above:

- Neovascular (wet or exudative) AMD
- DME
- DR

BEVACIZUMAB (AVASTIN) AND RELATED BIOSIMILARS

The intravitreal injection of VEGF antagonist bevacizumab (Avastin) and related biosimilars are considered medically necessary and, therefore, covered for vascular diseases of the eye including but not limited to the following:

- Choroidal neovascularization due to angioid streaks, central serous chorioretinopathy, choroidal rupture or trauma, idiopathic choroidal neovascularization, multifocal choroiditis, pathologic myopia, presumed ocular histoplasmosis syndrome, uveitis
- DME
- DR
- Macular edema following RVO
- Neovascular (wet) AMD
- Neovascular glaucoma
- ROP

BROLUCIZUMAB-DBLL (BEOVU) AND RELATED BIOSIMILARS

The intravitreal injection of VEGF antagonist brolucizumab-dbl (Beovu) and related biosimilars are considered medically necessary and, therefore, covered for individuals who have the following conditions and meet the requirements listed in the COMPANY-DESIGNATED PREFERRED PRODUCTS and NON-PREFERRED PRODUCTS sections above:

- Neovascular (wet or exudative) AMD
- DME

FARICIMAB-SVOA (VABYSMO) AND RELATED BIOSIMILARS

The intravitreal injection of faricimab-svoa (Vabysmo) and related biosimilars are considered medically necessary and, therefore, covered for individuals who have the following

conditions and meet the requirements listed in the COMPANY-DESIGNATED PREFERRED PRODUCTS and NON-PREFERRED PRODUCTS sections above:

- Neovascular (wet or exudative) AMD
- DME
- Macular edema following RVO

RANIBIZUMAB (LUCENTIS) AND RELATED BIOSIMILARS

The intravitreal injection of VEGF antagonist ranibizumab (Lucentis) and related biosimilars are considered medically necessary and, therefore, covered for individuals who have the following conditions and meet the requirements listed in the COMPANY-DESIGNATED PREFERRED PRODUCTS and NON-PREFERRED PRODUCTS sections above:

- Neovascular (wet or exudative) AMD
- Macular edema following RVO
- DME
- DR
- ROP
- Choroidal neovascularization due to angioid streaks, central serous chorioretinopathy, choroidal rupture or trauma, idiopathic choroidal neovascularization, multifocal choroiditis, pathologic myopia, presumed ocular histoplasmosis syndrome, uveitis

RANIBIZUMAB (SUSVIMO) OCULAR IMPLANT

The intravitreal ocular implant ranibizumab (Susvimo) is considered medically necessary and, therefore, covered for individuals who meet all of the following criteria and meet the requirements listed in the COMPANY-DESIGNATED PREFERRED PRODUCTS and NON-PREFERRED PRODUCTS sections above:

- Diagnosed with neovascular (wet or exudative) AMD and requires VEGF antagonist treatment every month
- Documented response to at least two intravitreal injections of a non-preferred product (e.g., Beovu, Eylea, Eylea HD, Vabysmo, and related biosimilars) within the last 6 months

Continuation Therapy

VEGF antagonists and VEGF/Ang-2 inhibitors are considered medically necessary and, therefore, covered for the continuation therapy when the individual meets **all** of the following:

- Individual has met the medical necessity criteria for Initial Therapy
- Medical records show **both** of the following:
 - Documented improvement or stabilization in visual acuity
 - The professional provider orders continued treatment with the requested drug

Duration of authorization: 12 months

Version Effective Date: 04/01/2025

Title: Abatacept (Orencia®) for Injection for Intravenous Use

MEDICALLY NECESSARY:

INITIAL THERAPY

Hematopoietic Cell Transplantation

Prophylaxis of Acute Graft-Versus-Host Disease (aGVHD)

Abatacept (Orencia) injection for intravenous use is considered medically necessary and, therefore, covered for the prophylaxis of acute graft-versus-host disease (aGVHD), in combination with a calcineurin inhibitor (e.g., cyclosporine, tacrolimus) and methotrexate up to four doses when all the following criteria are met:

- The individual is undergoing hematopoietic stem cell transplantation (HSCT) from a matched or one allele–mismatched unrelated donor.
- Active or latent tuberculosis (TB) has been ruled out.
- The individual is 2 years of age or older.
- Abatacept (Orencia) will not be used in combination with other biologic disease-modifying antirheumatic drugs [bDMARDs (tumor necrosis factor [TNF] antagonists, e.g., certolizumab, adalimumab, etanercept] or Janus kinase (JAK) inhibitors (e.g., baricitinib, tofacitinib, upadacitinib).

Treatment of Chronic Graft-Versus-Host Disease (GVHD)

Abatacept (Orencia) injection for intravenous use is considered medically necessary and, therefore, covered for the treatment of chronic GVHD as additional therapy in conjunction with systemic corticosteroids following no response (steroid-refractory disease) to first-line therapy options.

IMMUNE CHECKPOINT INHIBITOR–RELATED TOXICITIES

Abatacept (Orencia) injection for intravenous use is considered medically necessary and, therefore, covered as additional therapy for the management of the following immune checkpoint inhibitor–related (e.g., pembrolizumab [Keytruda], nivolumab [Opdivo]) autoimmune-like toxicity (also known as immune-related adverse event):

- Myocarditis, as a single agent if no improvement within 24 to 48 hours of starting high-dose methylprednisolone
- Concomitant myositis and myocarditis in combination with ruxolitinib (Jakavi)

POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS (pJIA)

Abatacept (Orencia) injection for intravenous use is considered medically necessary and, therefore, covered when used in individuals who have moderately to severely active pJIA. Abatacept (Orencia) injection for intravenous use may be covered as monotherapy or concomitantly with methotrexate when **all** of the following inclusion criteria are met:

- If the individual has not previously received a bDMARD to treat pJIA, abatacept (Orencia) injection for intravenous use is only eligible for coverage when the individual has a documented failure, contraindication, or intolerance to golimumab (Simponi Aria),

or there is a clinical reason that a trial of golimumab (Simponi Aria) would be otherwise inappropriate for the member.

- Active or latent TB has been ruled out.
- The individual has had an inadequate response after at least 3 months of one or more DMARDs, or the use of all DMARDs is contraindicated in the individual.
- The individual is 6 years of age or older.
- Abatacept (Orencia) will not be used in combination with other bDMARDs or JAK inhibitors.

PSORIATIC ARTHRITIS (PsA)

Abatacept (Orencia) injection for intravenous use is considered medically necessary and, therefore, covered for the treatment of active PsA. Abatacept (Orencia) injection for intravenous use may be covered as monotherapy or concomitantly with non-bDMARDs when **all** of the following inclusion criteria are met:

- If the individual has not previously received a bDMARD to treat adult rheumatoid arthritis (RA), abatacept (Orencia) injection for intravenous use is only eligible for coverage when the individual has a documented failure, contraindication, or intolerance to infliximab (Remicade), ustekinumab (Stelara), or golimumab (Simponi Aria), or there is a clinical reason that a trial of infliximab (Remicade), ustekinumab (Stelara), or golimumab (Simponi Aria) would be otherwise inappropriate for the member.
- Active or latent TB has been ruled out.
- The individual has had an inadequate response after at least 3 months of one or more DMARDs, or the use of all DMARDs is contraindicated in the individual.
- The individual is 18 years of age or older.
- Abatacept (Orencia) will not be used in combination with other bDMARDs or JAK inhibitors.

RHEUMATOID ARTHRITIS (RA)

Abatacept (Orencia) injection for intravenous use is considered medically necessary and, therefore, covered in individuals who have moderately to severely active RA. Abatacept (Orencia) injection for intravenous use may be covered as monotherapy or concomitantly with DMARDs, other than JAK inhibitors or biologic DMARDs (bDMARDs) when **all** of the following inclusion criteria are met:

- If the individual has not previously received a bDMARD to treat adult RA, abatacept (Orencia) injection for intravenous use is only eligible for coverage when the individual has a documented failure, contraindication, or intolerance to infliximab (Remicade) or golimumab (Simponi Aria), or there is a clinical reason that a trial of infliximab (Remicade) or golimumab (Simponi Aria) would be otherwise inappropriate for the member.
- Active or latent tuberculosis (TB) has been ruled out.
- The individual has had an inadequate response after at least 3 months to one or more non-bDMARDs or tumor necrosis factor (TNF) antagonists, or the use of all non-bDMARDs or TNF-antagonists is contraindicated in the individual.
- The individual is 18 years of age or older.

- Abatacept (Orencia) will not be used in combination with other bDMARDs or JAK inhibitors.

CONTINUATION THERAPY

CHRONIC GVHD

Abatacept (Orencia) injection for intravenous use is considered medically necessary for the treatment of chronic GVHD and, therefore, covered for the continuation therapy when the individual meets **both** of the following:

- Individual continues to experience chronic GVHD
- There is documentation of positive clinical response to therapy (e.g., reduction in symptoms, Global Scoring of Chronic GVHD, and steroid dose)

POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS, RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS

Abatacept (Orencia) injection for intravenous use is considered medically necessary for the treatment of pJIA, RA, and PsA, and, therefore, covered for the continuation therapy when the individual meets **both** of the following:

- Individual has met the medical necessity criteria for initial therapy
- There is documentation of positive clinical response or stabilization to therapy as evidenced by at least one of the following:
 - Reduction in total active (swollen and tender) joint count from baseline
 - Improvement in symptoms (e.g., pain, stiffness, inflammation) from baseline

Duration of authorization: 12 months

Version Effective Date: 09/23/2024

Title: Abatacept (Orencia®) for Injection for Intravenous Use

ICD-10 CODES AND NARRATIVES

D89.811 Chronic graft-versus-host disease
D89.812 Acute on chronic graft-versus-host disease
I40.8 Other acute myocarditis
I40.9 Acute myocarditis, unspecified
I51.4 Myocarditis, unspecified
L40.50 Arthropathic psoriasis, unspecified
L40.51 Distal interphalangeal psoriatic arthropathy
L40.52 Psoriatic arthritis mutilans
L40.53 Psoriatic spondylitis
L40.59 Other psoriatic arthropathy
M05.011 Felty's syndrome, right shoulder
M05.012 Felty's syndrome, left shoulder
M05.021 Felty's syndrome, right elbow
M05.022 Felty's syndrome, left elbow
M05.031 Felty's syndrome, right wrist
M05.032 Felty's syndrome, left wrist
M05.041 Felty's syndrome, right hand
M05.042 Felty's syndrome, left hand
M05.051 Felty's syndrome, right hip
M05.052 Felty's syndrome, left hip
M05.061 Felty's syndrome, right knee
M05.062 Felty's syndrome, left knee
M05.071 Felty's syndrome, right ankle and foot
M05.072 Felty's syndrome, left ankle and foot
M05.09 Felty's syndrome, multiple sites
M05.111 Rheumatoid lung disease with rheumatoid arthritis of right shoulder
M05.112 Rheumatoid lung disease with rheumatoid arthritis of left shoulder
M05.121 Rheumatoid lung disease with rheumatoid arthritis of right elbow
M05.122 Rheumatoid lung disease with rheumatoid arthritis of left elbow
M05.131 Rheumatoid lung disease with rheumatoid arthritis of right wrist
M05.132 Rheumatoid lung disease with rheumatoid arthritis of left wrist
M05.141 Rheumatoid lung disease with rheumatoid arthritis of right hand
M05.142 Rheumatoid lung disease with rheumatoid arthritis of left hand

M05.151 Rheumatoid lung disease with rheumatoid arthritis of right hip
M05.152 Rheumatoid lung disease with rheumatoid arthritis of left hip
M05.161 Rheumatoid lung disease with rheumatoid arthritis of right knee
M05.162 Rheumatoid lung disease with rheumatoid arthritis of left knee
M05.171 Rheumatoid lung disease with rheumatoid arthritis of right ankle and foot
M05.172 Rheumatoid lung disease with rheumatoid arthritis of left ankle and foot
M05.19 Rheumatoid lung disease with rheumatoid arthritis of multiple sites
M05.211 Rheumatoid vasculitis with rheumatoid arthritis of right shoulder
M05.212 Rheumatoid vasculitis with rheumatoid arthritis of left shoulder
M05.221 Rheumatoid vasculitis with rheumatoid arthritis of right elbow
M05.222 Rheumatoid vasculitis with rheumatoid arthritis of left elbow
M05.231 Rheumatoid vasculitis with rheumatoid arthritis of right wrist
M05.232 Rheumatoid vasculitis with rheumatoid arthritis of left wrist
M05.241 Rheumatoid vasculitis with rheumatoid arthritis of right hand
M05.242 Rheumatoid vasculitis with rheumatoid arthritis of left hand
M05.251 Rheumatoid vasculitis with rheumatoid arthritis of right hip
M05.252 Rheumatoid vasculitis with rheumatoid arthritis of left hip
M05.261 Rheumatoid vasculitis with rheumatoid arthritis of right knee
M05.262 Rheumatoid vasculitis with rheumatoid arthritis of left knee
M05.271 Rheumatoid vasculitis with rheumatoid arthritis of right ankle and foot
M05.272 Rheumatoid vasculitis with rheumatoid arthritis of left ankle and foot
M05.29 Rheumatoid vasculitis with rheumatoid arthritis of multiple sites
M05.311 Rheumatoid heart disease with rheumatoid arthritis of right shoulder
M05.312 Rheumatoid heart disease with rheumatoid arthritis of left shoulder
M05.321 Rheumatoid heart disease with rheumatoid arthritis of right elbow
M05.322 Rheumatoid heart disease with rheumatoid arthritis of left elbow
M05.331 Rheumatoid heart disease with rheumatoid arthritis of right wrist
M05.332 Rheumatoid heart disease with rheumatoid arthritis of left wrist
M05.341 Rheumatoid heart disease with rheumatoid arthritis of right hand
M05.342 Rheumatoid heart disease with rheumatoid arthritis of left hand
M05.351 Rheumatoid heart disease with rheumatoid arthritis of right hip
M05.352 Rheumatoid heart disease with rheumatoid arthritis of left hip
M05.361 Rheumatoid heart disease with rheumatoid arthritis of right knee
M05.362 Rheumatoid heart disease with rheumatoid arthritis of left knee
M05.371 Rheumatoid heart disease with rheumatoid arthritis of right ankle and foot
M05.372 Rheumatoid heart disease with rheumatoid arthritis of left ankle and foot

M05.39 Rheumatoid heart disease with rheumatoid arthritis of multiple sites
M05.411 Rheumatoid myopathy with rheumatoid arthritis of right shoulder
M05.412 Rheumatoid myopathy with rheumatoid arthritis of left shoulder
M05.421 Rheumatoid myopathy with rheumatoid arthritis of right elbow
M05.422 Rheumatoid myopathy with rheumatoid arthritis of left elbow
M05.431 Rheumatoid myopathy with rheumatoid arthritis of right wrist
M05.432 Rheumatoid myopathy with rheumatoid arthritis of left wrist
M05.441 Rheumatoid myopathy with rheumatoid arthritis of right hand
M05.442 Rheumatoid myopathy with rheumatoid arthritis of left hand
M05.451 Rheumatoid myopathy with rheumatoid arthritis of right hip
M05.452 Rheumatoid myopathy with rheumatoid arthritis of left hip
M05.461 Rheumatoid myopathy with rheumatoid arthritis of right knee
M05.462 Rheumatoid myopathy with rheumatoid arthritis of left knee
M05.471 Rheumatoid myopathy with rheumatoid arthritis of right ankle and foot
M05.472 Rheumatoid myopathy with rheumatoid arthritis of left ankle and foot
M05.49 Rheumatoid myopathy with rheumatoid arthritis of multiple sites
M05.511 Rheumatoid polyneuropathy with rheumatoid arthritis of right shoulder
M05.512 Rheumatoid polyneuropathy with rheumatoid arthritis of left shoulder
M05.521 Rheumatoid polyneuropathy with rheumatoid arthritis of right elbow
M05.522 Rheumatoid polyneuropathy with rheumatoid arthritis of left elbow
M05.531 Rheumatoid polyneuropathy with rheumatoid arthritis of right wrist
M05.532 Rheumatoid polyneuropathy with rheumatoid arthritis of left wrist
M05.541 Rheumatoid polyneuropathy with rheumatoid arthritis of right hand
M05.542 Rheumatoid polyneuropathy with rheumatoid arthritis of left hand
M05.551 Rheumatoid polyneuropathy with rheumatoid arthritis of right hip
M05.552 Rheumatoid polyneuropathy with rheumatoid arthritis of left hip
M05.561 Rheumatoid polyneuropathy with rheumatoid arthritis of right knee
M05.562 Rheumatoid polyneuropathy with rheumatoid arthritis of left knee
M05.571 Rheumatoid polyneuropathy with rheumatoid arthritis of right ankle and foot
M05.572 Rheumatoid polyneuropathy with rheumatoid arthritis of left ankle and foot
M05.59 Rheumatoid polyneuropathy with rheumatoid arthritis of multiple sites
M05.611 Rheumatoid arthritis of right shoulder with involvement of other organs and systems
M05.612 Rheumatoid arthritis of left shoulder with involvement of other organs and systems
M05.621 Rheumatoid arthritis of right elbow with involvement of other organs and systems
M05.622 Rheumatoid arthritis of left elbow with involvement of other organs and systems
M05.631 Rheumatoid arthritis of right wrist with involvement of other organs and systems

M05.632 Rheumatoid arthritis of left wrist with involvement of other organs and systems
M05.641 Rheumatoid arthritis of right hand with involvement of other organs and systems
M05.642 Rheumatoid arthritis of left hand with involvement of other organs and systems
M05.651 Rheumatoid arthritis of right hip with involvement of other organs and systems
M05.652 Rheumatoid arthritis of left hip with involvement of other organs and systems
M05.661 Rheumatoid arthritis of right knee with involvement of other organs and systems
M05.662 Rheumatoid arthritis of left knee with involvement of other organs and systems
M05.671 Rheumatoid arthritis of right ankle and foot with involvement of other organs and systems
M05.672 Rheumatoid arthritis of left ankle and foot with involvement of other organs and systems
M05.69 Rheumatoid arthritis of multiple sites with involvement of other organs and systems
M05.7A Rheumatoid arthritis with rheumatoid factor of other specified site without organ or systems involve
M05.8A Other rheumatoid arthritis with rheumatoid factor of other specified site
M05.711 Rheumatoid arthritis with rheumatoid factor of right shoulder without organ or systems involvement
M05.712 Rheumatoid arthritis with rheumatoid factor of left shoulder without organ or systems involvement
M05.721 Rheumatoid arthritis with rheumatoid factor of right elbow without organ or systems involvement
M05.722 Rheumatoid arthritis with rheumatoid factor of left elbow without organ or systems involvement
M05.731 Rheumatoid arthritis with rheumatoid factor of right wrist without organ or systems involvement
M05.732 Rheumatoid arthritis with rheumatoid factor of left wrist without organ or systems involvement
M05.741 Rheumatoid arthritis with rheumatoid factor of right hand without organ or systems involvement
M05.742 Rheumatoid arthritis with rheumatoid factor of left hand without organ or systems involvement
M05.751 Rheumatoid arthritis with rheumatoid factor of right hip without organ or systems involvement
M05.752 Rheumatoid arthritis with rheumatoid factor of left hip without organ or systems involvement
M05.761 Rheumatoid arthritis with rheumatoid factor of right knee without organ or systems involvement
M05.762 Rheumatoid arthritis with rheumatoid factor of left knee without organ or systems involvement
M05.771 Rheumatoid arthritis with rheumatoid factor of right ankle and foot without organ or systems involve
M05.772 Rheumatoid arthritis with rheumatoid factor of left ankle and foot without organ or systems involvem
M05.79 Rheumatoid arthritis with rheumatoid factor of multiple sites without organ or systems involvement
M05.811 Other rheumatoid arthritis with rheumatoid factor of right shoulder
M05.812 Other rheumatoid arthritis with rheumatoid factor of left shoulder
M05.821 Other rheumatoid arthritis with rheumatoid factor of right elbow
M05.822 Other rheumatoid arthritis with rheumatoid factor of left elbow
M05.831 Other rheumatoid arthritis with rheumatoid factor of right wrist
M05.832 Other rheumatoid arthritis with rheumatoid factor of left wrist
M05.841 Other rheumatoid arthritis with rheumatoid factor of right hand
M05.842 Other rheumatoid arthritis with rheumatoid factor of left hand
M05.851 Other rheumatoid arthritis with rheumatoid factor of right hip

M05.852 Other rheumatoid arthritis with rheumatoid factor of left hip
M05.861 Other rheumatoid arthritis with rheumatoid factor of right knee
M05.862 Other rheumatoid arthritis with rheumatoid factor of left knee
M05.871 Other rheumatoid arthritis with rheumatoid factor of right ankle and foot
M05.872 Other rheumatoid arthritis with rheumatoid factor of left ankle and foot
M05.89 Other rheumatoid arthritis with rheumatoid factor of multiple sites
M05.9 Rheumatoid arthritis with rheumatoid factor, unspecified
M06.0A Rheumatoid arthritis without rheumatoid factor, other specified site
M06.8A Other specified rheumatoid arthritis, other specified site
M06.011 Rheumatoid arthritis without rheumatoid factor, right shoulder
M06.012 Rheumatoid arthritis without rheumatoid factor, left shoulder
M06.021 Rheumatoid arthritis without rheumatoid factor, right elbow
M06.022 Rheumatoid arthritis without rheumatoid factor, left elbow
M06.031 Rheumatoid arthritis without rheumatoid factor, right wrist
M06.032 Rheumatoid arthritis without rheumatoid factor, left wrist
M06.041 Rheumatoid arthritis without rheumatoid factor, right hand
M06.042 Rheumatoid arthritis without rheumatoid factor, left hand
M06.051 Rheumatoid arthritis without rheumatoid factor, right hip
M06.052 Rheumatoid arthritis without rheumatoid factor, left hip
M06.061 Rheumatoid arthritis without rheumatoid factor, right knee
M06.062 Rheumatoid arthritis without rheumatoid factor, left knee
M06.071 Rheumatoid arthritis without rheumatoid factor, right ankle and foot
M06.072 Rheumatoid arthritis without rheumatoid factor, left ankle and foot
M06.08 Rheumatoid arthritis without rheumatoid factor, vertebrae
M06.09 Rheumatoid arthritis without rheumatoid factor, multiple sites
M06.811 Other specified rheumatoid arthritis, right shoulder
M06.812 Other specified rheumatoid arthritis, left shoulder
M06.821 Other specified rheumatoid arthritis, right elbow
M06.822 Other specified rheumatoid arthritis, left elbow
M06.831 Other specified rheumatoid arthritis, right wrist
M06.832 Other specified rheumatoid arthritis, left wrist
M06.841 Other specified rheumatoid arthritis, right hand
M06.842 Other specified rheumatoid arthritis, left hand
M06.851 Other specified rheumatoid arthritis, right hip
M06.852 Other specified rheumatoid arthritis, left hip
M06.861 Other specified rheumatoid arthritis, right knee

M06.862 Other specified rheumatoid arthritis, left knee
M06.871 Other specified rheumatoid arthritis, right ankle and foot
M06.872 Other specified rheumatoid arthritis, left ankle and foot
M06.88 Other specified rheumatoid arthritis, vertebrae
M06.89 Other specified rheumatoid arthritis, multiple sites
M06.9 Rheumatoid arthritis, unspecified
M08.3 Juvenile rheumatoid polyarthritis (seronegative)
M60.811 Other myositis, right shoulder
M60.812 Other myositis, left shoulder
M60.821 Other myositis, right upper arm
M60.822 Other myositis, left upper arm
M60.831 Other myositis, right forearm
M60.832 Other myositis, left forearm
M60.841 Other myositis, right hand
M60.842 Other myositis, left hand
M60.851 Other myositis, right thigh
M60.852 Other myositis, left thigh
M60.861 Other myositis, right lower leg
M60.862 Other myositis, left lower leg
M60.871 Other myositis, right ankle and foot
M60.872 Other myositis, left ankle and foot
M60.88 Other myositis, other site
M60.89 Other myositis, multiple sites
M60.9 Myositis, unspecified
Z94.84 Stem cell transplantation status
Z29.89 Encounter for other specified prophylactic measures

Duration of authorization: 12 months

Version Effective Date: 09/23/2024

Title: ADAMTS13, recombinant-krhn (Adzynma)

MEDICALLY NECESSARY:

INITIAL THERAPY

PROPHYLACTIC TREATMENT

ADAMTS13, recombinant-krhn (Adzynma), is considered medically necessary and, therefore, covered for the **prophylactic** treatment of congenital thrombotic thrombocytopenic purpura (cTTP) in adult and pediatric individuals, when all of the following criteria are met, including dosing and frequency:

Initial Criteria

- Diagnosis of cTTP:
 - ADAMTS13 mutation is confirmed by molecular genetic testing with biallelic mutations in the ADAMTS13 gene
 - The individual has an ADAMTS13 activity level of less than 10% at the time of diagnosis
- ADAMTS13, recombinant-krhn (Adzynma) is being prescribed for routine prophylactic treatment to prevent thrombotic thrombocytopenic purpura (TTP) events
- Prescribed by or in consultation with a hematologist
- Dosing and frequency for ADAMTS13, recombinant-krhn (Adzynma):
 - 40 IU/kg body weight once every other week intravenously
 - The prophylaxis dosing frequency may be adjusted to 40 IU/kg body weight once weekly based on prior prophylactic dosing regimen or clinical response

Continuation Criteria

- The individual has previously received routine prophylactic treatment with ADAMTS13, recombinant-krhn (Adzynma)
- Documentation of positive clinical response to ADAMTS13, recombinant-krhn (Adzynma) therapy (e.g., reduction or maintenance of number of TTP events, increase in platelet count, decrease in lactate dehydrogenase [LDH] level)
- Prescribed by or in consultation with a hematologist

TREATMENT

ADAMTS13, recombinant-krhn (Adzynma) is considered medically necessary and, therefore, covered for **on demand treatment** of an acute TTP event in adult and pediatric individuals, when all of the following criteria are met, including dosing and frequency:

- Diagnosis of congenital thrombotic thrombocytopenic purpura (cTTP):
 - ADAMTS13 mutation is confirmed by molecular genetic testing with biallelic mutations in the ADAMTS13 gene
 - The individual has an ADAMTS13 activity level of less than 10% at the time of diagnosis

- ADAMTS13, recombinant-krhn (Adzynma) is being prescribed for on demand treatment of an acute thrombotic thrombocytopenic purpura (TTP) event
- Prescribed by or in consultation with a hematologist
- Dosing and frequency for ADAMTS13, recombinant-krhn (Adzynma):
 - 40 IU/kg body weight on day one
 - 20 IU/kg body weight on day two
 - 15 IU/kg body weight on day three and beyond until two days after the acute event is resolved

Duration of authorization: 12 months

Version Effective Date: 05/28/2025

Title: Ado-Trastuzumab Emtansine (Kadcyla®)

MEDICALLY NECESSARY:

Ado-trastuzumab emtansine (Kadcyla®) is considered medically necessary and, therefore, covered for the indication(s) identified below, in individuals who meet the applicable criteria, and whose tumors have human epidermal growth factor receptor 2 (HER2) protein overexpression verified as a positive result by US Food and Drug Administration (FDA)–approved diagnostic tests for the following indications:

BREAST CANCER

Ado-trastuzumab emtansine (Kadcyla®) is considered medically necessary and, therefore, covered for individuals with HER2-positive breast cancer and the individual has a left ventricular ejection fraction of 50 percent or greater for any of the following indications:

Early Breast Cancer

- As adjuvant therapy for individuals with HER2-positive early breast cancer who have residual invasive disease after neoadjuvant taxane and trastuzumab-based treatment.

Metastatic breast cancer

- As a single agent therapy for the treatment of individuals with HER2-positive, metastatic breast cancer who previously received trastuzumab and a taxane, separately or in combination, when any of the following criteria are met:
 - The individual received prior therapy for metastatic disease
 - The individual developed disease recurrence during or within 6 months of completing adjuvant therapy.

Inflammatory breast cancer

- National Comprehensive Cancer Network (NCCN)-preferred adjuvant systemic therapy for individuals with inflammatory breast cancer who have residual disease following preoperative therapy for HER2-positive tumors
- As third-line and beyond (or second-line if not a candidate for fam-trastuzumab deruxtecan) as a single-agent therapy for individuals with no response to preoperative systemic therapy, or for recurrent unresectable (local or regional) or stage IV (M1) HER2-positive inflammatory breast cancer for one of the following:
 - Hormone receptor–negative
 - Hormone receptor–positive with or without endocrine therapy
- Adjuvant systemic therapy for individuals who had a response to preoperative systemic therapy, followed by surgery, and need to complete planned chemotherapy, with HER2-positive tumors

Invasive breast cancer

- NCCN-preferred therapy for individuals with HER2-positive tumors and locally advanced clinical stage $\geq T2$ or cN+ and M0, or cT1c, cN0 invasive breast cancer and all of the following:
 - The individual completed planned chemotherapy and following mastectomy or breast-conserving surgery (BCS) with surgical axillary staging for:
 - ypT1-4N0
 - ypN ≥ 1
- Third line and beyond (or second-line if not a candidate for fam-trastuzumab deruxtecan) as a single-agent therapy for recurrent unresectable (local or regional) or stage IV (M1) HER2-positive invasive breast cancer for one of the following:
 - Hormone receptor–negative
 - Hormone receptor–positive with or without endocrine therapy
- Adjuvant systemic therapy for individuals with HER2-positive tumors and cT1c-3 and and pN0 or pN+ tumors disease

CENTRAL NERVOUS SYSTEM (CNS) CANCERS

Breast cancer with brain metastases

Ado-trastuzumab emtansine (Kadcyla®) is considered medically necessary and, therefore, covered for individuals with HER2-positive breast cancer with brain metastases and the individual has a left ventricular ejection fraction of 50 percent or greater for any of the following indications criteria:

- As a single-agent treatment for limited brain metastases in individuals with HER2-positive breast cancer:
 - Initial treatment in select individuals (e.g., individuals with small asymptomatic brain metastases)
 - Treatment for recurrent brain metastases
 - Treatment for relapsed disease with either stable systemic disease or reasonable systemic treatment options
- As a single-agent treatment for extensive brain metastases in individuals with HER2-positive breast cancer:
 - Primary treatment in select individuals (e.g., individuals with small asymptomatic brain metastases)
 - Treatment for recurrent disease with stable systemic disease or reasonable systemic treatment options

HEAD AND NECK CANCERS - SALIVARY GLAND TUMORS

Ado-trastuzumab emtansine (Kadcyla®) is considered medically necessary and, therefore, covered for individuals with HER2-positive recurrent disease and the individual has a left ventricular ejection fraction of 50 percent or greater for any of the following criteria:

- As a single-agent systemic therapy for recurrent disease with:
 - Distant metastases in individuals with a performance status (PS) of 0–3

- Unresectable locoregional recurrence or second primary with prior radiation therapy

NON-SMALL CELL LUNG CANCER

Ado-trastuzumab emtansine (Kadcyla®) is considered medically necessary and, therefore, covered as a single-agent therapy for individuals with a left ventricular ejection fraction of 50 percent or greater for one of the following indications (except for locoregional recurrence or symptomatic local disease [excluding mediastinal lymph node recurrence with prior radiation therapy] with no evidence of disseminated disease):

- As subsequent therapy for ERBB2/(HER2) mutation–positive recurrent, advanced, or metastatic disease
- Advanced disease, previously treated, HER2 mutation–positive

Duration of authorization: 12 months

Version Effective Date: 03/11/2024

Title: Ado-Trastuzumab Emtansine (Kadcyla®)

ICD-10-CM CODES AND NARRATIVES

C06.9 Malignant neoplasm of mouth, unspecified
C07 Malignant neoplasm of parotid gland
C08.0 Malignant neoplasm of submandibular gland
C08.1 Malignant neoplasm of sublingual gland
C08.9 Malignant neoplasm of major salivary gland, unspecified
C33 Malignant neoplasm of trachea
C34.00 Malignant neoplasm of unspecified main bronchus
C34.01 Malignant neoplasm of right main bronchus
C34.02 Malignant neoplasm of left main bronchus
C34.10 Malignant neoplasm of upper lobe, unspecified bronchus or lung
C34.11 Malignant neoplasm of upper lobe, right bronchus or lung
C34.12 Malignant neoplasm of upper lobe, left bronchus or lung
C34.2 Malignant neoplasm of middle lobe, bronchus or lung
C34.30 Malignant neoplasm of lower lobe, unspecified bronchus or lung
C34.31 Malignant neoplasm of lower lobe, right bronchus or lung
C34.32 Malignant neoplasm of lower lobe, left bronchus or lung
C34.80 Malignant neoplasm of overlapping sites of unspecified bronchus and lung
C34.81 Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82 Malignant neoplasm of overlapping sites of left bronchus and lung
C34.90 Malignant neoplasm of unspecified part of unspecified bronchus or lung
C34.91 Malignant neoplasm of unspecified part of right bronchus or lung
C34.92 Malignant neoplasm of unspecified part of left bronchus or lung
C50.011 Malignant neoplasm of nipple and areola, right female breast
C50.012 Malignant neoplasm of nipple and areola, left female breast
C50.019 Malignant neoplasm of nipple and areola, unspecified female breast
C50.021 Malignant neoplasm of nipple and areola, right male breast
C50.022 Malignant neoplasm of nipple and areola, left male breast
C50.029 Malignant neoplasm of nipple and areola, unspecified male breast
C50.111 Malignant neoplasm of central portion of right female breast
C50.112 Malignant neoplasm of central portion of left female breast
C50.119 Malignant neoplasm of central portion of unspecified female breast
C50.121 Malignant neoplasm of central portion of right male breast
C50.122 Malignant neoplasm of central portion of left male breast
C50.129 Malignant neoplasm of central portion of unspecified male breast
C50.211 Malignant neoplasm of upper-inner quadrant of right female breast
C50.212 Malignant neoplasm of upper-inner quadrant of left female breast
C50.219 Malignant neoplasm of upper-inner quadrant of unspecified female breast
C50.221 Malignant neoplasm of upper-inner quadrant of right male breast
C50.222 Malignant neoplasm of upper-inner quadrant of left male breast
C50.229 Malignant neoplasm of upper-inner quadrant of unspecified male breast

C50.311 Malignant neoplasm of lower-inner quadrant of right female breast
C50.312 Malignant neoplasm of lower-inner quadrant of left female breast
C50.319 Malignant neoplasm of lower-inner quadrant of unspecified female breast
C50.321 Malignant neoplasm of lower-inner quadrant of right male breast
C50.322 Malignant neoplasm of lower-inner quadrant of left male breast
C50.329 Malignant neoplasm of lower-inner quadrant of unspecified male breast
C50.411 Malignant neoplasm of upper-outer quadrant of right female breast
C50.412 Malignant neoplasm of upper-outer quadrant of left female breast
C50.419 Malignant neoplasm of upper-outer quadrant of unspecified female breast
C50.421 Malignant neoplasm of upper-outer quadrant of right male breast
C50.422 Malignant neoplasm of upper-outer quadrant of left male breast
C50.429 Malignant neoplasm of upper-outer quadrant of unspecified male breast
C50.511 Malignant neoplasm of lower-outer quadrant of right female breast
C50.512 Malignant neoplasm of lower-outer quadrant of left female breast
C50.519 Malignant neoplasm of lower-outer quadrant of unspecified female breast
C50.521 Malignant neoplasm of lower-outer quadrant of right male breast
C50.522 Malignant neoplasm of lower-outer quadrant of left male breast
C50.529 Malignant neoplasm of lower-outer quadrant of unspecified male breast
C50.611 Malignant neoplasm of axillary tail of right female breast
C50.612 Malignant neoplasm of axillary tail of left female breast
C50.619 Malignant neoplasm of axillary tail of unspecified female breast
C50.621 Malignant neoplasm of axillary tail of right male breast
C50.622 Malignant neoplasm of axillary tail of left male breast
C50.629 Malignant neoplasm of axillary tail of unspecified male breast
C50.811 Malignant neoplasm of overlapping sites of right female breast
C50.812 Malignant neoplasm of overlapping sites of left female breast
C50.819 Malignant neoplasm of overlapping sites of unspecified female breast
C50.821 Malignant neoplasm of overlapping sites of right male breast
C50.822 Malignant neoplasm of overlapping sites of left male breast
C50.829 Malignant neoplasm of overlapping sites of unspecified male breast
C50.911 Malignant neoplasm of unspecified site of right female breast
C50.912 Malignant neoplasm of unspecified site of left female breast
C50.919 Malignant neoplasm of unspecified site of unspecified female breast
C50.921 Malignant neoplasm of unspecified site of right male breast
C50.922 Malignant neoplasm of unspecified site of left male breast
C50.929 Malignant neoplasm of unspecified site of unspecified male breast
C72.9 Malignant neoplasm of central nervous system, unspecified
C79.31 Secondary malignant neoplasm of brain

Duration of authorization: 12 months

Version Effective Date: 03/11/2024

Title: Afamitresgene autoleucel (Tecelra®)

MEDICALLY NECESSARY:

Afamitresgene autoleucel (Tecelra®) for intravenous (IV) infusion is considered medically necessary and, therefore, covered for the palliative treatment of individuals with synovial sarcoma when all of the following criteria listed below are met:

- The individual is at least 18 years of age
- Documented diagnosis of unresectable or metastatic synovial sarcoma
- The individual has received at least one prior systemic chemotherapy agent
- The individual is positive for human leukocyte antigen HLA-A*02:01P, HLA-A*02:02P, HLA-A*02:03P, or HLA-A*02:06P alleles (see Guidelines)
- Tumor expresses the MAGE-A4 antigen (melanoma-associated antigen 4)
- The individual is not heterozygous or homozygous for HLA-A*02:05P (see Guidelines)

Duration of authorization: 12 months

Version Effective Date: 04/14/2025

Title: Agalsidase beta (Fabrazyme®) and pegunigalsidase alfa-iwxj (Elfabrio)

MEDICALLY NECESSARY:

Agalsidase beta (Fabrazyme) is considered medically necessary and, therefore, covered for individuals 2 years of age and older with Fabry disease to reduce globotriaosylceramide (GL-3) deposition in the capillary endothelium of the kidney and certain other cell types when all of the following criteria are met, including dosing and frequency:

- Diagnosis is confirmed by one of the following:
 - Deficiency of alpha-galactosidase A (α -Gal A) in plasma or peripheral leukocytes
 - Confirmation of a hemizygous pathogenic variant(s) in the galactosidase alpha (GLA) gene
- Dosing and frequency: 1 mg/kg intravenous (IV) infusion every 2 weeks
- No concomitant use of migalastat (Galafold)

Pegunigalsidase alfa-iwxj (Elfabrio) is considered medically necessary and, therefore, covered for adult individuals with confirmed Fabry disease when all of the following criteria are met, including dosing and frequency:

- Diagnosis of Fabry disease as confirmed by one the following:
 - Absence or deficiency (<5% of mean) of normal α -Gal A enzyme activity in leukocytes, dried blood spots, or serum analysis
- Molecular genetic testing demonstrating deletion or mutations in the GLA gene
- Medication is prescribed by, or in consultation with, a geneticist, endocrinologist, a metabolic disorder subspecialist, or a physician who specializes in the treatment of lysosomal storage disorders
- Presence of clinical signs and symptoms of the disease (e.g., acroparesthesias, angiokeratomas, whorls, anhidrosis/hypohidrosis, renal disease, exercise/heat/cold intolerance, etc.)
- Dosing and frequency: 1 mg/kg administered intravenously once every 2 weeks
- No concomitant use of migalastat (Galafold)

Duration of authorization: 12 months

Version Effective Date: 05/28/2025

Title: Alemtuzumab (Lemtrada®)

MEDICALLY NECESSARY:

Alemtuzumab (Lemtrada®) is considered medically necessary and, therefore, covered for **ONE** of the following:

- Individuals with relapsing forms of multiple sclerosis (MS), including relapsing-remitting multiple sclerosis and active secondary progressive disease, when **BOTH** the following criteria are met:
 - **ONE** of the following scenarios is met:
 - Inadequate clinical response to two or more drugs indicated for the treatment of multiple sclerosis as defined by relapse, and/or accumulating disability, and/or multiple new or enlarging of lesions of brain and/or spinal cord
 - Inadequate clinical response to one or more drugs, if individual is considered high risk for disability (e.g., the spinal MRI shows high burden of lesions, but the physical exam does not demonstrate the extent of disability)
 - Human immunodeficiency virus (HIV)-negative
- Individuals with aggressive relapsing-remitting multiple sclerosis defined as, but not limited to, accumulating disability, multiple new or enlarging of lesions of brain and/or spinal cord in the first year of illness
 - Human immunodeficiency virus (HIV)-negative

Duration of authorization: 12 months

Version Effective Date: 04/02/2025

Title: Alglucosidase alfa (e.g., Lumizyme®), Avalglucosidase alfa-ngpt (Nexviazyme®),
Cipaglucosidase alfa-atga (Pombiliti™)

MEDICALLY NECESSARY:

ALGLUCOSIDASE ALFA (LU MIZYME)

Alglucosidase alfa (Lumizyme) is considered medically necessary and, therefore, covered for the treatment of symptomatic individuals 1 month of age and older with infantile-onset or juvenile/adult-onset Pompe disease (lysosomal acid alpha-glucosidase [GAA] deficiency) when all of the following criteria are met, including dosing and frequency:

- Diagnosis is confirmed by either of the following:
 - Deficiency of acid alpha-glucosidase in leukocytes or skin fibroblasts or muscles
 - Confirmation of biallelic pathogenic variant(s) in the GAA gene
- Dosing and frequency: infants 1 month of age and older, children, adolescents and adult dosing IV: 20 mg/kg every 2 weeks

AVALGLUCOSIDASE ALFA-NGPT (NEXVIAZYME)

Avalglucosidase alfa-ngpt (Nexviazyme) is considered medically necessary and, therefore, covered for the treatment of individuals 1 year of age and older with late-onset Pompe disease (LOPD) (GAA deficiency) when all of the following criteria are met, including dosing and frequency:

- The participant has confirmed GAA enzyme deficiency from any tissue source (e.g., skin, fibroblasts, muscle, or blood) and/or two confirmed GAA gene mutations.
- Dosing and frequency:
 - ≥30 kg, the recommended dosage is 20 mg/kg (of actual body weight) every 2 weeks
 - <30 kg, the recommended dosage is 40 mg/kg (of actual body weight) every 2 weeks

CIPAGLUCOSIDASE ALFA-ATGA (POMBILITI)

Cipaglucosidase alfa-atga (Pombiliti) is considered medically necessary and, therefore, covered for the treatment of adult individuals with diagnosis of LOPD when all of the following criteria are met, including dosing and frequency:

- Diagnosis of LOPD (e.g., presence of clinical signs and symptoms of the disease (e.g., respiratory distress, skeletal muscle weakness) confirmed by either of the following:
 - Deficiency of GAA enzyme from any tissue sources (e.g., leukocytes or skin fibroblasts or muscles)
 - Confirmation of biallelic pathogenic variant(s) in the GAA gene.
- Individual's weight is greater than or equal to 40 kg
- Inadequate response or inability to tolerate an enzyme replacement therapy for Pompe disease (PD) (e.g., alglucosidase alfa or avalglucosidase alfa-ngpt)
- Medication must not be used in combination with other miglustat products (e.g., Zavesca, Yargesa)

- Dosing and frequency: 20 mg/kg (of actual body weight) administered every other week as an intravenous infusion

Note: medication must be used in combination with oral miglustat (Opfolda).

Duration of authorization: 12 months

Version Effective Date: 04/22/2024

Title: Allogeneic Processed Thymus Tissue-agdc (Rethymic®)

MEDICALLY NECESSARY:

Allogeneic processed thymus tissue-agdc (Rethymic) is considered medically necessary and, therefore, covered for the treatment of congenital athymia when ALL of the following criteria are met:

- The individual is 3 years of age or younger; AND
- The individual has a diagnosis of congenital athymia confirmed by flow cytometry demonstrating fewer than 50 naïve T-cells/mm³ (CD45RA⁺, CD62L⁺) in the peripheral blood or less than 05% of total T-cells being naïve in phenotype; AND
- The individual has complete DiGeorge syndrome (cDGS) and at least one of the following:
 - a. Congenital heart defect; OR
 - b. Hypoparathyroidism or hypocalcemia requiring calcium replacement; OR
 - c. 22q11.2 deletion syndrome; OR
 - d. 10p13 hemizyosity; OR
 - e. CHARGE (coloboma, heart defects, choanal atresia, growth and development retardation, genital hypoplasia, and ear anomalies including deafness) syndrome; OR
 - f. clinically-supported & established pathogenic mutation(s)/variation(s) in CHD7, FOXP1, TBX1, TBX2, and/or the PAX1 genes leading to confirmed congenital athymia; AND
- The individual is NOT being treated for severe combined immunodeficiency (SCID); AND
- The individual has been screened for anti-HLA antibodies prior to receiving treatment with the requested agent; AND
- For individuals who received prior solid organ (e.g., thymus) or hematopoietic cell transplantation, the patient has undergone HLA matching of the requested agent to recipient alleles; AND
- The requested quantity does NOT exceed the maximum units, (i.e. 22,000) allowed for the duration of approval (i.e. 180 days (one treatment course per lifetime); AND
- Dosing is administered per the FDA-approval: 5,000 to 22,000 mm² of Rethymic surface area/m² recipient body surface area (BSA) administered by surgical procedure.

Duration of authorization: 12 months

Version Effective Date: 03/06/2024

Title: Alpha 1-Antitrypsin Therapy (e.g., Prolastin-C®, Aralast NP®, Glassia®, Zemaira®)

MEDICALLY NECESSARY:

EMPHYSEMA WITH ALPHA 1-ANTITRYPSIN DEFICIENCY

Alpha 1-antitrypsin therapy (e.g., Prolastin-C, Aralast NP, Glassia, Zemaira) is considered medically necessary and, therefore, covered for individuals 18 years of age and older who have alpha 1-antitrypsin (AAT) deficiency and clinical evidence of chronic emphysema without evidence of alpha 1-antitrypsin-associated liver disease, when all of the following criteria are met:

- The individual has a low serum concentration of alpha 1-antitrypsin (AAT) less than 80 mg/dL (radial immunodiffusion) or 50 mg/dl (nephelometry) or less than 11 uM/L (nephelometry) or less than 0.8 g/L (35 percent of normal), which is considered the threshold thought to protect against emphysema.
- The individual has a documented diagnosis of congenital alpha1-antitrypsin deficiency confirmed by one of the following:
 - Pi*ZZ, Pi*Z(null) or Pi(null)(null) protein phenotypes (homozygous)
 - Other rare AAT disease-causing alleles associated with serum alpha1-antitrypsin (AAT) level <11uM/L
- The individual has progressive panacinar emphysema with a documented rate of decline in forced expiratory volume in 1 second (FEV1).
- The individual is a non-smoker.

ACUTE GRAFT VERSUS HOST DISEASE (GVHD) AFTER HEMATOPOIETIC CELL TRANSPLANTATION

Alpha 1-antitrypsin therapy (e.g., Prolastin-C, Aralast NP, Glassia, Zemaira) administered intravenously is considered medically necessary and, therefore, covered for individuals 18 years of age and older who have acute graft-versus-host disease (GVHD) following hematopoietic cell transplantation in conjunction with systemic corticosteroids following no response (steroid-refractory disease) to first-line therapy options.

Duration of authorization: 12 months

Version Effective Date: 05/01/2024

Title: Amivantamab-vmjw (Rybrevant®)

MEDICALLY NECESSARY:

Initial Approval

Amivantamab-vmjw (Rybrevant) is considered medically necessary and, therefore, covered as a single agent for the treatment of adult individuals with treatment of non-small cell lung cancer (NSCLC) when ALL of the following criteria are met:

- The individual has recurrent, locally advanced or metastatic disease; *and*
- The individual has EGFR exon 20 insertion pathogenic variations*; *and*
- Disease has progressed on or after platinum-based chemotherapy; *or as subsequent therapy*

Amivantamab-vmjw (Rybrevant) is considered medically necessary and, therefore, covered in combination with carboplatin and pemetrexed in adult individuals with NSCLC when either of the following criteria are met:

- First-line treatment with locally advanced or metastatic disease with epidermal growth factor receptor (EGFR) exon 20 insertion mutations* as National Comprehensive Cancer Network (NCCN) preferred therapy
- Subsequent therapy for EGFR exon 19 deletion or exon 21 L858R or EGFR S768I, L861Q, and/or G719X mutation positive recurrent, advanced, or metastatic disease (nonsquamous) following disease progression on osimertinib (Tagrisso) for symptomatic systemic disease with multiple lesions as NCCN-preferred therapy.

*as detected by a U.S. Food and Drug Administration (FDA)-approved test.

Continuation of Therapy

Continuation of amivantamab-vmjw (Rybrevant) therapy is medically necessary in individuals requesting reauthorization for an indication listed in Section I when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

Duration of authorization: 12 months

Version Effective Date: 05/20/2024

Title: Anifrolumab-fnia (Saphnelo®)

MEDICALLY NECESSARY:

INITIAL THERAPY

Anifrolumab-fnia (Saphnelo), administered by intravenous infusion, is considered medically necessary and, therefore, covered for the treatment of adult individuals with moderate to severe systemic lupus erythematosus (SLE) who are receiving standard therapy* and **do not** have severe active lupus nephritis or severe active central nervous system lupus.

*Standard therapy for SLE with the use of anifrolumab-fnia (Saphnelo) includes, but is not limited to, oral corticosteroids, antimalarials (e.g., hydroxychloroquine, chloroquine), and/or immunosuppressants (e.g., azathioprine, methotrexate, mycophenolate mofetil/mycophenolic acid) but excluding other biologic agents (including B-cell targeted therapies) and cyclophosphamide.

CONTINUATION THERAPY

Continuation of anifrolumab-fnia (Saphnelo) is considered medically necessary and, therefore, covered when all of the following criteria are met:

- All criteria under "Initial Therapy" as stated above are met.
- There is documented improvement or stabilization in disease activity due to anifrolumab-fnia (Saphnelo) treatment based on scoring instruments in SLE-associated disease area and severity (e.g., Systemic Lupus Erythematosus Disease Activity INDEX 2000 [SLEDAI-2K], British Isles Lupus Assessment Group [BILAG], and the Physician's Global Assessment [PGA] scores). It is expected that the same objective measurement scale will be used for both baseline and response to treatment.

Duration of authorization: 12 months

Version Effective Date: 05/28/2025

Title: Asparaginase Erwinia Chrysanthemi (recombinant)-rywn (Rylaze®)

MEDICALLY NECESSARY:

ASPARAGINASE ERWINIA CHRISANTHEMI [RECOMBINANT]-RYWN (RYLAZE)

Acute Lymphoblastic Leukemia (ALL) and Lymphoblastic Lymphoma (LBL)

Asparaginase erwinia chrysanthemi [recombinant]-rywn (Rylaze) is considered medically necessary and, therefore, covered for the treatment of ALL and LBL in adult and pediatric individuals 1 month or older when **all** of the following criteria are met:

- Asparaginase erwinia chrysanthemi [recombinant]-rywn (Rylaze) is being used as a component of a multiagent chemotherapeutic regimen
- The individual has a history of documented hypersensitivity to *Escherichia coli* (*E. coli*)–derived asparaginase (e.g., calaspargase pegol-mknl [Asparlas], pegaspargase [Oncaspar]) (and has fully recovered), or has silent inactivation
- The individual does **not** have **any** of the following conditions/contraindications:
 - History of serious hypersensitivity reactions to asparaginase erwinia chrysanthemi (Erwinaze), including anaphylaxis
 - History of Grade 3 or higher pancreatitis with prior L-asparaginase therapy
 - History of asparaginase-associated Grade 3 or higher hemorrhagic event or asparaginase-associated thrombus requiring anticoagulation therapy, excluding catheter-related thrombotic events with prior L-asparaginase therapy
 - History of severe hepatic impairment

Extranodal natural killer (NK)/T-cell lymphomas

Asparaginase erwinia chrysanthemi [recombinant]-rywn (Rylaze) is considered medically necessary and, therefore, covered for the treatment of extranodal NK/T-cell lymphomas when **all** of the following criteria are met:

- Asparaginase erwinia chrysanthemi [recombinant]-rywn (Rylaze) is being used as a component of a multiagent chemotherapeutic regimen
- The individual has a history of documented hypersensitivity to pegaspargase [Oncaspar])
- The individual does **not** have **any** of the following contraindications:
 - History of serious hypersensitivity reactions to asparaginase erwinia chrysanthemi (Erwinaze), including anaphylaxis
 - History of Grade 3 or higher pancreatitis with prior L-asparaginase therapy
 - History of asparaginase-associated Grade 3 or higher hemorrhagic event or asparaginase-associated thrombus requiring anticoagulation therapy, excluding catheter-related thrombotic events with prior L-asparaginase therapy
 - History of severe hepatic impairment

Duration of authorization: 12 months

Version Effective Date: 01/02/2025

Title: Atezolizumab (Tecentriq®) and Atezolizumab with Hyaluronidase-tqjs (Tecentriq Hybreza™)

ICD-10 Codes and Narratives

ATEZOLIZUMAB (TECENTRIQ®) AND ATEZOLIZUMAB WITH HYALURONIDASE-TQJS (TECENTRIQ HYBREZA™) ARE MEDICALLY NECESSARY WHEN REPORTED WITH THE FOLLOWING DIAGNOSIS CODES:

C22.0	Liver cell carcinoma
C22.8	Malignant neoplasm of liver, primary, unspecified as to type
C22.9	Malignant neoplasm of liver, not specified as primary or secondary
C33	Malignant neoplasm of trachea
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus
C34.11	Malignant neoplasm of upper lobe, right bronchus or lung
C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.81	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus and lung
C34.91	Malignant neoplasm of unspecified part of right bronchus or lung
C34.92	Malignant neoplasm of unspecified part of left bronchus or lung
C43.0	Malignant melanoma of lip
C43.111	Malignant melanoma of right upper eyelid, including canthus
C43.112	Malignant melanoma of right lower eyelid, including canthus
C43.121	Malignant melanoma of left upper eyelid, including canthus
C43.122	Malignant melanoma of left lower eyelid, including canthus
C43.21	Malignant melanoma of right ear and external auricular canal
C43.22	Malignant melanoma of left ear and external auricular canal
C43.30	Malignant melanoma of unspecified part of face
C43.31	Malignant melanoma of nose
C43.39	Malignant melanoma of other parts of face
C43.4	Malignant melanoma of scalp and neck
C43.51	Malignant melanoma of anal skin
C43.52	Malignant melanoma of skin of breast
C43.59	Malignant melanoma of other part of trunk

C43.61 Malignant melanoma of right upper limb, including shoulder
C43.62 Malignant melanoma of left upper limb, including shoulder
C43.71 Malignant melanoma of right lower limb, including hip
C43.72 Malignant melanoma of left lower limb, including hip
C43.8 Malignant melanoma of overlapping sites of skin
C43.9 Malignant melanoma of skin, unspecified
C45.1 Mesothelioma of peritoneum
C45.2 Mesothelioma of pericardium
C45.7 Mesothelioma of other sites
C45.9 Mesothelioma, unspecified
C49.0 Malignant neoplasm of connective and soft tissue of head, face and neck
C49.11 Malignant neoplasm of connective and soft tissue of right upper limb, including shoulder
C49.12 Malignant neoplasm of connective and soft tissue of left upper limb, including shoulder
C49.21 Malignant neoplasm of connective and soft tissue of right lower limb, including hip
C49.22 Malignant neoplasm of connective and soft tissue of left lower limb, including hip
C49.3 Malignant neoplasm of connective and soft tissue of thorax
C49.4 Malignant neoplasm of connective and soft tissue of abdomen
C49.5 Malignant neoplasm of connective and soft tissue of pelvis
C49.6 Malignant neoplasm of connective and soft tissue of trunk, unspecified
C49.8 Malignant neoplasm of overlapping sites of connective and soft tissue
C49.9 Malignant neoplasm of connective and soft tissue, unspecified
C53.0 Malignant neoplasm of endocervix
C53.1 Malignant neoplasm of exocervix
C53.8 Malignant neoplasm of overlapping sites of cervix uteri
C53.9 Malignant neoplasm of cervix uteri, unspecified
C78.01 Secondary malignant neoplasm of right lung
C78.02 Secondary malignant neoplasm of left lung
C79.31 Secondary malignant neoplasm of brain
C79.51 Secondary malignant neoplasm of bone
C79.52 Secondary malignant neoplasm of bone marrow
C7A.1 Malignant poorly differentiated neuroendocrine tumors

Duration of authorization: 12 months

Version Effective Date: 04/01/2025

Title: Atezolizumab (Tecentriq®) and Atezolizumab with Hyaluronidase-tqjs (Tecentriq Hybreza TM)

MEDICALLY NECESSARY:

ALVEOLAR SOFT PART SARCOMA

Atezolizumab (Tecentriq) and atezolizumab with hyaluronidase-tqjs (Tecentriq Hybreza) are considered medically necessary and, therefore, covered for the treatment of unresectable or metastatic alveolar soft part sarcoma (ASPS) when **BOTH** of the following are met:

- **ONE** of the following:
 - Atezolizumab (Tecentriq) is approved for use in adults and pediatric individuals age 2 years and older for this indication only
 - Atezolizumab with hyaluronidase-tqjs (Tecentriq Hybreza) is approved for use in adults only
- **BOTH** of the following:
 - ASPS has been histologically or cytologically confirmed
 - Used as single-agent therapy (National Comprehensive Cancer Network [NCCN] preferred)

CERVICAL CANCER

Atezolizumab (Tecentriq) and atezolizumab with hyaluronidase-tqjs (Tecentriq Hybreza) are considered medically necessary and, therefore, covered for adult individuals with persistent, recurrent, or metastatic small cell neuroendocrine carcinoma of the cervix (NECC) as first-line, second-line, or subsequent therapy as clinically appropriate (if not used previously as first-line) in **EITHER** of the following regimens:

- In combination with cisplatin and etoposide, and continued as a single-agent for maintenance therapy
- In combination with carboplatin and etoposide, and continued as a single-agent for maintenance therapy

HEPATOCELLULAR CARCINOMA (HCC)

Atezolizumab (Tecentriq) and atezolizumab with hyaluronidase-tqjs (Tecentriq Hybreza) are considered medically necessary and, therefore, covered, in combination with bevacizumab (NCCN-preferred regimen) for the treatment of adult individuals with hepatocellular carcinoma (Child-Pugh Class A only) with **EITHER** of the following:

- As first-line systemic therapy with **ANY** of the following:
 - Unresectable disease and not a transplant candidate
 - Liver-confined, unresectable disease, and are deemed ineligible for transplant
 - Metastatic/extrahepatic disease and are deemed ineligible for resection, transplant, or locoregional therapy
- As adjuvant therapy following resection or ablation for individuals with **ALL** of the following:
 - Initial clinical presentation is operable by performance status or comorbidity
 - Meet resection criteria

- Are at high risk of recurrence (defined as size >5 cm, >3 tumors, macrovascular invasion or microvessel invasion on histology, or grade 3/4 histology)

MELANOMA: CUTANEOUS

Atezolizumab (Tecentriq) and atezolizumab with hyaluronidase-tqjs (Tecentriq Hybreza) are considered medically necessary and, therefore, covered in combination with cobimetinib and vemurafenib for adult individuals with cutaneous melanoma that is proto-oncogene B-Raf (BRAF) V600 mutation positive in **EITHER** of the following:

- Second-line or subsequent treatment of unresectable or metastatic disease following progression or intolerance if BRAF/mitogen-activated protein kinase (MEK) and/or programmed death-ligand 1 (PD-L1) checkpoint inhibition was not previously used
- As re-induction therapy if prior combination BRAF/MEK with PD-L1 checkpoint inhibition resulted in disease control (complete response, partial response, or stable disease), no residual toxicity, and disease progression/relapse more than 3 months after treatment discontinuation

MESOTHELIOMA: PERITONEAL

Atezolizumab (Tecentriq) and atezolizumab with hyaluronidase-tqjs (Tecentriq Hybreza) are considered medically necessary and, therefore, covered for adult individuals with biphasic, epithelioid, or sarcomatoid peritoneal mesothelioma (may also be used for pericardial mesothelioma and tunica vaginalis testis mesothelioma) and with **ALL** of the following:

- As subsequent systemic therapy
- Eastern Cooperative Oncology Group (ECOG) performance status (PS) 0 to 2
- In combination with bevacizumab if not previously treated with immune checkpoint inhibitors

NON-SMALL CELL LUNG CANCER (NSCLC)

Initial Therapy for NSCLC

Atezolizumab (Tecentriq) and atezolizumab with hyaluronidase-tqjs (Tecentriq Hybreza) are considered medically necessary and, therefore, covered for the treatment of adult individuals with recurrent (excluding locoregional recurrence or symptomatic local disease with no evidence of disseminated disease; however, including mediastinal lymph node recurrence with prior radiation therapy [RT]), advanced or metastatic non-small cell lung cancer (NSCLC) in **ANY** of the following regimens:

- First-line systemic therapy (NCCN preferred) when **ALL** of the following criteria are met:
 - PD-L1 expression positive (50 percent or greater or PD-L1 stained tumor-infiltrating immune cells [IC] covering 10 percent or greater of the tumor area [IC 10 percent or greater]) tumors (as determined by a US Food and Drug Administration [FDA]-approved test) that are negative for actionable molecular biomarkers*
 - No contraindications** to PD-1 or PD-L1 inhibitors
 - PS 0-2
 - Adenocarcinoma (with mixed subtypes), large cell carcinoma, or squamous cell carcinoma histology

- First-line systemic therapy when **ALL** of the following criteria are met:
 - In combination with **EITHER** of the following regimens:
 - Bevacizumab, carboplatin, and paclitaxel (if no history of recent hemoptysis)
 - Carboplatin and albumin-bound paclitaxel
 - PD-L1 expression positive (1 percent or greater) tumors that are negative for actionable molecular biomarkers*
 - No contraindications** to PD-1 or PD-L1 inhibitors
 - PS 0-2
 - Nonsquamous cell history (i.e., adenocarcinoma [with mixed subtypes], large cell carcinoma)
- Single-agent as subsequent therapy (NCCN preferred) when **ALL** of the following criteria are met:
 - PS 0-2
 - No contraindications** to PD-1 or PD-L1 inhibitors
 - No prior progression on a PD-1 or PD-L1 inhibitor
 - Adenocarcinoma (with mixed subtypes), large cell carcinoma, or squamous cell carcinoma histology
- Single-agent treatment for recurrent, advanced, or metastatic disease for individuals with PS 3, no contraindications** to PD-1 or PD-L1 inhibitors, and squamous cell carcinoma, adenocarcinoma (with mixed subtypes), or large cell carcinoma histology, as monotherapy for **ANY** of the following:
 - First-line therapy option regardless of PD-L1 status and negative for actionable molecular biomarkers* (may be KRAS G12C mutation positive)
 - First-line therapy for EGFR exon 20 insertion mutation positive* tumors
 - First-line or subsequent therapy for BRAF V600E mutation positive* tumors
 - First-line or subsequent therapy for NTRK1/2/3 gene fusion positive* tumors
 - First-line or subsequent therapy for MET exon 14 skipping mutation positive* tumors
 - First-line or subsequent therapy for RET rearrangement positive* tumors
 - First-line therapy for ERBB2 (HER2) mutation positive* tumors
 - Subsequent therapy for EGFR exon 19 deletion or exon 21 L858R* tumors and prior erlotinib with or without (ramucirumab or bevacizumab), afatinib, gefitinib, osimertinib, amivantamab-vmjw with lazertinib, or dacomitinib therapy
 - Subsequent therapy for EGFR S768I, L861Q, and/or G719X mutation positive* tumors and prior afatinib, osimertinib, erlotinib, gefitinib, or dacomitinib therapy
 - Subsequent therapy for ALK rearrangement positive* tumors and prior crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib therapy
 - Subsequent therapy for ROS1 rearrangement positive* tumors and prior crizotinib, entrectinib, repotrectinib, ceritinib, or lorlatinib therapy
- Combination systemic therapy with carboplatin, paclitaxel, and bevacizumab (if no history of recent hemoptysis), or in combination with carboplatin and albumin-bound paclitaxel, for the treatment of individuals with PS 0-1, no contraindications** to PD-1

or PD-L1 inhibitors, and tumors of nonsquamous cell histology (i.e., adenocarcinoma [with mixed subtypes], large cell carcinoma histology) in **ANY** of the following regimens:

- Initial systemic therapy for tumors that are negative for actionable molecular biomarkers* and PD-L1 expression positive (<1 percent) (may be KRAS G12C mutation positive)
- First-line therapy for EGFR exon 20 insertion mutation positive* tumors
- First-line or subsequent therapy for BRAF V600E mutation positive* tumors
- First-line or subsequent therapy for NTRK 1/2/3 gene fusion positive* tumors
- First-line or subsequent therapy for MET exon 14 skipping mutation positive* tumors
- First-line or subsequent therapy for RET rearrangement positive* tumors
- First-line therapy for ERBB2 (HER2) mutation positive* tumors
- Subsequent therapy for EGFR exon 19 deletion or exon 21 L858R tumors* and prior erlotinib with or without (ramucirumab or bevacizumab), afatinib, gefitinib, osimertinib, amivantamab-vmjw with lazertinib, or dacomitinib therapy
- Subsequent therapy for EGFR S768I, L861Q, and/or G719X mutation positive tumors* and prior afatinib, osimertinib, erlotinib, gefitinib, or dacomitinib therapy
- Subsequent therapy for ALK rearrangement positive tumors* and prior crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib therapy
- Subsequent systemic therapy for ROS1 rearrangement positive* tumors and prior crizotinib, entrectinib, lorlatinib, or ceritinib therapy
- For the treatment of individuals with metastatic NSCLC who have disease progression during or following platinum-containing chemotherapy. Individuals with EGFR or ALK genomic tumor aberrations should have disease progression on an FDA-approved therapy for NSCLC harboring these aberrations prior to receiving atezolizumab (Tecentriq) or atezolizumab with hyaluronidase-tqjs (Tecentriq Hybreza)
- As single-agent treatment for individuals with completely resected stage IIB to IIIA, high-risk stage IIA, or stage IIIB (T3, N2) who have **ALL** of the following:
 - Tumors have PD-L1 expression on 1 percent or greater of tumor cells, as determined by a FDA-approved test
 - Negative for EGFR exon 19 deletion or exon 21 L858R mutations, or ALK rearrangements*
 - Who received previous adjuvant chemotherapy
 - Have adenocarcinoma (with mixed subtypes), large cell carcinoma, or squamous cell carcinoma histology
 - No contraindications to immune checkpoint inhibitors**

*If there is insufficient tissue to allow testing for all of the actionable molecular biomarkers of epidermal growth factor receptor (EGFR), Kirsten rat sarcoma viral oncogene homolog (KRAS), erythroblastic oncogene B2 (ERBB2 [human epidermal growth factor receptor 2 {HER2}]), anaplastic lymphoma kinase (ALK), c-ros oncogene 1 (ROS1), BRAF, neurotrophic tyrosine kinase receptor (NTRK) 1/2/3, mesenchymal-epithelial transition (MET) exon 14 skipping mutation, and rearranged during transfection (RET), repeat biopsy and/or plasma testing should be done. If these are not feasible, treatment is guided by available results and, if unknown, these

individuals are treated as though they do not have driver oncogenes.

****Contraindications** for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or current use of immunosuppressive agents, and/or presence of some oncogenic drivers (i.e., EGFR exon 19 deletions or exon 21 L858R, ALK rearrangements), which have been shown to be associated with less benefit from PD-1/PD-L1 inhibitors.

Continuation Maintenance Therapy for NSCLC

Atezolizumab (Tecentriq) and atezolizumab with hyaluronidase-tqjs (Tecentriq Hybreza) are considered medically necessary and, therefore, covered for continuation maintenance therapy for the treatment of individuals with NSCLC, recurrent (excluding locoregional recurrence or symptomatic local disease with no evidence of disseminated disease; however, including mediastinal lymph node recurrence with prior RT), advanced, or metastatic disease in **ANY** of the following:

- As a single-agent for PD-L1 expression positive (<1 percent) tumors that are negative for actionable molecular biomarkers* and experienced tumor response or stable disease following first-line systemic combination therapy with atezolizumab (Tecentriq) or atezolizumab with hyaluronidase-tqjs (Tecentriq Hybreza), carboplatin, and albumin-bound paclitaxel with **ALL** of the following:
 - No contraindications** to PD-1 or PD-L1 inhibitors
 - PS 0-2
 - Non-squamous cell histology (i.e., adenocarcinoma [with mixed subtypes], large cell carcinoma histology)
- In combination with bevacizumab for PD-L1 expression positive (<1 percent) tumors that are negative for actionable molecular biomarkers* and experienced tumor response or stable disease following first-line systemic combination therapy with atezolizumab (Tecentriq) or atezolizumab with hyaluronidase-tqjs (Tecentriq Hybreza), carboplatin, paclitaxel, and bevacizumab with **ALL** of the following:
 - No contraindications** to PD-1 or PD-L1 inhibitors
 - PS 0-
 - Non-squamous cell histology (i.e., adenocarcinoma [with mixed subtypes], large cell carcinoma histology)
- No history of recent hemoptysis
- In combination with bevacizumab for PD-L1 expression positive (1 percent or greater) tumors that are negative for actionable molecular biomarkers* (may be KRAS G12C mutation positive) with **ALL** of the following:
 - Tumor response or stable disease following first-line systemic combination therapy with atezolizumab (Tecentriq) or atezolizumab with hyaluronidase-tqjs (Tecentriq Hybreza), carboplatin, paclitaxel, and bevacizumab
 - No contraindications** to PD-1 or PD-L1 inhibitors
 - PS 0-2

- Nonsquamous cell histology (i.e., adenocarcinoma [with mixed subtypes], large cell carcinoma histology)
 - No history of recent hemoptysis
- As a single-agent for PD-L1 expression positive (1 percent or greater) tumors that are negative for actionable molecular tumor biomarkers* and with **ALL** of the following:
 - Tumor response or stable disease following first-line systemic combination therapy with atezolizumab (Tecentriq) or atezolizumab with hyaluronidase-tqjs (Tecentriq Hybreza), carboplatin, and albumin-bound paclitaxel
 - No contraindications** to PD-1 or PD-L1 inhibitors
 - PS 0-2
 - Nonsquamous cell history (i.e., adenocarcinoma [with mixed subtypes], large cell carcinoma histology)
- As a single-agent for PD-L1 expression positive (50 percent or greater) tumors that are negative for actionable molecular biomarkers* and with **ALL** of the following:
 - Tumor response or stable disease following first-line therapy with single-agent atezolizumab (Tecentriq) or atezolizumab with hyaluronidase-tqjs (Tecentriq Hybreza)
 - No contraindications** to PD-1 or PD-L1 inhibitors
 - PS 0-2
 - Adenocarcinoma (with mixed subtypes), large cell carcinoma, or squamous cell carcinoma histology

*If there is insufficient tissue to allow testing for all of the actionable molecular biomarkers of EGFR, KRAS, ERBB2 (HER2), ALK, ROS1, BRAF, NTRK 1/2/3, MET, and RET, repeat biopsy and/or plasma testing should be done. If these are not feasible, treatment is guided by available results and, if unknown, these individuals are treated as though they do not have driver oncogenes.

**Contraindications for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or current use of immunosuppressive agents, and/or presence of some oncogenic drivers (i.e., EGFR exon 19 deletions or exon 21 L858R, ALK rearrangements), which have been shown to be associated with less benefit from PD-1/PD-L1 inhibitors.

SMALL CELL LUNG CANCER (SCLC)

Atezolizumab (Tecentriq) and atezolizumab with hyaluronidase-tqjs (Tecentriq Hybreza) are considered medically necessary and, therefore, covered for first-line systemic combination therapy with etoposide and carboplatin (followed by single-agent maintenance) for the treatment of adult individuals with extensive-stage*** small cell lung cancer (NCCN-preferred regimen) and in **ANY** of the following scenarios:

- Without localized symptomatic sites or brain metastases and good PS (0-2)
- Without localized symptomatic sites or brain metastases and poor PS (3-4) due to SCLC
- With localized symptomatic sites (used with radiation therapy [typically sequential] if spinal cord compression)
- With brain metastases

***Extensive stage: Stage IV (T any, N any, M 1a/b/c), or T3-4 due to multiple lung nodules that are too extensive or have tumor/nodal volume that is too large to be encompassed in a tolerable radiation plan (American Joint Committee on Cancer, 8th edition).

Duration of authorization: 12 months

Version Effective Date: 04/01/2025

Title: Atidarsagene autotemcel (Lenmeldy)

MEDICALLY NECESSARY:

Atidarsagene autotemcel (Lenmeldy) is considered medically necessary and, therefore, covered as a one-time administration for the treatment of metachromatic leukodystrophy (MLD) in individuals younger than 18 years of age when ALL of the following criteria are met:

- Individual has a confirmed diagnosis of MLD (also known as arylsulfatase A deficiency [ARSA]) as evidenced by the following biochemical and molecular markers:
 - ARSA enzyme activity below the normal range in peripheral blood mononuclear cells-leukocytes or fibroblasts OR increased urinary excretion of sulfatides; AND
 - Presence of biallelic ARSA pathogenic or likely pathogenic variation(s) of known polymorphisms identified by gene sequencing and/or deletion/duplication assessment (Note: for individuals with novel mutations, a 24-hour urine collection must show elevated sulfatide levels)
 - For the initial individual within a family with one of the below clinical classifications (i.e., a potential proband), both of the following are present:
 1. ARSA enzyme activity in leukocytes below reference values; AND
 2. Urinary sulfatide levels above reference values; AND
- Individual has confirmed clinical classification of pre-symptomatic late infantile (PSLI), presymptomatic, early juvenile (PSEJ) or early symptomatic early juvenile (ESEJ) MLD disease based on phenotypes including age and presence of applicable signs and symptoms (see Guidelines Section)
- The biologic is used as single-agent therapy (Note: not inclusive of busulfan-conditioning regimen); AND
- Individual has not received a prior allogeneic stem cell transplant (or has, but is without evidence of residual donor cells present), and is a candidate for autologous stem cell transplantation (e.g., adequate renal and hepatic function); AND
- Individual has not received other gene therapy for MLD; AND
- Individual is negative for hepatitis B virus (HBV), hepatitis C virus (HCV), human T-lymphotropic virus 1 and 2 (HTLV-1/HTLV-2), human immunodeficiency virus 1 and 2 (HIV-1/HIV-2), and mycoplasma infection before collection of cells for manufacturing.

NOTE: Evio has been selected by the Company to administer clinical outcomes monitoring for individuals receiving certain high-cost drug therapies. Atidarsagene autotemcel (Lenmeldy) is included in the portfolio of high-cost drug/biologic therapies for which Evio will be tracking clinical outcomes. If an individual meets all medical policy criteria, the requesting physician and/or individual being treated must agree to providing clinical outcomes data and information via Evio's secure web portal as requested.

Duration of authorization: 12 months

Version Effective Date: 05/28/2025

Title: Avelumab (Bavencio®)

ICD-10 Codes and Narratives

AVELUMAB (BAVENCIO®) IS MEDICALLY NECESSARY WHEN REPORTED WITH THE FOLLOWING DIAGNOSIS CODES:

C37	Malignant neoplasm of thymus
C4A.0	Merkel cell carcinoma of lip
C4A.111	Merkel cell carcinoma of right upper eyelid, including canthus
C4A.112	Merkel cell carcinoma of right lower eyelid, including canthus
C4A.121	Merkel cell carcinoma of left upper eyelid, including canthus
C4A.122	Merkel cell carcinoma of left lower eyelid, including canthus
C4A.21	Merkel cell carcinoma of right ear and external auricular canal
C4A.22	Merkel cell carcinoma of left ear and external auricular canal
C4A.31	Merkel cell carcinoma of nose
C4A.39	Merkel cell carcinoma of other parts of face
C4A.4	Merkel cell carcinoma of scalp and neck
C4A.51	Merkel cell carcinoma of anal skin
C4A.52	Merkel cell carcinoma of skin of breast
C4A.59	Merkel cell carcinoma of other part of trunk
C4A.61	Merkel cell carcinoma of right upper limb, including shoulder
C4A.62	Merkel cell carcinoma of left upper limb, including shoulder
C4A.71	Merkel cell carcinoma of right lower limb, including hip
C4A.72	Merkel cell carcinoma of left lower limb, including hip
C4A.8	Merkel cell carcinoma of overlapping sites
C4A.9	Merkel cell carcinoma, unspecified
C54.0	Malignant neoplasm of isthmus uteri
C54.1	Malignant neoplasm of endometrium
C54.2	Malignant neoplasm of myometrium
C54.3	Malignant neoplasm of fundus uteri
C54.8	Malignant neoplasm of overlapping sites of corpus uteri
C54.9	Malignant neoplasm of corpus uteri, unspecified
C55	Malignant neoplasm of uterus, part unspecified
C58	Malignant neoplasm of placenta
C61	Malignant neoplasm of prostate
C64.1	Malignant neoplasm of right kidney, except renal pelvis

C64.2	Malignant neoplasm of left kidney, except renal pelvis
C65.1	Malignant neoplasm of right renal pelvis
C65.2	Malignant neoplasm of left renal pelvis
C66.1	Malignant neoplasm of right ureter
C66.2	Malignant neoplasm of left ureter
C67.0	Malignant neoplasm of trigone of bladder
C67.1	Malignant neoplasm of dome of bladder
C67.2	Malignant neoplasm of lateral wall of bladder
C67.3	Malignant neoplasm of anterior wall of bladder
C67.4	Malignant neoplasm of posterior wall of bladder
C67.5	Malignant neoplasm of bladder neck
C67.6	Malignant neoplasm of ureteric orifice
C67.7	Malignant neoplasm of urachus
C67.8	Malignant neoplasm of overlapping sites of bladder
C67.9	Malignant neoplasm of bladder, unspecified
C68.0	Malignant neoplasm of urethra
C7A.091	Malignant carcinoid tumor of the thymus
C7B.1	Secondary Merkel cell carcinoma
D09.0	Carcinoma in situ of bladder
D39.2	Neoplasm of uncertain behavior of placenta
O01.9	Hydatidiform mole, unspecified

Duration of authorization: 12 months

Version Effective Date: 01/06/2025

Title: Avelumab (Bavencio®)

MEDICALLY NECESSARY:

GESTATIONAL TROPHOBLASTIC NEOPLASIA

Avelumab (Bavencio®) is considered medically necessary and, therefore, covered for adult individuals as a single agent for multiagent chemotherapy-resistant disease in **either** of the following:

- High-risk disease
- Recurrent or progressive intermediate trophoblastic tumor (placental site trophoblastic tumor or epithelioid trophoblastic tumor)

MERKEL CELL CARCINOMA (MCC)

Avelumab (Bavencio) is considered medically necessary and, therefore, covered in adult and pediatric individuals 12 years and older with MCC as single-agent therapy:

- Metastatic (M1 disseminated disease) (National Comprehensive Cancer Network [NCCN] preferred regimen)
- Primary clinical N0 locally advanced disease if curative surgery and curative radiation therapy (RT) are not feasible (preferred) or for progression on neoadjuvant nivolumab (Opdivo)
- Recurrent N+ regional disease or N0 locally advanced disease if curative surgery and curative RT are not feasible

RENAL CELL CARCINOMA (RCC)

Avelumab (Bavencio) in combination with axitinib (Inlyta) is considered medically necessary and, therefore, covered for adult individuals with advanced RCC as first-line therapy for relapse or stage IV disease and clear cell histology.

UROTHELIAL CARCINOMA (UC)

Avelumab (Bavencio) is considered medically necessary and, therefore, covered as single-agent therapy for the treatment of adult individuals for **one** of the following indications:

- Locally advanced or metastatic UC in individuals with disease progression, in **one** of the following scenarios:
 - During or post-platinum-containing chemotherapy
 - Within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy
- Locally advanced or metastatic UC as single-agent maintenance therapy if there is no progression on first-line platinum-containing chemotherapy that consisted of **any** of the following regimens:
 - Gemcitabine and cisplatin
 - Gemcitabine and carboplatin
 - DDMVAC (dose-dense methotrexate, vinblastine, doxorubicin, cisplatin)

- Recurrent or metastatic primary carcinoma of the urethra that is not recurrent stage T3-4 disease and is without palpable inguinal lymph nodes, as a single-agent, second-line systemic therapy, post-platinum or other chemotherapy (NCCN alternative preferred)
- Metastatic UC of the prostate or metastatic upper genitourinary tract (GU) tumors, as a single-agent, second-line systemic therapy, post-platinum or other chemotherapy (NCCN alternative preferred),
- Locally advanced or metastatic bladder cancer, as a single-agent (NCCN preferred), second-line systemic therapy, post-platinum or other chemotherapy, in **any** of the following clinical stages:
 - Stage II (cT2, N0) disease or stage IIIA (cT3, N0; cT4a, N0; cT1-T4a, N1) disease if tumor is present following reassessment of tumor status 2 to 3 months after primary treatment with concurrent bladder-preserving chemoradiotherapy and maximal transurethral resection of bladder tumor (TURBT)
 - Stage IIIB (cT1-T4a, N2,3) disease following partial response or progression after primary treatment with downstaging systemic therapy or concurrent chemoradiotherapy
 - Stage IVA (cT4b, any N, M0) disease if tumor is present following reassessment of tumor status after primary treatment with first-line systemic therapy or concurrent chemoradiotherapy
 - Stage IVA (any T, any N, M1a) disease if stable disease or progression following reassessment of tumor status after primary treatment with first-line systemic therapy
 - Metastatic stage IVB (any T, any N, M1b) disease
 - Muscle invasive local recurrence or persistent disease in a preserved bladder treated with curative intent
 - Metastatic or local recurrence postcystectomy treated with curative intent

UTERINE NEOPLASMS

Avelumab (Bavencio) is considered medically necessary and, therefore, covered for adult individuals with endometrial carcinoma (i.e., serous carcinoma, clear cell carcinoma, carcinosarcoma, endometrioid adenocarcinoma, undifferentiated/dedifferentiated carcinoma histology types), as a single-agent second-line or subsequent treatment for recurrent, or metastatic, microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) tumors in **one** of the following:

- Isolated metastases
- Disseminated metastases with or without sequential palliative external beam radiation therapy (EBRT)
- With sequential EBRT and with or without brachytherapy for locoregional recurrence in individuals with no prior RT to site of recurrence, or previous vaginal brachytherapy only
- After surgical exploration, with sequential EBRT for locoregional recurrence in individuals with disease confined to the vagina or paravaginal soft tissue, or in pelvic, para-aortic or common iliac lymph nodes
- After surgical exploration, with or without sequential EBRT for locoregional recurrence in individuals with upper abdominal or peritoneal disease

- With or without sequential palliative EBRT or brachytherapy for locoregional recurrence in individuals who have received prior EBRT to site of recurrence

THYMOMAS AND THYMIC CARCINOMAS

Avelumab (Bavencio) is considered medically necessary and, therefore, covered for adult individuals with thymic carcinoma after R1 or R2 resection for postoperative systemic therapy in combination with axitinib (Inlyta) for those who cannot tolerate first-line combination regimens.

First-line systemic therapy in combination with axitinib (Inlyta) for recurrent, advanced, or metastatic disease (for thymic carcinomas only) for individuals who cannot tolerate first-line combination regimens for one of the following:

- Potentially resectable locally advanced disease
- Potentially resectable solitary metastasis or ipsilateral pleural metastasis
- Consideration following surgery for solitary metastasis or ipsilateral pleural metastasis
- Medically inoperable/unresectable solitary metastasis or ipsilateral pleural metastasis
- Extrathoracic metastatic disease

Second-line systemic therapy (for thymic carcinomas only) in combination with axitinib (Inlyta) for one of the following:

- Unresectable locally advanced disease
- Solitary metastasis or ipsilateral pleural metastasis
- Extrathoracic metastatic disease

Duration of authorization: 12 months

Version Effective Date: 01/06/2025

Title: Belimumab (Benlysta®) for Intravenous Use

MEDICALLY NECESSARY:

SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

Belimumab (Benlysta) for **intravenous** use is considered medically necessary and, therefore, covered when used for the treatment of individuals with systemic lupus erythematosus ((SLE) five years of age and older who meet **all** of the following criteria:

- Active systemic lupus erythematosus (SLE)
- Positive autoantibody test (e.g., antinuclear antibody test [ANA], antibodies to DNA [Anti-dsDNA], Anti-Smith [Anti-Sm])
- Concurrent treatment with at least one of the following: steroids, antimalarials, immunosuppressives, or nonsteroidal anti-inflammatory drugs (NSAIDS)

LUPUS NEPHRITIS (LN)

Belimumab (Benlysta) for **intravenous** use is considered medically necessary and, therefore, covered when used for the treatment of individuals with lupus nephritis (LN) five years of age and older who meet **all** of the following criteria:

- Active systemic lupus erythematosus
- Biopsy-proven LN Class III, IV, and/or V and have active renal disease at screening
- Concurrent standard treatment for LN (e.g., corticosteroids along with one of the following regimens: mycophenolate for induction followed by mycophenolate for maintenance or cyclophosphamide for induction followed by azathioprine for maintenance)

Duration of authorization: 12 months

Version Effective Date: 05/28/2025

Title: Beremagene Geperpavec (Vyjuvek™)

MEDICALLY NECESSARY:

INITIATION THERAPY

Beremagene geperpavec (Vyjuvek™) is considered medically necessary and, therefore, covered in individuals 6 months and older for the treatment of wounds in individuals with dystrophic epidermolysis bullosa (DEB) when ALL of the following criteria are met:

- Individual has diagnosis of DEB; and
- Submission of medical records (e.g., chart notes, laboratory values) confirming a pathogenic variation in the collagen type VII alpha 1 chain (COL7A1) gene; and
- At least one recurrent or chronic open wound that meets all of the following criteria:
 - Adequate granulation tissue
 - Excellent vascularization
 - No evidence of active wound infection
 - No evidence or history of squamous cell carcinoma
- Individual has not had a skin graft in the past 3 months
- Beremagene geperpavec (Vyjuvek) prescribed by, or in consultation with, a dermatologist with expertise in the treatment of DEB; and
- Dosing in accordance with the US Food and Drug Administration (FDA)–approved labeling; and
- Initial authorization to be issued for no more than 6 months and no more than 26 doses

CONTINUATION THERAPY

Continued therapy with beremagene geperpavec (Vyjuvek) is considered medically necessary and, therefore, covered when ALL of the following criteria are met:

- Individual has previously been treated with beremagene geperpavec (Vyjuvek) therapy
- Individual had a positive clinical response to beremagene geperpavec (Vyjuvek) therapy (e.g., decrease in wound size, increase in granulation tissue, complete wound closure); and
- Wound(s) being treated meet all of the following criteria:
 - Adequate granulation tissue
 - Excellent vascularization
 - No evidence of active wound infection
 - No evidence or history of squamous cell carcinoma
- Individual did not have a skin graft in the past 3 months
- Beremagene geperpavec (Vyjuvek) is prescribed by, or in consultation with, a dermatologist with expertise in the treatment of DEB; and
- Dosing is in accordance with the FDA-approved labeling; and
- Reauthorization will be issued for no more than 6 months and no more than 26 doses

NOTE:

Evio has been selected by the Company to administer clinical outcomes monitoring for patients receiving certain high-cost drug therapies. Beremagene geperpavec (Vyjuvek™) is included in the portfolio of high-cost drug therapies for which Evio will be tracking clinical outcomes. If a patient meets all medical policy provisions and is approved to receive treatment, the requesting physician or member must attest and agree to providing clinical outcomes data and information via Evio's secure web portal as requested.

Duration of authorization: 12 months

Version Effective Date: 07/15/2024

Title: Betibeglogene Autotemcel [Beti-Cel (ZYNTEGLO®)]

MEDICALLY NECESSARY:

Betibeglogene autotemcel [Beti-Cel (Zynteglo®)] is considered medically necessary and, therefore, covered for the treatment of individuals with β -thalassemia who require regular peripheral blood transfusions to maintain target hemoglobin levels when prescribed by or in consultation with a hematologist when ALL of the following criteria are also met:

- Individual has genetically confirmed diagnosis of β -thalassemia
- Individual meets one of the following:
 - Age ≥ 5 years and ≤ 50 years
 - If age < 5 years, individual meets both of the following:
 - Weight ≥ 6 kg
 - Provider submits medical rationale that individual is anticipated to be able to provide at least the minimum number of cells required to initiate the manufacturing process
- Individual has a Karnofsky performance status (PS) of ≥ 80 for adults (≥ 16 years of age) or a Lansky PS of ≥ 80 for adolescents (< 16 years of age)
- Individual has a clinical diagnosis of transfusion-dependent β -thalassemia (β -thalassemia major or TDT), and has documentation of one of the following in the 2 previous years
 - Receipt of ≥ 8 transfusions of packed red blood cells (pRBC) per year
 - Receipt of ≥ 100 mL/kg pRBC per year
- Individual is eligible for an allogeneic hematopoietic stem cell transplantation (HSCT)
- Individual has not received prior allogeneic HSCT or gene therapy
- Individual does not have any of the following:
 - Availability of human leukocyte antigen–identical or human leukocyte antigen–matched donor
 - T2*-weighted magnetic resonance imaging measurement of myocardial iron of less than 10 msec or other evidence of severe iron overload in the opinion of treating physician
 - Advanced liver disease (meets any one of the following)
 - Persistent aspartate transaminase, alanine transaminase, or direct bilirubin value greater than three times the upper limit of normal
 - Baseline prothrombin time or partial thromboplastin time greater than 1.5 times the upper limit of normal
 - Magnetic resonance imaging of the liver demonstrating clear evidence of cirrhosis
 - Liver biopsy demonstrating cirrhosis, any evidence of bridging fibrosis, or active hepatitis
 - Baseline estimated glomerular filtration rate less than 70 mL/min/1.73 m²
 - History of receiving prior gene therapy or allogeneic hematopoietic stem cell transplant

- Any prior or current malignancy (with the exception of adequately treated cone-biopsied *in situ* carcinoma of the cervix uteri and basal or squamous cell carcinoma of the skin) or myeloproliferative or significant immunodeficiency disorder
- Any immediate family member (i.e., parent or siblings) with a known familial cancer syndrome (including but not limited to hereditary breast and ovarian cancer syndrome, hereditary nonpolyposis colorectal cancer syndrome and familial adenomatous polyposis)
- Active, uncontrolled hepatitis C virus or hepatitis B virus infection
- Contraindication to the use of granulocyte colony stimulating factor (G-CSF), plerixafor, busulfan, or any other medicinal products required during myeloablative conditioning, including hypersensitivity to the active substances or to any of the excipients
- A white blood cell count less than $3 \times 10^9/L$, and/or platelet count less than $100 \times 10^9/L$ not related to hypersplenism

NOTE: Evio has been selected by the Company to administer clinical outcomes monitoring for individuals receiving certain high-cost drug therapies. Betibeglogene autotemcel [Beti-Cel (Zynteglo)] is included in the portfolio of high-cost drug/biologic therapies for which Evio will be tracking clinical outcomes. If an individual meets all medical policy criteria, the requesting physician and/or individual being treated must agree to providing clinical outcomes data and information via Evio's secure web portal as requested.

Duration of authorization: 12 months

Version Effective Date: 05/28/2025

Title: Bevacizumab (Avastin®) and Related Biosimilars For Oncologic Use

ICD 10 Diagnosis Codes

C17.0 Malignant neoplasm of duodenum
C17.1 Malignant neoplasm of jejunum
C17.2 Malignant neoplasm of ileum
C17.3 Meckel's diverticulum, malignant
C17.8 Malignant neoplasm of overlapping sites of small intestine
C17.9 Malignant neoplasm of small intestine, unspecified
C18.0 Malignant neoplasm of cecum
C18.1 Malignant neoplasm of appendix
C18.2 Malignant neoplasm of ascending colon
C18.3 Malignant neoplasm of hepatic flexure
C18.4 Malignant neoplasm of transverse colon
C18.5 Malignant neoplasm of splenic flexure
C18.6 Malignant neoplasm of descending colon
C18.7 Malignant neoplasm of sigmoid colon
C18.8 Malignant neoplasm of overlapping sites of colon
C18.9 Malignant neoplasm of colon, unspecified
C19 Malignant neoplasm of rectosigmoid junction
C20 Malignant neoplasm of rectum
C21.8 Malignant neoplasm of overlapping sites of rectum, anus and anal canal
C22.0 Liver cell carcinoma
C22.1 Intrahepatic bile duct carcinoma
C22.2 Hepatoblastoma
C22.3 Angiosarcoma of liver
C22.4 Other sarcomas of liver
C22.7 Other specified carcinomas of liver
C22.8 Malignant neoplasm of liver, primary, unspecified as to type
C22.9 Malignant neoplasm of liver, not specified as primary or secondary
C24.1 Malignant neoplasm of ampulla of Vater
C33 Malignant neoplasm of trachea
C34.01 Malignant neoplasm of right main bronchus
C34.02 Malignant neoplasm of left main bronchus
C34.11 Malignant neoplasm of upper lobe, right bronchus or lung
C34.12 Malignant neoplasm of upper lobe, left bronchus or lung
C34.2 Malignant neoplasm of middle lobe, bronchus or lung
C34.31 Malignant neoplasm of lower lobe, right bronchus or lung
C34.32 Malignant neoplasm of lower lobe, left bronchus or lung
C34.81 Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82 Malignant neoplasm of overlapping sites of left bronchus and lung
C34.91 Malignant neoplasm of unspecified part of right bronchus or lung
C34.92 Malignant neoplasm of unspecified part of left bronchus or lung

C45.0 Mesothelioma of pleura

C45.1 Mesothelioma of peritoneum

C45.2 Mesothelioma of pericardium

C45.7 Mesothelioma of other sites

C45.9 Mesothelioma, unspecified

C48.0 Malignant neoplasm of retroperitoneum

C48.1 Malignant neoplasm of specified parts of peritoneum

C48.2 Malignant neoplasm of peritoneum, unspecified

C48.8 Malignant neoplasm of overlapping sites of retroperitoneum and peritoneum

C49.0 Malignant neoplasm of connective and soft tissue of head, face and neck

C49.3 Malignant neoplasm of connective and soft tissue of thorax

C49.4 Malignant neoplasm of connective and soft tissue of abdomen

C49.5 Malignant neoplasm of connective and soft tissue of pelvis

C49.8 Malignant neoplasm of overlapping sites of connective and soft tissue

C49.9 Malignant neoplasm of connective and soft tissue, unspecified

C49.11 Malignant neoplasm of connective and soft tissue of right upper limb, including shoulder

C49.12 Malignant neoplasm of connective and soft tissue of left upper limb, including shoulder

C49.21 Malignant neoplasm of connective and soft tissue of right lower limb, including hip

C49.22 Malignant neoplasm of connective and soft tissue of left lower limb, including hip

C49.3 Malignant neoplasm of connective and soft tissue of thorax

C49.4 Malignant neoplasm of connective and soft tissue of abdomen

C49.5 Malignant neoplasm of connective and soft tissue of pelvis

C49.6 Malignant neoplasm of connective and soft tissue of trunk, unspecified

C49.8 Malignant neoplasm of overlapping sites of connective and soft tissue

C49.9 Malignant neoplasm of connective and soft tissue, unspecified

C51.0 Malignant neoplasm of labium majus

C51.1 Malignant neoplasm of labium minus

C51.2 Malignant neoplasm of clitoris

C51.8 Malignant neoplasm of overlapping sites of vulva

C51.9 Malignant neoplasm of vulva, unspecified

C52 Malignant neoplasm of vagina

C53.0 Malignant neoplasm of endocervix

C53.1 Malignant neoplasm of exocervix

C53.8 Malignant neoplasm of overlapping sites of cervix uteri

C53.9 Malignant neoplasm of cervix uteri, unspecified

C54.0 Malignant neoplasm of isthmus uteri

C54.1 Malignant neoplasm of endometrium

C54.2 Malignant neoplasm of myometrium

C54.3 Malignant neoplasm of fundus uteri

C54.8 Malignant neoplasm of overlapping sites of corpus uteri

C54.9 Malignant neoplasm of corpus uteri, unspecified

C55 Malignant neoplasm of uterus, part unspecified

C56.1 Malignant neoplasm of right ovary
C56.2 Malignant neoplasm of left ovary
C56.3 Malignant neoplasm of bilateral ovaries
C57.01 Malignant neoplasm of right fallopian tube
C57.02 Malignant neoplasm of left fallopian tube
C57.11 Malignant neoplasm of right broad ligament
C57.12 Malignant neoplasm of left broad ligament
C57.21 Malignant neoplasm of right round ligament
C57.22 Malignant neoplasm of left round ligament
C57.3 Malignant neoplasm of parametrium
C57.4 Malignant neoplasm of uterine adnexa, unspecified
C57.7 Malignant neoplasm of other specified female genital organs
C57.8 Malignant neoplasm of overlapping sites of female genital organs
C57.9 Malignant neoplasm of female genital organ, unspecified
C64.1 Malignant neoplasm of right kidney, except renal pelvis
C64.2 Malignant neoplasm of left kidney, except renal pelvis
C65.1 Malignant neoplasm of right renal pelvis
C65.2 Malignant neoplasm of left renal pelvis
C70.0 Malignant neoplasm of cerebral meninges
C70.1 Malignant neoplasm of spinal meninges
C70.9 Malignant neoplasm of meninges, unspecified
C71.0 Malignant neoplasm of cerebrum, except lobes and ventricles
C71.1 Malignant neoplasm of frontal lobe
C71.2 Malignant neoplasm of temporal lobe
C71.3 Malignant neoplasm of parietal lobe
C71.4 Malignant neoplasm of occipital lobe
C71.5 Malignant neoplasm of cerebral ventricle
C71.6 Malignant neoplasm of cerebellum
C71.7 Malignant neoplasm of brain stem
C71.8 Malignant neoplasm of overlapping sites of brain
C71.9 Malignant neoplasm of brain, unspecified
C72.0 Malignant neoplasm of spinal cord
C72.1 Malignant neoplasm of cauda equina
C72.9 Malignant neoplasm of central nervous system, unspecified
C78.01 Secondary malignant neoplasm of right lung
C78.02 Secondary malignant neoplasm of left lung
C78.6 Secondary malignant neoplasm of retroperitoneum and peritoneum
C78.7 Secondary malignant neoplasm of liver and intrahepatic bile duct
C79.31 Secondary malignant neoplasm of brain
C83.30 Diffuse large B-cell lymphoma, unspecified site
C83.390 Primary central nervous system lymphoma
C83.398 Diffuse large B-cell lymphoma of other extranodal and solid organ sites
C83.59 Lymphoblastic (diffuse) lymphoma, extranodal and solid organ sites

C83.79 Burkitt lymphoma, extranodal and solid organ sites
C83.80 Other non-follicular lymphoma, unspecified site
C83.89 Other non-follicular lymphoma, extranodal and solid organ sites
C84.49 Peripheral T-cell lymphoma, not elsewhere classified, extranodal and solid organ sites
C85.89 Other specified types of non-Hodgkin lymphoma, extranodal and solid organ sites
C85.99 Non-Hodgkin lymphoma, unspecified, extranodal and solid organ sites
D39.11 Neoplasm of uncertain behavior of right ovary
D39.12 Neoplasm of uncertain behavior of left ovary
D39.8 Neoplasm of uncertain behavior of other specified female genital organs
D39.9 Neoplasm of uncertain behavior of female genital organ, unspecified
D42.0 Neoplasm of uncertain behavior of cerebral meninges

D42.1 Neoplasm of uncertain behavior of spinal meninges
D42.9 Neoplasm of uncertain behavior of meninges, unspecified
D43.0 Neoplasm of uncertain behavior of brain, supratentorial

D43.1 Neoplasm of uncertain behavior of brain, infratentorial
D43.4 Neoplasm of uncertain behavior of spinal cord
D43.9 Neoplasm of uncertain behavior of central nervous system, unspecified
G93.6 Cerebral edema
I67.89 Other cerebrovascular disease
I67.9 Cerebrovascular disease, unspecified
Q85.02 Neurofibromatosis, type 2
Q85.03 Schwannomatosis
Q85.83 Von Hippel-Lindau syndrome

Duration of authorization: 12 months

Version Effective Date: 01/01/2025

Title: Bevacizumab (Avastin®) and Related Biosimilars For Oncologic Use

MEDICALLY NECESSARY:

COMPANY-DESIGNATED PREFERRED PRODUCTS

Although there are many bevacizumab products on the market (e.g., bevacizumab [Avastin®], bevacizumab-maly (Alymsys®), bevacizumab-awwb [Mvasi™], bevacizumab-bvzr [Zirabev™]), there is no reliable evidence of the superiority of any one product of bevacizumab compared to other products. The Company has designated the following bevacizumab biosimilar products as its preferred products: bevacizumab-awwb (Mvasi™) and bevacizumab-bvzr (Zirabev™).

These products are less costly and and at least as likely to produce equivalent therapeutic results as the non-preferred products, which include, but are not limited to bevacizumab (Avastin®) and any other non-preferred bevacizumab biosimilars.

According to the U.S. Food and Drug Administration (FDA) “a biosimilar is a biological product that has no clinically meaningful differences from the existing FDA-approved reference product. All biosimilar products meet the FDA’s rigorous standards for approval for the indications described in the product labeling. Once a biosimilar has been approved by the FDA, the safety and effectiveness of these products have been established, just as they have been for the reference product.” Coverage of a biosimilar product as an alternate to a reference product is not considered a form of step therapy by the Company.

NON-PREFERRED PRODUCTS

Use of non-preferred products, bevacizumab (Avastin®) or any non-preferred biosimilar, is considered medically necessary and, therefore, covered only for individuals who are currently receiving or have previously received a non-preferred product for the specified bevacizumab indication.

If the individual has not previously received a non-preferred product to treat the specified indication, these non-preferred products are eligible for coverage when the individual has documented contraindication(s) or intolerance(s) to the Company designated preferred products.

BEVACIZUMAB AND RELATED BIOSIMILARS

Bevacizumab and related biosimilars are considered medically necessary and, therefore, covered for the following indications when the requirements listed in the COMPANY-DESIGNATED PREFERRED PRODUCTS and NON-PREFERRED PRODUCTS Sections above are met:

AMPULLARY ADENOCARCINOMA

- First-line therapy in individuals with good performance status (ECOG 0-1, with good biliary drainage and adequate nutritional intake) in combination with

- FOLFIRINOX (fluorouracil, leucovorin, oxaliplatin, and irinotecan) regimen
 - FOLFOX (fluorouracil, leucovorin, and oxaliplatin) regimen
 - FOLFIRI (fluorouracil, leucovorin, and irinotecan) regimen
 - CapeOx (capecitabine and oxaliplatin) regimen
- The above regimens are used for intestinal type
 - unresectable localized disease
 - stage IV resected ampullary cancer
 - metastatic disease at initial presentation
- First-line therapy for intestinal type in select individuals with poor performance status (PS) and ECOG PS 2 for unresectable localized disease, stage IV resected ampullary cancer, metastatic disease at initial presentation in combination with any of the following:
 - FOLFOX (fluorouracil, leucovorin, and oxaliplatin) regimen
 - FOLFIRI (fluorouracil, leucovorin, and irinotecan) regimen
 - Capecitabine and fluorouracil
 - CapeOx (capecitabine and oxaliplatin) regimen
- Subsequent therapy for disease progression in individuals with good performance status (ECOG 0-1, with good biliary drainage and adequate nutritional intake) and intestinal type if previously treated with oxaliplatin-based therapy in combination with FOLFIRI (fluorouracil, leucovorin, and irinotecan) regimen
- Subsequent therapy to be considered for disease progression in select individuals with poor performance status (PS) and ECOG PS 2 with intestinal type in combination with any of the following:
 - Capecitabine
 - Fluorouracil
 - FOLFOX (fluorouracil, leucovorin, and oxaliplatin) regimen
 - FOLFIRI (fluorouracil, leucovorin, and irinotecan) regimen
 - CapeOx (capecitabine and oxaliplatin) regimen

CENTRAL NERVOUS SYSTEM TUMORS

Pediatric Central Nervous System Cancers

Pediatric Diffuse High-Grade Gliomas

- Treatment for palliation of recurrent or progressive disease for pediatric diffuse high-grade glioma*

National Comprehensive Cancer Network (NCCN) note: *Except oligodendroglioma, IDH-mutant and 1p/19q co-deleted or astrocytoma IDH-mutant (see NCCN Guidelines for Central Nervous System Cancers in Adults)

- Treatment for recurrent or progressive disease for all risk categories as part of TEMR (temozolomide, irinotecan, bevacizumab) regimen

- Treatment for recurrent or progressive disease for all risk categories as part of MEMMAT (thalidomide, celecoxib, fenofibrate, etoposide, cyclophosphamide, bevacizumab) regimen

Adult Central Nervous System Cancers

- For symptomatic mass effect, brain edema, radiation necrosis:
 - Extensive Brain Metastases
 - Metastatic Spine Tumors
 - Limited Brain Metastases
 - Meningiomas
 - Primary Spinal Cord Tumors
 - Primary CNS Lymphoma
 - Adult Medulloblastoma
 - Adult Intracranial and Spinal Ependymoma (Excluding Subependymoma)
 - High-Grade Glioma: Other
 - Adult Glioma: Glioblastoma
 - Adult Glioma: Circumscribed Glioma
 - Adult Glioma: IDH-mutant Astrocytoma
 - Adult Glioma: Oligodendroglioma (IDH-mutant, 1p19q codeleted)
- Treatment for recurrent or progressive disease for adult glioma (glioblastoma, high-grade glioma)
 - as a single agent (NCCN preferred)
 - in combination with carmustine, lomustine, or temozolomide if disease progression on bevacizumab monotherapy and it is desirable to continue the steroid-sparing effects of bevacizumab
- Treatment for recurrent or progressive disease of high-grade glioma or glioblastoma as a single agent (NCCN-preferred) or in combination with carmustine, lomustine, or temozolomide if bevacizumab monotherapy fails and it is desirable to continue the steroid-sparing effects of bevacizumab
- Treatment as a single agent for progression or recurrent disease in individuals who are refractory to surgery or radiation therapy (RT), if received prior RT for intracranial and spinal ependymoma (excluding subependymoma), and any of the following conditions:
 - gross total or subtotal resection with negative cerebrospinal fluid (CSF) cytology
 - subtotal resection and evidence of metastasis (brain, spine, or CSF)
 - unresectable disease
 - Adult medulloblastoma:
 - treatment for recurrence in combination with temozolomide and irinotecan
 - Primary central nervous system lymphoma
 - Meningiomas:
 - treatment to be considered as single agent for surgically inaccessible recurrent or progressive disease when radiation is not possible
 - Brain metastases (limited or extensive)

- Primary Spinal Cord Tumors:
 - as single-agent treatment for neurofibromatosis type 2 vestibular schwannomas with hearing loss
- Treatment for recurrent WHO grade 3 oligodendroglioma (IDH-mutant, 1p19q codeleted) in individuals with Karnofsky Performance Status (KPS) $\geq$ 60, recurrent or progressive WHO grade 3 or 4 IDH-mutant astrocytoma for individuals with KPS $\geq$ 60/Glioblastoma, recurrent or progressive adult glioblastoma for the following:
 - as a single agent (preferred)
 - may be considered in combination with carmustine, lomustine, or temozolomide if bevacizumab monotherapy fails and it is desirable to continue the steroid sparing effects of bevacizumab

CERVICAL CANCER

- Persistent, recurrent, or metastatic cervical cancer, in combination with paclitaxel and cisplatin, or paclitaxel and topotecan.
- NCCN preferred first-line, second-line, or subsequent therapy as clinically appropriate (if not used previously as first-line) in combination with pembrolizumab, paclitaxel, and cisplatin or carboplatin for PD-L1 positive (combined positive score [CPS] $\geq$ 1) as determined by an FDA-approved assay or test validated test performed in a CLIA-certified laboratory for:
 - local/regional recurrence
 - stage IVB or distant metastases
- First-line, second-line, or subsequent therapy as clinically appropriate (if not used previously as first-line) in combination with paclitaxel and cisplatin or carboplatin (preferred regimens), or in combination with paclitaxel and topotecan and continued for maintenance therapy for the following:
 - local/regional recurrence
 - stage IVB or recurrence with distant metastases
- Second-line or subsequent therapy as a single agent for:
 - local/regional recurrence
 - stage IVB or or recurrence with distant metastases
- First-line, second-line, or subsequent therapy as clinically appropriate (if not used previously as first-line) for persistent, recurrent, or metastatic small cell neuroendocrine carcinoma of the cervix (NECC) in combination with topotecan and paclitaxel and continued for maintenance therapy
- Second-line or subsequent therapy for persistent, recurrent, or metastatic small cell neuroendocrine carcinoma of the cervix (NECC) as a single agent

RECTAL CANCER

- Primary treatment for T3, N Any; T1-2, N1-2; T4, N Any; or locally unresectable or medically inoperable disease if resection is contraindicated following total neoadjuvant therapy (proficient mismatch repair/microsatellite-stable [pMMR/MSS] or ineligible for or progressed on checkpoint inhibitor immunotherapy for deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] or polymerase epsilon/delta

[POLE/POLD1] mutation) or neoadjuvant/definitive immunotherapy (dMMR/MSI-H) if intensive therapy recommended

- in CapeOX (capecitabine and oxaliplatin) regimen
 - in FOLFOX (fluorouracil, leucovorin, and oxaliplatin) regimen
 - in FOLFIRI (fluorouracil, leucovorin, and irinotecan) regimen
- Primary treatment for T3, N Any; T1-2, N1-2; T4, N Any; or locally unresectable or medically inoperable disease if resection is contraindicated following total neoadjuvant therapy (proficient mismatch repair/microsatellite-stable [pMMR/MSS] or ineligible for or progressed on checkpoint inhibitor immunotherapy for deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] or polymerase epsilon/delta [POLE/POLD1] mutation) or neoadjuvant/definitive immunotherapy (dMMR/MSI-H) if intensive therapy not recommended
 - in combination with capecitabine
 - in 5-FU/leucovorin (fluorouracil and leucovorin) regimen
- Therapy in combination with FOLFOX (fluorouracil, leucovorin, and oxaliplatin), FOLFIRI (fluorouracil, leucovorin, and irinotecan), CapeOX (capecitabine and oxaliplatin), or FOLFIRINOX (fluorouracil, leucovorin, irinotecan, and oxaliplatin) regimen (strongly consider FOLFIRINOX for individuals with excellent performance status) if intensive therapy recommended (proficient mismatch repair/microsatellite-stable [pMMR/MSS] or ineligible for or progressed on checkpoint inhibitor immunotherapy for deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] or polymerase epsilon/delta [POLE/POLD1] mutation)
 - as primary treatment for synchronous abdominal/peritoneal metastases that are nonobstructing, or following local therapy for individuals with existing or imminent obstruction
 - as primary treatment for synchronous unresectable metastases of other sites
 - as primary treatment for unresectable isolated pelvic/anastomotic recurrence
 - as initial treatment for unresectable metachronous metastases in individuals who have not received previous FOLFOX or CapeOX within the past 12 months, who have received previous fluorouracil/leucovorin (5-FU/LV) or capecitabine therapy, or who have not received any previous chemotherapy
 - and progressed on non-intensive therapy, except if received previous fluoropyrimidine, with improvement in functional status
- Therapy in combination with capecitabine or 5-FU/leucovorin (fluorouracil and leucovorin) regimen if intensive therapy not recommended (proficient mismatch repair/microsatellite-stable [pMMR/MSS] or ineligible for or progressed on checkpoint inhibitor immunotherapy for deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] or polymerase epsilon/delta [POLE/POLD1] mutation)
 - as primary treatment for synchronous abdominal/peritoneal metastases that are nonobstructing, or following local therapy for individuals with existing or imminent obstruction
 - as primary treatment for synchronous unresectable metastases of other sites
 - as primary treatment for unresectable isolated pelvic/anastomotic recurrence

- as initial treatment for unresectable metachronous metastases in individuals who have not received previous FOLFOX or CapeOX within the past 12 months, who have received previous fluorouracil/leucovorin (5-FU/LV) or capecitabine therapy, or who have not received any previous chemotherapy
- Primary treatment for synchronous liver only and/or lung only metastases (proficient mismatch repair/microsatellite-stable [pMMR/MSS]; deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] or polymerase epsilon/delta [POLE/POLD1] mutation and not a candidate for immunotherapy) that are unresectable or medically inoperable in combination with
 - FOLFIRI (fluorouracil, leucovorin, and irinotecan) regimen
 - FOLFOX (fluorouracil, leucovorin, and oxaliplatin) regimen
 - CapeOX (capecitabine and oxaliplatin) regimen
 - FOLFIRINOX (fluorouracil, leucovorin, irinotecan, and oxaliplatin) regimen
- Preferred anti-angiogenic therapy as initial treatment for individuals with unresectable metachronous metastases (proficient mismatch repair/microsatellite-stable [pMMR/MSS]) and previous FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin) within the past 12 months
 - in combination with irinotecan
 - in combination with FOLFIRI (fluorouracil, leucovorin, and irinotecan) regimen
- Second-line and subsequent therapy for progression of advanced or metastatic disease (proficient mismatch repair/microsatellite-stable [pMMR/MSS] or ineligible for or progressed on checkpoint inhibitor immunotherapy for deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] or polymerase epsilon/delta [POLE/POLD1] mutation)
 - as the preferred anti-angiogenic agent in combination with irinotecan or FOLFIRI (fluorouracil, leucovorin, and irinotecan) regimen, if not previously given and if previously treated with oxaliplatin-based therapy without irinotecan
 - in combination with FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin) regimen, if not previously given and if previously treated with irinotecan-based therapy without oxaliplatin
 - in combination with FOLFOX, CapeOX, FOLFIRI (preferred), irinotecan and oxaliplatin, irinotecan (preferred), or FOLFIRINOX (fluorouracil, leucovorin, irinotecan and oxaliplatin), if not previously given and if previously treated without irinotecan or oxaliplatin
- For the treatment of individuals with unresectable or metastatic MSI-H or dMMR colorectal cancer (CRC) as determined by an FDA-approved test

COLON CANCER

- In combination with FOLFOX (fluorouracil, leucovorin, and oxaliplatin), FOLFIRI (fluorouracil, leucovorin, and irinotecan), CapeOX (capecitabine and oxaliplatin), or FOLFIRINOX (fluorouracil, leucovorin, oxaliplatin, and irinotecan) regimen, in individuals appropriate for intensive therapy (proficient mismatch repair/microsatellite-stable [pMMR/MSS] or ineligible for or progressed on checkpoint inhibitor immunotherapy for deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] or polymerase

epsilon/delta [POLE/POLD1] mutation), if intensive therapy recommended for any of the following indications:

- as primary treatment for locally unresectable or medically inoperable disease
 - as primary treatment for synchronous abdominal/peritoneal metastases that are nonobstructing, or following local therapy for individuals with existing or imminent obstruction
 - for synchronous unresectable metastases of other sites
 - as primary initial treatment for unresectable metachronous metastases in individuals who have not received previous adjuvant FOLFOX or CapeOX within the past 12 months, who have received previous fluorouracil/leucovorin (5-FU/LV) or capecitabine therapy, or who have not received any previous chemotherapy
 - and progressed on non-intensive therapy, except if received previous fluoropyrimidine, with improvement in functional status
- Primary treatment for unresectable synchronous liver and/or lung metastases (proficient mismatch repair/microsatellite-stable [pMMR/MSS]; deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] or polymerase epsilon/delta [POLE/POLD1] mutation and individual is not a candidate for immunotherapy) in combination with any of the following regimens:
 - FOLFOX (fluorouracil, leucovorin, and oxaliplatin) regimen
 - FOLFIRI (fluorouracil, leucovorin, and irinotecan) regimen
 - FOLFIRINOX (fluorouracil, leucovorin, irinotecan, and oxaliplatin) regimen
 - CapeOX (capecitabine and oxaliplatin) regimen
- Second-line and subsequent therapy, if not previously given, for progression of advanced or metastatic disease (proficient mismatch repair/microsatellite-stable [pMMR/MSS] or ineligible for or progressed on checkpoint inhibitor immunotherapy for deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] or polymerase epsilon/delta [POLE/POLD1] mutation) in combination with trifluridine and tipiracil (preferred), if not previously given, in individuals who have progressed through all available regimens
- In combination with capecitabine or with 5-FU/leucovorin (fluorouracil and leucovorin) regimen (proficient mismatch repair/microsatellite-stable [pMMR/MSS] or ineligible for or progressed on checkpoint inhibitor immunotherapy for deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] or polymerase epsilon/delta [POLE/POLD1] mutation), in individuals not appropriate for intensive therapy for any of the following indications:
 - as primary treatment for locally unresectable or medically inoperable disease
 - as primary treatment for synchronous abdominal/peritoneal metastases that are nonobstructing, or following local therapy for individuals with existing or imminent obstruction
 - for synchronous unresectable metastases of other sites
 - as initial treatment for unresectable metachronous metastases in individuals who have not received previous adjuvant FOLFOX or CapeOX within the past 12

months, who have received previous fluorouracil/leucovorin (5-FU/LV) or capecitabine therapy, or who have not received any previous chemotherapy

- As NCCN-preferred antiangiogenic therapy as initial treatment for individuals with unresectable metachronous metastases (proficient mismatch repair/microsatellite-stable [pMMR/MSS] only or deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] and previous adjuvant FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin) within the past 12 months for any of the following regimens:
 - in combination with irinotecan
 - in combination with FOLFIRI (fluorouracil, leucovorin, and irinotecan) regimen
- Therapy in combination with FOLFOX (fluorouracil, leucovorin, and oxaliplatin), FOLFIRI (fluorouracil, leucovorin and irinotecan), CapeOX (capecitabine and oxaliplatin), or FOLFIRINOX (fluorouracil, leucovorin, irinotecan, and oxaliplatin) regimen (strongly consider FOLFIRINOX for individuals with excellent performance status) if intensive therapy recommended for any of the following:
 - as adjuvant treatment following synchronized or staged resection and/or local therapy for synchronous liver and/or lung metastases that converted from unresectable to resectable disease after primary treatment. Biologic therapy is only appropriate for continuation of favorable response from conversion therapy.
 - as adjuvant treatment following resection and/or local therapy for resectable metachronous metastases in individuals who have received previous chemotherapy
 - as adjuvant treatment for unresectable metachronous metastases that converted to resectable disease after primary treatment. Biologic therapy is only appropriate for continuation of favorable response from conversion therapy.
- Therapy in combination with capecitabine or 5-FU/leucovorin (fluorouracil and leucovorin) regimen, if intensive therapy not recommended, for advanced or metastatic disease for any of the following:
 - adjuvant treatment following synchronized or staged resection and/or local therapy for synchronous liver and/or lung metastases that converted from unresectable to resectable disease after primary treatment. Biologic therapy is only appropriate for continuation of favorable response from conversion therapy (proficient mismatch repair/microsatellite-stable [pMMR/MSS] or ineligible for or progression on checkpoint inhibitor immunotherapy for deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H])
 - adjuvant treatment following resection and/or local therapy for resectable metachronous metastases in individuals who have received previous chemotherapy (pMMR/MSS or ineligible for or progression on checkpoint inhibitor immunotherapy for dMMR/MSI-H)
 - adjuvant treatment following resection and/or local therapy for resectable metachronous metastases in individuals who have received previous immunotherapy (dMMR/MSI-H)

- adjuvant treatment for unresectable metachronous metastases that converted to resectable disease after primary treatment. Biologic therapy is only appropriate for continuation of favorable response from conversion therapy (pMMR/MSS or ineligible for or progression on checkpoint inhibitor immunotherapy for dMMR/MSI-H)
- As second-line and subsequent therapy for progression of advanced or metastatic disease (proficient mismatch repair/microsatellite-stable [pMMR/MSS] or ineligible for or progressed on checkpoint inhibitor immunotherapy for deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] or polymerase epsilon/delta [POLE/POLD1] mutation) for any of the following:
 - NCCN-preferred anti-angiogenic agent in combination with irinotecan or FOLFIRI (fluorouracil, leucovorin, and irinotecan) regimen if previously treated with oxaliplatin-based therapy without irinotecan
 - in combination with FOLFOX (fluorouracil, leucovorin, and oxaliplatin) regimen or CapeOX (capecitabine and oxaliplatin) regimen if previously treated with irinotecan-based therapy without oxaliplatin
 - NCCN preferred anti-angiogenic agent in combination with irinotecan or FOLFIRI if previously treated without irinotecan or oxaliplatin
 - in combination with FOLFOX, CapeOX, FOLFIRINOX (fluorouracil, leucovorin, irinotecan, oxaliplatin) or irinotecan and oxaliplatin, if not previously given and if previously treated without irinotecan or oxaliplatin

Appendiceal Adenocarcinoma

- Initial systemic therapy for advanced or metastatic disease (proficient mismatch repair/microsatellite-stable [pMMR/MSS] or ineligible for or progressed on checkpoint inhibitor immunotherapy for deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] or polymerase epsilon/delta [POLE/POLD1] mutation) in combination with FOLFOX (fluorouracil, leucovorin, and oxaliplatin) regimen, CapeOX (capecitabine and oxaliplatin) regimen, FOLFIRI (fluorouracil, leucovorin, and irinotecan) regimen, or FOLFIRINOX (fluorouracil, leucovorin, irinotecan, and oxaliplatin) regimen (strongly NCCN recommended for individuals with excellent performance status) for one of the following:
 - if intensive therapy recommended
 - if intensive therapy recommended and progressed on non-intensive therapy, except if received previous fluoropyrimidine, with improvement in functional status
- Initial systemic therapy for advanced or metastatic disease (proficient mismatch repair/microsatellite-stable [pMMR/MSS] or ineligible for or progressed on checkpoint inhibitor immunotherapy for deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] or polymerase epsilon/delta [POLE/POLD1] mutation) in combination with capecitabine or with 5-FU/leucovorin (fluorouracil and leucovorin) regimen if intensive therapy not recommended
- Second line and subsequent therapy for progression of advanced or metastatic disease (proficient mismatch repair/microsatellite-stable [pMMR/MSS] or ineligible for

or progressed on checkpoint inhibitor immunotherapy for deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] or polymerase epsilon/delta [POLE/POLD1] mutation) for any of the following:

- as NCCN preferred anti-angiogenic agent in combination with irinotecan or FOLFIRI (fluorouracil, leucovorin, and irinotecan) regimen if previously treated with oxaliplatin-based therapy without irinotecan
 - in combination with FOLFOX (fluorouracil, leucovorin, and oxaliplatin) regimen or CapeOX (capecitabine and oxaliplatin) regimen if previously treated with irinotecan-based therapy without oxaliplatin
 - as NCCN preferred antiangiogenic agent in combination with irinotecan or FOLFIRI if previously treated without irinotecan or oxaliplatin
 - in combination with FOLFOX, CapeOX, or irinotecan and oxaliplatin if previously treated without irinotecan or oxaliplatin
- Second line and subsequent therapy for progression of advanced or metastatic disease (proficient mismatch repair/microsatellite-stable [pMMR/MSS] or ineligible for or progressed on checkpoint inhibitor immunotherapy for deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] or polymerase epsilon/delta [POLE/POLD1] mutation) in combination with trifluridine and tipiracil (NCCN preferred) if not previously given in individuals who have progressed through all available regimens

SMALL BOWEL ADENOCARCINOMA

- In combination with FOLFOX (fluorouracil, leucovorin, and oxaliplatin), CapeOX (capecitabine and oxaliplatin), or FOLFOXIRI (fluorouracil, leucovorin, oxaliplatin, and irinotecan) regimen for advanced or metastatic disease if intensive therapy is appropriate:
 - as initial therapy
 - as second-line and subsequent therapy
- In combination with FOLFIRINOX (fluorouracil, leucovorin, irinotecan, and oxaliplatin) regimen for advanced or metastatic disease if intensive therapy is appropriate:
 - as initial therapy
 - as subsequent therapy in individuals who previously received initial therapy with nivolumab with or without ipilimumab, or pembrolizumab
- In combination with FOLFOXIRI (fluorouracil, leucovorin, oxaliplatin, and irinotecan) regimen for advanced or metastatic disease if intensive therapy recommended
 - as initial therapy
 - as second-line and subsequent therapy (if not previously given)
- Initial therapy in combination with FOLFIRINOX (fluorouracil, leucovorin, irinotecan, and oxaliplatin) for advanced or metastatic disease if intensive therapy is recommended
- Initial therapy in combination with capecitabine or 5-FU/leucovorin (fluorouracil and leucovorin) regimen for advanced or metastatic disease in individuals not appropriate for intensive therapy

- Initial therapy in combination with FOLFIRI (fluorouracil, leucovorin, and irinotecan) for advanced or metastatic disease and if individuals received previous FOLFOX/CAPEOX in the adjuvant setting within the past 12 months or contraindication

HEPATOCELLULAR CARCINOMA

- In individuals with hepatocellular carcinoma (HCC) who have been previously treated with sorafenib
- As adjuvant therapy in combination with atezolizumab following resection or ablation for those whose initial clinical presentation is operable by performance status or comorbidity and meet resection criteria, and are at high risk of recurrence (defined as size > 5 cm, >3 tumors, macrovascular invasion or microvessel invasion on histology or grade 3/4 histology)
- As NCCN-preferred first-line treatment in combination with atezolizumab for individuals who have any of the following indications:
 - liver-confined, unresectable disease and are deemed ineligible for transplant
 - extrahepatic/metastatic disease and are deemed ineligible for resection, transplant, or locoregional therapy

KIDNEY CARCINOMA

- In individuals with metastatic renal cell carcinoma in combination with interferon alfa.
- Treatment for relapse or stage IV disease for the following regimens:
 - in combination with everolimus as systemic therapy for non-clear cell histology (if first-line therapy and stage IV, then M1 or unresectable T4, M0 only)
- In individuals with relapsed or stage IV hereditary renal cell carcinoma in combination with erlotinib for non-clear cell histology in selected individuals with advanced papillary renal cell carcinoma including hereditary leiomyomatosis and renal cell carcinoma (HLRCC) associated RCC

MALIGNANT PLEURAL MESOTHELIOMA

- In combination with (cisplatin or carboplatin) pemetrexed (NCCN preferred for epithelioid histology) as first-line systemic therapy for any of the following:
 - unresectable clinical stage I-III A disease after surgical exploration (if induction chemotherapy was not given) and epithelioid histology
 - clinical stage I-III A disease and epithelioid histology who have not undergone surgical exploration (if induction chemotherapy was not given)
 - clinical stage IIIB or IV disease, sarcomatoid or biphasic histology, or medically inoperable tumors in individuals with performance status (PS) 0-2

NCCN note: *May also be used for pericardial mesothelioma and tunica vaginalis testis mesothelioma

- Treatment in those who are not candidates for cisplatin in combination with pemetrexed and carboplatin (preferred for epithelioid histology) as first-line systemic therapy for the following indications:

- unresectable clinical stage I-IIIa disease after surgical exploration (if induction chemotherapy was not given) and epithelioid histology
- clinical stage I-IIIa disease and epithelioid histology who have not undergone surgical exploration (if induction chemotherapy was not given)
- for individuals with performance status (PS) 0-2 and: clinical stage IIIB or IV disease, sarcomatoid or biphasic histology, or medically inoperable tumors in individuals with performance status (PS) 0-2

NCCN note: *May also be used for pericardial mesothelioma and tunica vaginalis testis mesothelioma

- NCCN preferred subsequent systemic therapy, if immunotherapy was administered as first-line treatment or to be considered as a rechallenge if good response to front-line pemetrexed-based treatment for the following regimens:
 - in combination with pemetrexed and cisplatin
 - in combination with pemetrexed and carboplatin in those who are not candidates for cisplatin

NCCN note: *May also be used for pericardial mesothelioma and tunica vaginalis testis mesothelioma

MALIGNANT PERITONEAL MESOTHELIOMA

- Used in combination with pemetrexed and (cisplatin or carboplatin) (NCCN preferred for epithelioid histology) as first-line systemic therapy for
 - adjuvant treatment of peritoneal mesothelioma (PeM) with unicavitary, epithelioid histology that is medically operable and complete cytoreduction achievable, following cytoreductive surgery (CRS) + hyperthermic intraperitoneal chemotherapy (HIPEC), if surgical/pathologic high-risk features** and no neoadjuvant therapy given
 - PeM with unicavitary, epithelioid histology that is medically inoperable and/or complete cytoreduction not achievable (including high-risk features**) and ECOG performance status (PS) 0-2
 - PeM with biphasic/sarcomatoid histology or bicavitary disease and ECOG PS 0-2
 - ECOG PS 0-2 and: recurrence of PeM with unicavitary, epithelioid histology after prior cytoreductive surgery (CRS) + hyperthermic intraperitoneal chemotherapy (HIPEC) if no previous adjuvant systemic therapy given
 - ECOG PS 0-2 and: recurrence of PeM with biphasic/sarcomatoid histology after prior CRS + HIPEC

NCCN notes: *May also be used for pericardial mesothelioma and tunica vaginalis testis mesothelioma

**High-risk features include Ki-67 >9%, nodal metastasis, high tumor burden (Peritoneal Cancer Index [PCI] >17), completeness of cytoreduction (CC) score >1, biphasic disease, or bicavitary disease

- In combination with pemetrexed and cisplatin or carboplatin (preferred for epithelioid histology) as first-line systemic therapy for :

- diffuse peritoneal mesothelioma (PeM) with unicavitary, epithelioid histology that is medically inoperable and/or complete cytoreduction not achievable (including high-risk features**) and ECOG performance status (PS) 0-2
- diffuse PeM with biphasic/sarcomatoid histology or bicavitary disease and ECOG PS 0-2
- recurrence of diffuse PeM with unicavitary, epithelioid histology after prior cytoreductive surgery (CRS) + hyperthermic intraperitoneal chemotherapy (HIPEC), if no previous adjuvant systemic therapy given and ECOG PS 0-2
- recurrence of benign multicystic or well-differentiated papillary PeM after prior CRS ± HIPEC for ECOG PS 0-2

NCCN notes: *May also be used for pericardial mesothelioma and tunica vaginalis testis mesothelioma

**High-risk features include Ki-67 >9%, nodal metastasis, high tumor burden (Peritoneal Cancer Index [PCI] >17), completeness of cytoreduction (CC) score >1, biphasic disease, or bicavitary disease

- Treatment in individuals who are not candidates for cisplatin in combination with pemetrexed and carboplatin (preferred for epithelioid histology) as first-line systemic therapy for any of the following:
 - unresectable clinical stage I-IIIa disease after surgical exploration (if induction chemotherapy was not given) and epithelioid histology
 - clinical stage I-IIIa disease and epithelioid histology in those who have not undergone surgical exploration (if induction chemotherapy was not given)
 - those with performance status (PS) 0-2 and: clinical stage IIIB or IV disease, sarcomatoid or biphasic histology, or if medically inoperable

NCCN notes: *May also be used for pericardial mesothelioma and tunica vaginalis testis mesothelioma

**High-risk features include Ki-67 >9%, nodal metastasis, high tumor burden (Peritoneal Cancer Index [PCI] >17), completeness of cytoreduction (CC) score >1, biphasic disease, or bicavitary disease

- Subsequent systemic therapy for ECOG performance status (PS) 0-2 in combination with atezolizumab if not previously treated with immune checkpoint inhibitors

NCCN note: *May also be used for pericardial mesothelioma and tunica vaginalis testis mesothelioma

- NCCN preferred subsequent systemic therapy, in combination with pemetrexed and cisplatin or carboplatin, if immunotherapy was administered as first-line treatment or to be considered as a rechallenge if good response to front-line pemetrexed-based treatment and ECOG performance status (PS) 0-2

NCCN note: *May also be used for pericardial mesothelioma and tunica vaginalis testis mesothelioma

NON-SQUAMOUS NON-SMALL CELL LUNG CANCER (NSCLC): ADENOCARCINOMA AND LARGE CELL CARCINOMA

- In individuals who have unresectable, locally advanced, recurrent, or metastatic NSCLC, as first-line treatment in combination with paclitaxel (Taxol®) and carboplatin (Paraplatin®)
- In combination with erlotinib for EGFR mutation-positive (e.g., exon 19 deletion or L858R) nonsquamous cell histology, recurrent, advanced, or metastatic disease with no history of hemoptysis as (except for locoregional recurrence or symptomatic local disease (excluding mediastinal lymph node recurrence with prior radiation therapy) with no evidence of disseminated disease) either first-line therapy or continuation of therapy following disease progression on combination of erlotinib with bevacizumab for asymptomatic disease, symptomatic brain lesions, or symptomatic systemic limited progression (if T790M negative)
- As first-line therapy treatment for recurrent, advanced, or metastatic disease** as first-line therapy for PD-L1 expression positive ($\geq 1\%$) tumors that are negative for actionable molecular biomarkers* and no contraindications to PD-1 or PD-L1 inhibitors and performance status (PS) 0-2 in combination with atezolizumab, carboplatin and paclitaxel for nonsquamous cell histology
- Treatment for recurrent, advanced, or metastatic disease in individuals with performance status 0-1, tumors of nonsquamous cell histology, and no history of recent hemoptysis (excluding mediastinal lymph node recurrence with prior radiation therapy) with no evidence of disseminated disease in combination with:
 - carboplatin and either paclitaxel or pemetrexed (if contraindications** to PD-1 or PD-L1 inhibitors)
 - cisplatin and pemetrexed (if contraindications** to PD-1 or PD-L1 inhibitors)
- The above regimens are used as:
 - initial systemic therapy for PD-L1 expression positive ($\geq 1\%$) and negative for actionable molecular markers* (may be KRAS G12C mutation positive) with contraindications to PD-1 or PD-L1 inhibitors
 - initial systemic therapy for PD-L1 $< 1\%$ and negative for actionable molecular markers* (may be KRAS G12C mutation positive)
 - first-line therapy for EGFR exon 20 mutation positive tumors
 - first-line or subsequent therapy for BRAF V600E mutation positive tumors
 - first-line or subsequent therapy for NTRK1/2/3 gene fusion positive tumors
 - first-line or subsequent therapy for MET exon 14 skipping mutation positive tumors
 - first-line or subsequent therapy for RET rearrangement positive tumors
 - first-line therapy for ERBB2 (HER2) mutation positive tumors
 - subsequent therapy for EGFR mutation positive (e.g., exon 19 deletion or L858R) tumors and prior erlotinib +/- (ramucirumab or bevacizumab), afatinib, gefitinib, osimertinib, amivantamab-vmjw + lazertinib or dacomitinib therapy
 - subsequent therapy for EGFR S768I, L861Q, and/or G719X mutation positive tumors and prior afatinib, osimertinib, erlotinib, gefitinib, or dacomitinib therapy

- subsequent therapy for ALK rearrangement positive tumors and prior crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib therapy
- subsequent therapy for ROS1 rearrangement positive tumors and prior crizotinib, entrectinib, or ceritinib therapy
- subsequent therapy for PD-L1 expression positive ($\geq 1\%$) tumors and negative for actionable molecular markers* after prior PD-1/PD-L1 inhibitor but no prior platinum-containing chemotherapy
- Treatment for recurrent, advanced, or metastatic disease in individuals with performance status 0-1, tumors of nonsquamous cell histology, and no history of recent hemoptysis in combination with atezolizumab, carboplatin and paclitaxel (if no contraindications** to PD-1 or PD-L1 inhibitors) for any of the following indications:
 - initial systemic therapy for PD-L1 $< 1\%$ and negative for actionable molecular markers* (may be KRAS G12C mutation positive)
 - first-line therapy for EGFR exon 20 mutation–positive tumors
 - first-line or subsequent therapy for BRAF V600E mutation–positive tumors
 - first-line or subsequent therapy for NTRK1/2/3 gene fusion–positive tumors
 - first-line or subsequent therapy for MET exon 14 skipping mutation–positive tumors
 - first-line or subsequent therapy for RET rearrangement positive tumors
 - first-line therapy for ERBB2 (HER2) mutation positive tumors
 - subsequent therapy for EGFR exon 19 deletion or exon 21 L858R tumors and prior erlotinib $\pm$ (ramucirumab or bevacizumab), afatinib, gefitinib, osimertinib, amivantamab-vmjw + lazertinib or dacomitinib therapy
 - subsequent therapy for EGFR S768I, L861Q, and/or G719X mutation positive–tumors and prior afatinib, osimertinib, erlotinib, gefitinib, or dacomitinib therapy
 - subsequent therapy for ALK rearrangement–positive tumors and prior crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib therapy
 - subsequent therapy for ROS1 rearrangement–positive tumors and prior crizotinib, entrectinib, or ceritinib therapy
- Treatment for recurrent, advanced, or metastatic disease as first-line therapy for PD-L1 expression–positive ($\geq 1\%$) tumors that are negative for actionable molecular markers* and no contraindications** to PD-1 or PD-L1 inhibitors and performance status 0-2 in combination with atezolizumab, carboplatin and paclitaxel for nonsquamous cell histology (except for locoregional recurrence or symptomatic local disease [with the exception of mediastinal lymph node recurrence with prior radiation therapy] with no evidence of disseminated disease)
- Continuation maintenance therapy in combination with atezolizumab for recurrent, advanced, or metastatic disease for PD-L1 expression–positive ($\geq 1\%$) tumors that are negative for actionable molecular markers* (may be KRAS G12C mutation positive) and no contraindications** to PD-1 or PD-L1 inhibitors in individuals with performance status 0-2 who achieve a response or stable disease following first-line therapy with atezolizumab/carboplatin/paclitaxel/bevacizumab for nonsquamous cell histology (except for locoregional recurrence or symptomatic local disease [with the exception of

mediastinal lymph node recurrence with prior radiation therapy] with no evidence of disseminated disease)

- Continuation maintenance therapy for recurrent, advanced, or metastatic disease (except for locoregional recurrence or symptomatic local disease [with the exception of mediastinal lymph node recurrence with prior radiation therapy] with no evidence of disseminated disease) with PD-L1 expression <1% that are negative for actionable molecular biomarkers* (may be KRAS G12C mutation positive) in individuals with performance status 0 to 2, tumors of nonsquamous cell histology, and no history of recent hemoptysis who achieve tumor response or stable disease following initial systemic therapy, with one of the following regimens:
 - as single-agent
 - in combination with pemetrexed (if previously used with a first-line pemetrexed/platinum chemotherapy regimen)
 - in combination with atezolizumab (if previously used first-line as part of an atezolizumab/carboplatin/paclitaxel/bevacizumab regimen) for nonsquamous cell histology and no contraindications** to PD-1 or PD-L1 inhibitors

NCCN notes:* Complete genotyping for EGFR, ALK, ROS1, BRAF, NTRK1/2/3, MET and RET, repeat biopsy and/or plasma testing should be done. If these are not feasible, treatment is guided by available results and, if unknown, these individuals are treated as though they do not have driver oncogenes

**Contraindications for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or current use of immunosuppressive agents, or presence of an oncogene (e.g., EGFR [exon 19 deletions, p.L858R point mutation in exon 21], ALK rearrangements, RET rearrangements), which would predict lack of benefit.

OVARIAN CANCER (EPITHELIAL), FALLOPIAN TUBE CANCER, OR PRIMARY PERITONEAL CANCER **Epithelial Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer**

- In combination with carboplatin and paclitaxel, followed by bevacizumab or related biosimilar as a single agent, for stage III or IV disease following initial surgical resection
- In combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan for platinum-resistant recurrent disease who received no more than two prior chemotherapy regimens
- In combination with carboplatin and paclitaxel or carboplatin and gemcitabine, followed by bevacizumab as a single agent, for platinum-sensitive recurrent disease
- Maintenance therapy as a single agent if used previously as part of combination therapy for individuals with partial response (PR) or complete response (CR) following recurrence therapy with chemotherapy plus bevacizumab for platinum-sensitive disease
- As an NCCN-preferred therapy for rising CA-125 levels or clinical relapse in individuals who have received no prior chemotherapy in combination with paclitaxel and carboplatin
- As an NCCN-preferred targeted therapy as a single agent for persistent disease or recurrence (except for immediate treatment of biochemical relapse)

- as immediate treatment for serially rising CA-125 in individuals who previously received chemotherapy
 - for progression on primary, maintenance, or recurrence therapy (platinum-resistant disease)
 - for stable or persistent disease (if not on maintenance therapy) (platinum-resistant disease)
 - for complete remission and relapse <6 months after completing chemotherapy (platinum-resistant disease)
 - for radiographic and/or clinical relapse in individuals with previous complete remission and relapse ≥6 months after completing prior chemotherapy (platinum-sensitive disease) completing prior chemotherapy
- As primary adjuvant therapy for pathologic stage II-IV disease in combination with oxaliplatin and docetaxel
- As an NCCN preferred primary adjuvant therapy in combination with carboplatin and paclitaxel (NCCN preferred with paclitaxel) or docetaxel for pathologic stage II-IV disease
- Maintenance therapy for stage II-IV high-grade serous or grade 2/3 endometrioid carcinoma if a CR or PR to primary therapy including bevacizumab
 - as a single agent in individuals BRCA1/2 wild-type or unknown and HR proficient or status unknown
 - in combination with olaparib in individuals BRCA1/2 wild-type or unknown and HR deficient
 - as a single agent in individuals BRCA1/2 wild-type or unknown and HR deficient
 - in combination with olaparib (or niraparib if unable to tolerate olaparib) in individuals with a germline or somatic BRCA1/2 mutation
- For platinum-sensitive persistent disease or recurrence (except for immediate treatment of biochemical relapse) for the following indications in combination with:
 - as immediate treatment for serially rising CA-125 in individuals who previously received chemotherapy (platinum-sensitive or platinum-resistant)
 - for progression on primary, maintenance, or recurrence therapy (platinum-resistant)
 - for stable or persistent disease (if not on maintenance therapy) (platinum-resistant)
 - for complete remission and relapse <6 months after completing chemotherapy (platinum-resistant)
 - in individuals with complete remission and relapse ≥6 months after completing prior chemotherapy (platinum-resistant) in combination with:
 - carboplatin and gemcitabine (preferred in platinum-sensitive disease)
 - carboplatin and paclitaxel (preferred in platinum-sensitive disease)
 - carboplatin and liposomal doxorubicin (preferred in platinum-sensitive disease)
- As therapy for platinum-resistant persistent disease or recurrence in combination with oral cyclophosphamide (NCCN preferred), cyclophosphamide and pembrolizumab, liposomal doxorubicin (NCCN preferred), weekly paclitaxel (NCCN preferred), or topotecan (NCCN preferred), mirvetuximab soravtansine-gynx (in folate receptor-

alpha expressing tumors; useful in certain circumstances), or gemcitabine (except for immediate treatment of biochemical relapse)

- as immediate treatment for serially rising CA-125 in individuals who previously received chemotherapy
 - for progression on primary, maintenance, or recurrence therapy
 - stable or persistent disease (if not on maintenance therapy)
 - for complete remission and relapse <6 months after completing chemotherapy
- As NCCN preferred therapy in combination with paclitaxel or docetaxel (NCCN preferred with paclitaxel) and carboplatin for individuals who are poor surgical candidates or have a low likelihood of optimal cytoreduction as:
 - neoadjuvant therapy
 - continued treatment for stable disease following neoadjuvant therapy
 - adjuvant therapy following interval debulking surgery (IDS) in individuals with response or stable disease to neoadjuvant therapy
- Maintenance therapy as a single agent (useful in certain circumstances) if used previously as part of a combination therapy for individuals with partial or CR following recurrence therapy with chemotherapy plus bevacizumab for platinum-sensitive disease

Carcinosarcoma (Malignant Mixed Müllerian Tumors)

- Adjuvant treatment with any of the following:
 - in combination with oxaliplatin and docetaxel for pathologic stage II-IV disease
 - in combination with carboplatin and paclitaxel or docetaxel for pathologic stage II-IV disease (preferred with paclitaxel)
- Maintenance therapy in combination with olaparib or niraparib (if unable to tolerate olaparib) for stage II-IV carcinosarcoma with a germline or somatic BRCA1/2 mutation if CR or PR to primary therapy including bevacizumab
- NCCN-preferred treatment for rising CA-125 levels or clinical relapse in individuals who have received no prior chemotherapy in combination with paclitaxel and carboplatin
- NCCN-preferred targeted therapy as a single agent for persistent disease or recurrence (except for immediate treatment of biochemical relapse)
 - as immediate treatment for serially rising CA-125 in individuals who previously received chemotherapy
 - for progression on primary, maintenance, or recurrence therapy (platinum-resistant disease)
 - for stable or persistent disease (if not on maintenance therapy) (platinum-resistant disease)
 - for complete remission and relapse <6 months after completing chemotherapy (platinum-resistant disease)
 - for radiographic and/or clinical relapse in individuals with previous complete remission and relapse ≥6 months after completing prior chemotherapy (platinum-sensitive disease)
- Treatment for persistent disease or recurrence (except for immediate treatment of biochemical relapse)

- as immediate treatment for serially rising CA-125 in individuals who previously received chemotherapy (platinum-sensitive or platinum-resistant)
- for progression on primary, maintenance, or recurrence therapy (platinum resistant)
- for stable or persistent disease (if not on maintenance therapy) (platinum resistant)
- for complete remission and relapse <6 months after completing chemotherapy (platinum resistant)
- in individuals with complete remission and relapse ≥6 months after completing prior chemotherapy (platinum sensitive)
 - in combination with any of the following:
 - carboplatin and gemcitabine (preferred in platinum-sensitive disease)
 - carboplatin and paclitaxel (preferred in platinum-sensitive disease)
 - carboplatin and liposomal doxorubicin (preferred in platinum-sensitive disease)
- Therapy for platinum-resistant persistent disease or recurrence in combination with oral cyclophosphamide (NCCN preferred), oral cyclophosphamide and pembrolizumab liposomal doxorubicin (NCCN preferred), weekly paclitaxel (NCCN preferred), topotecan (NCCN preferred), gemcitabine, mirvetuximab soravtansine-gynx (in folate receptor-alpha-expressing tumors), or ixabepilone (if previously treated with taxane) 2B for immediate treatment of biochemical relapse, or for combination with ixabepilone
 - as immediate treatment for serially rising CA-125 in individuals who previously received chemotherapy
 - for progression on primary, maintenance, or recurrence therapy
 - for stable or persistent disease (if not on maintenance therapy)
 - for complete remission and relapse <6 months after completing chemotherapy
- Maintenance therapy as a single agent if used previously as part of a combination therapy for individuals with PR or CR following recurrence therapy with chemotherapy plus bevacizumab for platinum-sensitive disease

Malignant Sex Cord-Stromal Tumors

- As a single agent for clinical relapse in individuals with stage II-IV disease

Clear Cell Carcinoma of the Ovary

- Maintenance therapy in combination with olaparib or niraparib (if unable to tolerate olaparib) for stage II-IV clear cell carcinoma with a germline or somatic BRCA1/2 mutation if CR or PR to primary therapy including bevacizumab
- As a therapy for platinum-resistant persistent disease or recurrence in combination with oral cyclophosphamide (NCCN-preferred), oral cyclophosphamide and pembrolizumab, liposomal doxorubicin (NCCN-preferred), weekly paclitaxel (NCCN-preferred), or topotecan (NCCN-preferred), gemcitabine, mirvetuximab soravtansine-

gynx (in folate receptor-alpha-expressing tumors; useful in certain circumstances) except for immediate treatment of biochemical relapse for any of the following:

- as immediate treatment for serially rising CA-125 in individuals who previously received chemotherapy
 - for progression on primary, maintenance, or recurrence therapy
 - stable or persistent disease (if not on maintenance therapy)
 - for complete remission and relapse <6 months after completing chemotherapy
- For persistent disease or recurrence (except for immediate treatment of biochemical relapse)
 - as immediate treatment for serially rising CA-125 in individuals who previously received chemotherapy
 - for progression on primary, maintenance, or recurrence therapy (platinum resistant)
 - for stable or persistent disease (if not on maintenance therapy) (platinum resistant)
 - in individuals with complete remission and relapse ≥ 6 months after completing prior chemotherapy (platinum resistant)
 - in individuals with complete remission and relapse ≥ 6 months after completing prior chemotherapy (platinum sensitive)
 - in combination with:
 - carboplatin and gemcitabine (NCCN preferred in platinum-sensitive disease)
 - carboplatin and paclitaxel (NCCN preferred in platinum-sensitive disease)
 - carboplatin and liposomal doxorubicin (NCCN preferred in platinum-sensitive disease)
- As NCCN-preferred targeted therapy as a single agent for persistent disease or recurrence (except for immediate treatment of biochemical relapse)
 - as immediate treatment for serially rising CA-125 in individuals who previously received chemotherapy
 - for progression on primary, maintenance, or recurrence therapy (platinum-resistant disease)
 - for stable or persistent disease (if not on maintenance therapy) (platinum-resistant disease)
 - for complete remission and relapse <6 months after completing chemotherapy (platinum-resistant disease)
 - for radiographic and/or clinical relapse in individuals with previous complete remission and relapse ≥ 6 months after completing prior chemotherapy (platinum-sensitive disease)
- As an NCCN-preferred therapy for rising CA-125 levels or clinical relapse in individuals who have received no prior chemotherapy in combination with paclitaxel and carboplatin

- Maintenance therapy as a single agent (useful in certain circumstances) if used previously as part of a combination therapy for individuals with PR or CR following recurrence therapy with chemotherapy plus bevacizumab for platinum-sensitive disease

Grade 1 Endometrioid Carcinoma

- Therapy for platinum-resistant persistent disease or recurrence in combination with oral cyclophosphamide (NCCN-preferred), oral cyclophosphamide and pembrolizumab, liposomal doxorubicin (NCCN preferred), weekly paclitaxel (NCCN preferred), or topotecan (NCCN preferred), gemcitabine, mirvetuximab, soravtansine-gynx (in folate receptor-alpha-expressing tumors; useful in certain circumstances) except for immediate treatment of biochemical relapse
 - as immediate treatment for serially rising CA-125 in individuals who previously received chemotherapy
 - for progression on primary, maintenance, or recurrence therapy
 - stable or persistent disease (if not on maintenance therapy)
 - for complete remission and relapse <6 months after completing chemotherapy
- As an NCCN-preferred targeted therapy as a single agent for persistent disease or recurrence except for immediate treatment of biochemical relapse
 - as immediate treatment for serially rising CA-125 in individuals who previously received chemotherapy
 - for progression on primary, maintenance, or recurrence therapy (platinum-resistant disease)
 - for stable or persistent disease (if not on maintenance therapy) (platinum-resistant disease)
 - for complete remission and relapse <6 months after completing chemotherapy (platinum-resistant disease)
 - for radiographic and/or clinical relapse in individuals with previous complete remission and relapse ≥6 months after completing prior chemotherapy (platinum-sensitive disease)
- Preferred treatment for rising CA-125 levels or clinical relapse in individuals who have received no prior chemotherapy in combination with paclitaxel and carboplatin
- As adjuvant therapy in combination with carboplatin and paclitaxel (NCCN preferred) for pathologic stage II-IV, grade 1 endometrioid carcinoma
- For persistent disease or recurrence (except for immediate treatment of biochemical relapse) for the following indications:
 - as immediate treatment for serially rising CA-125 in individuals who previously received chemotherapy (platinum sensitive or platinum resistant)
 - for progression on primary, maintenance, or recurrence therapy (platinum resistant)
 - for stable or persistent disease (if not on maintenance therapy) (platinum resistant)*
 - for complete remission and relapse <6 months after completing chemotherapy (platinum resistant)

- in individuals with complete remission and relapse ≥ 6 months after completing prior chemotherapy (platinum sensitive)
 - in combination with:
 - carboplatin and gemcitabine
 - carboplatin and paclitaxel
 - carboplatin and liposomal doxorubicin
- Maintenance therapy as a single agent if used previously as part of a combination therapy for individuals with PR or CR following recurrence therapy with chemotherapy plus bevacizumab for platinum-sensitive disease

Low-Grade Serous Carcinoma

- As NCCN-preferred treatment for recurrence in individuals who have received no prior chemotherapy in combination with paclitaxel and carboplatin
- As NCCN-preferred targeted therapy as a single agent for platinum-sensitive or platinum-resistant recurrence
- As therapy in combination with gemcitabine for platinum-resistant recurrence
- As therapy for platinum-resistant recurrence in combination with oral cyclophosphamide (NCCN preferred), oral cyclophosphamide and pembrolizumab, liposomal doxorubicin (NCCN preferred), weekly paclitaxel (NCCN preferred), or topotecan (NCCN preferred), mirvetuximab soravtansine-gynx (in folate receptor-alpha-expressing tumors)
- As treatment for platinum-sensitive or platinum-resistant persistent disease or recurrence (except for immediate treatment of biochemical relapse) as immediate treatment for serially rising CA-125 or in individuals who previously received chemotherapy in individuals with complete remission and relapse ≥ 6 months after completing prior chemotherapy in combination with:
 - carboplatin and gemcitabine (NCCN preferred in platinum-sensitive disease)
 - carboplatin and paclitaxel (NCCN preferred in platinum-sensitive disease)
 - carboplatin and liposomal doxorubicin (NCCN preferred in platinum-sensitive disease)
- As NCCN-preferred adjuvant therapy in combination with carboplatin and paclitaxel (NCCN preferred) for pathologic stage II-IV low-grade serous carcinoma
- Maintenance therapy as a single agent if used previously as part of a combination therapy for individuals with PR or CR following recurrence therapy with chemotherapy plus bevacizumab for platinum-sensitive disease

Mucinous Carcinoma

- As NCCN-preferred therapy for rising CA-125 levels or clinical relapse in individuals who have received no prior chemotherapy in combination with paclitaxel and carboplatin
- NCCN-preferred therapy for platinum-sensitive persistent disease or recurrence (except for immediate treatment of biochemical relapse)
 - as immediate treatment for serially rising CA-125 in individuals who previously received chemotherapy

- in individuals with complete remission and relapse ≥ 6 months after completing prior chemotherapy
 - in combination with
 - carboplatin and gemcitabine (NCCN preferred)
 - carboplatin and paclitaxel (NCCN preferred)
 - carboplatin and liposomal doxorubicin (NCCN preferred)
- Therapy for platinum-resistant persistent disease or recurrence (except for immediate treatment of biochemical relapse)
 - as immediate treatment for serially rising CA-125 in individuals who previously received chemotherapy
 - for progression on primary, maintenance, or recurrence therapy
 - for stable or persistent disease (if not on maintenance therapy)
 - for complete remission and relapse < 6 months after completing chemotherapy
 - in combination with any of the following:
 - carboplatin and gemcitabine
 - carboplatin and paclitaxel
 - carboplatin and liposomal doxorubicin
- As adjuvant treatment for pathologic stage II-IV disease in combination with carboplatin and paclitaxel
- As adjuvant treatment in combination with oxaliplatin and docetaxel for pathologic stage II-IV disease
- As NCCN-preferred targeted therapy as a single agent for persistent disease or recurrence except for immediate treatment of biochemical relapse
 - as immediate treatment for serially rising CA-125 in individuals who previously received chemotherapy
 - for progression on primary, maintenance, or recurrence therapy (platinum-resistant disease)
 - for stable or persistent disease (if not on maintenance therapy) (platinum-resistant disease)
 - for complete remission and relapse < 6 months after completing chemotherapy (platinum-resistant disease)
 - for radiographic and/or clinical relapse in individuals with previous complete remission and relapse ≥ 6 months after completing prior chemotherapy (platinum-sensitive disease)
- As therapy for platinum-resistant persistent disease or recurrence in combination with oral cyclophosphamide (NCCN preferred), oral cyclophosphamide and pembrolizumab liposomal doxorubicin (NCCN preferred), weekly paclitaxel (NCCN preferred), or topotecan (NCCN preferred) gemcitabine, mirvetuximab soravtansine-gynx (in folate receptor- α -expressing tumors), except for immediate treatment of biochemical relapse
 - as immediate treatment for serially rising CA-125 in individuals who previously received chemotherapy
 - for progression on primary, maintenance, or recurrence therapy
 - stable or persistent disease (if not on maintenance therapy)

- for complete remission and relapse <6 months after completing chemotherapy
- Maintenance therapy as a single agent if used previously as part of combination therapy for individuals with PR or CR following recurrence therapy with chemotherapy plus bevacizumab for platinum-sensitive disease

SOFT TISSUE SARCOMA

- In individuals with angiosarcoma as a single agent
- In individuals with solitary fibrous tumor or hemangiopericytoma in combination with temozolomide, as NCCN-preferred therapy.

UTERINE CANCER/ENDOMETRIAL CANCER

- First-line therapy (or Second-line or subsequent therapy as clinically appropriate if not used previously) in combination with carboplatin and paclitaxel and continued as a single agent for maintenance therapy for advanced and recurrent disease only for any of the following:
 - second-line or subsequent therapy for isolated metastases
 - for disseminated metastases with or without sequential palliative external beam radiation therapy (EBRT)
 - after surgical exploration, with sequential EBRT for locoregional recurrence in individuals with disease confined to the vagina or paravaginal soft tissue, or in pelvic, para-aortic or common iliac lymph nodes
 - after surgical exploration, with or without sequential EBRT for locoregional recurrence in individuals with upper abdominal or peritoneal disease
 - with or without sequential palliative EBRT or brachytherapy for locoregional recurrence in individuals who have received prior EBRT to site of recurrence
- Second-line or subsequent therapy as a single agent for recurrent disease that has progressed on prior cytotoxic chemotherapy for any of the following indications:
 - may be considered for isolated metastases
 - for disseminated metastases with or without sequential palliative external beam radiation therapy (EBRT)
 - with sequential EBRT and with or without brachytherapy for locoregional recurrence in individuals with no prior RT to site of recurrence, or previous brachytherapy only
 - after surgical exploration, with sequential EBRT for locoregional recurrence in individuals with disease confined to the vagina or paravaginal soft tissue, or in pelvic, para-aortic or common iliac lymph nodes
 - after surgical exploration, with or without sequential EBRT for locoregional recurrence in individuals with upper abdominal or peritoneal disease
 - with or without sequential palliative EBRT or brachytherapy for locoregional recurrence in individuals who have received prior EBRT to site of recurrence

VAGINAL CANCER

- or:
 - local/regional recurrence if prior intracavitary brachytherapy only, or prior EBRT with or without brachytherapy and noncentral disease

- stage IVB or recurrent distant metastases
- First-line, second-line, or subsequent therapy as clinically appropriate (if not used previously as first-line) in combination with paclitaxel and cisplatin or carboplatin (preferred regimens), or in combination with paclitaxel and topotecan for
 - local/regional recurrence if prior intracavitary brachytherapy only, or prior EBRT with or without brachytherapy and noncentral disease
 - stage IVB or recurrent distant metastases
- Second-line or subsequent therapy as a single agent for
 - local/regional recurrence
 - stage IVB or recurrent distant metastases

VULVAR CANCER

- First-line therapy for advanced or recurrent/metastatic disease (or second-line or subsequent therapy as clinically appropriate if not used previously) in combination with cisplatin (NCCN-preferred regimen) for any of the following:
 - as additional treatment following primary therapy with concurrent chemoradiation for locally advanced unresectable disease (larger T2, T3) or initially unresectable nodes regardless of T stage that is clinically positive for residual tumor at the primary site and/or nodes
 - as additional treatment following primary therapy with concurrent chemoradiation for locally advanced disease or initially unresectable nodes regardless of T stage with positive margins for invasive disease following resection
 - as primary treatment for metastatic disease beyond the pelvis (Stage IVB)
 - for confirmed isolated inguinofemoral/pelvic lymph node recurrence if prior external beam radiation therapy (EBRT)
 - for confirmed nodal or distant recurrence with multiple pelvic nodes, distant metastasis, or prior pelvic EBRT

Duration of authorization: 12 months

Version Effective Date: 01/01/2025

Title: Blinatumomab (Blinicyto®)

MEDICALLY NECESSARY:

Blinatumomab (Blinicyto) is considered medically necessary and, therefore, covered for individuals with acute lymphoblastic leukemia (ALL) who meet any of the following criteria, including Dosing and Frequency Requirements:

MINIMAL RESIDUAL DISEASE–POSITIVE (MRD+) DISEASE

- CD19-positive B-cell precursor acute lymphoblastic leukemia (B-ALL) in adult or pediatric individuals in first or second complete remission with minimal residual disease (MRD) greater than or equal to 0.1%
- Philadelphia chromosome (Ph)-negative or Ph-like B-ALL that is MRD+ in pediatric individuals as a single agent, incorporated into frontline consolidation therapy
- Ph-negative or Ph-like B-ALL that is MRD+ in pediatric individuals, after intensified consolidation therapy as a single agent
- Ph-positive B-ALL in pediatric individuals MRD+ at end of consolidation, as a single agent incorporated into frontline consolidation therapy with imatinib or dasatinib

MINIMAL RESIDUAL DISEASE–NEGATIVE (MRD-) DISEASE

- Ph-negative or Ph-like B-ALL MRD- disease in pediatric individuals as a single agent, incorporated into frontline consolidation therapy
- Ph-negative or Ph-like B-ALL MRD- disease in pediatric individuals after intensified consolidation therapy, as a single agent incorporated into continuation of frontline consolidation therapy
- Ph-positive B-ALL if refractory to TKIs in adults with MRD- as part of maintenance as a single agent alternating with POMP (mercaptopurine, vincristine, methotrexate, prednisone), if induced with inotuzumab ozogamicin + mini-hyperCVD + sequential blinatumomab

MINIMAL RESIDUAL DISEASE–NEGATIVE (MRD-) OR MRD-UNAVAILABLE DISEASE

- Consolidation as a single agent for Ph-negative B-ALL in one of the following:
 - Adolescent and Young Adult (AYA) without substantial comorbidities and adults, alternating with frontline[†] multiagent therapy (if not already included in a multi-part regimen)
 - AYA without substantial comorbidities and adults[†], after multiagent therapy, or if multiagent therapy is contraindicated
 - Alternating with ECOG1910: cyclophosphamide, cytarabine, daunorubicin, dexamethasone, etoposide, mercaptopurine, high-dose methotrexate, pegaspargase, vincristine, rituximab for CD20-positive disease, in one of the following:
 - Frontline therapy in AYA without substantial comorbidities and adults (National Comprehensive Cancer Network [NCCN]-preferred regimen for adults aged <65 years without substantial comorbidities)

- Refractory therapy in adults aged ≥ 65 years or adults with substantial comorbidities
 - Late relapse (>3 years from initial diagnosis) if regimen used in frontline in AYA without substantial comorbidities and adults
- Sequential Consolidation therapy for Ph-negative B-ALL, as a single agent after dose-adjusted HyperCVAD[§] (hyperfractionated cyclophosphamide, mesna, vincristine, doxorubicin, dexamethasone, IT methotrexate, IT cytarabine alternating with high-dose methotrexate, leucovorin, dose-adjusted cytarabine, IT methotrexate, IT cytarabine), in one of the following:
 - Frontline therapy in AYA without substantial comorbidities and adults
 - Refractory therapy in adults aged ≥ 65 years or adults with substantial comorbidities
 - Late relapse (>3 years from initial diagnosis) if regimen used in frontline in AYA without substantial comorbidities and adults
- Maintenance in Ph-negative ALL in AYA without substantial comorbidities and adult individuals as a single agent alternating with POMP[¶] (prednisone, vincristine, methotrexate, and mercaptopurine) in individuals with negative MRD or MRD unavailable after induction therapy with dose-adjusted HyperCVAD (hyperfractionated cyclophosphamide, mesna, vincristine, doxorubicin, dexamethasone, IT methotrexate, IT cytarabine alternating with high-dose methotrexate, leucovorin, dose-adjusted cytarabine, IT methotrexate, IT cytarabine; plus sequential blinatumomab as part of consolidation
- Frontline[†] therapy for Ph-negative B-ALL in adults with negative MRD or MRD unavailable, as a single agent in one of the following regimens:
 - Consolidation when used sequentially with inotuzumab ozogamicin + mini-hyperCVD (cyclophosphamide, vincristine, dexamethasone, inotuzumab ozogamicin alternating with cytarabine, methotrexate, inotuzumab ozogamicin)
 - Maintenance when alternating with POMP (mercaptopurine, vincristine, methotrexate, prednisone), if induced with inotuzumab ozogamicin + mini-hyperCVD + sequential blinatumomab
- Relapsed/refractory for Ph-negative B-ALL in adults with negative MRD or MRD unavailable as a single agent in one of the following regimens:
 - Consolidation when used sequentially with inotuzumab ozogamicin + mini-hyperCVD (cyclophosphamide, vincristine, dexamethasone, inotuzumab ozogamicin alternating with cytarabine, methotrexate, inotuzumab ozogamicin)
 - Maintenance when alternating with POMP (mercaptopurine, vincristine, methotrexate, prednisone), if induced with inotuzumab ozogamicin + mini-hyperCVD + sequential blinatumomab
- Sequential Consolidation therapy for Ph-positive B-ALL in adults refractory to TKIs with negative MRD or MRD unavailable disease as a single agent after inotuzumab ozogamicin + mini-hyperCVD (cyclophosphamide, vincristine, dexamethasone, inotuzumab ozogamicin alternating with cytarabine, methotrexate, inotuzumab ozogamicin)

§ Dose-adjusted HyperCVAD used with rituximab for AYA without substantial comorbidities and adults with CD20-positive disease; include methylprednisolone if CD20-positive B-ALL.

¶ POMP used with rituximab for AYA without substantial comorbidities and adults with CD20-positive disease; include methylprednisolone if CD20-positive.

PERSISTENT/RISING MINIMAL/MEASURABLE RESIDUAL DISEASE (MRD)

- Frontline[†] consolidation as a single agent if persistent/rising minimal/MRD for Ph-positive B-ALL in adolescent and young adult (AYA) without substantial comorbidities and adults.
- Consolidation[†] as a single agent for Ph-negative B-ALL in AYA without substantial comorbidities and adults with persistent/rising minimal/MRD (NCCN-preferred if have not previously received blinatumomab)

ALL REGARDLESS OF MINIMAL RESIDUAL DISEASE (MRD) DISEASE

- Ph-positive B-ALL in combination with a TKI* during frontline[†] induction or frontline[†] consolidation therapy for adolescent and young adult (AYA) without substantial comorbidities and adults (NCCN-preferred in consolidation regardless of MRD status for those who have not previously received blinatumomab)

RELAPSED OR REFRACTORY DISEASE

- Relapsed or refractory Ph-negative CD19-positive B-ALL in pediatric and adult individuals as a single agent (NCCN-preferred regimen in adults)
- Relapsed or refractory Ph-negative B-ALL in pediatric individuals
 - as a single agent
 - as a component of COG AALL1331 regimen
- Relapsed or refractory Ph-positive CD19-positive B-ALL as a single agent in pediatric and adult individuals
- Relapsed or refractory Ph-positive B-ALL in pediatric individuals who are TKI* intolerant/refractory
- Relapsed or refractory Ph-positive B-ALL in combination with a TKI* (NCCN-preferred in consolidation regardless of MRD status for those who have not previously received blinatumomab)
- Relapsed or refractory Ph-positive B-ALL in pediatric individuals in combination with dasatinib or imatinib, as a component of COG AALL1331 regimen

ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) IN INFANTS

- Induction in combination with Interfant regimens for infant ALL with KMT2A status (11q23) rearranged
- Infant ALL with KMT2A status (11q23) not rearranged (standard risk) as a single agent, incorporated into frontline consolidation therapy

ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) IN PEDIATRIC INDIVIDUALS WITH STANDARD OR HIGH-RISK DISEASE[‡]

- Ph-positive B-ALL with standard risk disease[‡] and low MRD, as a single agent incorporated into frontline consolidation therapy with imatinib or dasatinib

- Ph-positive B-ALL with high risk disease[†] and less than complete response at end of consolidation, as a single agent incorporated into frontline consolidation therapy with imatinib or dasatinib
- Ph-positive B-ALL as consolidation therapy in combination with imatinib or dasatinib for individuals with high-risk disease[†] and less than complete response, or MRD+ at end of consolidation

*TKI options include bosutinib, dasatinib, imatinib, nilotinib, or ponatinib. Imatinib use in first line should be restricted to those who cannot tolerate broader acting

TKIs. TKI/mutation contraindications: Bosutinib - T315I, V299L, G250E, or F317L; Dasatinib - T315I/A, F317L/V/I/C or V299L; Imatinib too numerous to include; Nilotinib - T315I, Y253H, E255K/V, F359V/C/I or G250E.

[†] There are data to support the benefit of rituximab for CD20-positive disease in addition to chemotherapy (excluding immunotherapy) for AYA and adults aged less than 65 years without substantial comorbidities (especially if aged <60 years).

[‡] Risk Stratification of ALL:

- Standard risk criteria: Aged ≥1 y to <10 y and white blood cell (WBC) count <50,000/mm³
- High-risk criteria: Aged <1 y or ≥10 y, and/or WBC count ≥50,000/mm³

DOSING AND FREQUENCY REQUIREMENTS

The Company reserves the right to modify the Dosing and Frequency Requirements listed in this policy to ensure consistency with the most recently published recommendations for the use of blinatumomab (Blinicyto). Changes to these guidelines are based on a consensus of information obtained from resources such as, but not limited to, the US Food and Drug Administration (FDA); Company-recognized authoritative pharmacology compendia; or published peer-reviewed clinical research. The professional provider must supply supporting documentation (i.e., published peer-reviewed literature) in order to request coverage for an amount of blinatumomab (Blinicyto) outside of the Dosing and Frequency Requirements listed in this policy. For a list of Company-recognized pharmacology compendia, view our policy on off-label coverage for prescription drugs and biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of this drug. If the member's dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider must submit those changes to the Company for a new approval based on those changes as part of the precertification process. The Company reserves the right to conduct postpayment review and audit procedures for any claims submitted for blinatumomab (Blinicyto).

Ph-POSITIVE OR Ph-NEGATIVE B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA (B-ALL)

For Ph-positive or Ph-Negative B-ALL, a treatment course consists of one cycle of blinatumomab (Blinicyto) for induction (Cycle 1), followed by up to three additional cycles for consolidation treatment (Cycles 2–4). Each cycle consists of 4 weeks of continuous intravenous infusion followed by a 2-week treatment-free interval (total, 42 days). Do not exceed a maximum of 875 mcg, or 25 vials, per month.

Induction Cycle 1 and Consolidation Cycles 2–4

- Days 1–28
 - Weight ≥ 45 kg: 28 mcg/day
 - Weight < 45 kg: 15 mcg/m²/day, not to exceed 28 mcg/day
- Days 29–42: 14-day treatment-free interval

RELAPSED OR REFRACTORY B-CELL ALL

For relapsed or refractory B-ALL, a treatment course consists of up to two cycles of blinatumomab (Blinicyto) for induction (Cycles 1–2), followed by three additional cycles for consolidation treatment (Cycles 3–5) and up to four additional cycles of continued therapy (Cycles 6–9). Each induction or consolidation therapy cycle consists of 4 weeks of continuous intravenous infusion followed by a 2-week treatment-free interval (total, 42 days). Each continued therapy cycle consists of 4 weeks of continuous intravenous infusion followed by an 8-week treatment-free interval (total, 84 days). Do not exceed a maximum of 875 mcg, or 25 vials, per month.

Induction Cycle 1, Days 1–7

- Weight ≥ 45 kg: 9 mcg/day
- Weight < 45 kg: 5 mcg/m²/day, not to exceed 9 mcg/day

Induction Cycle 1, Days 8–28

- Weight ≥ 45 kg: 28 mcg/day
- Weight < 45 kg: 15 mcg/m²/day, not to exceed 28 mcg/day

Induction Cycle 1, Days 29–42: 14-day treatment-free interval

Induction Cycle 2 and Consolidation Cycles 3–5

- Days 1–28
 - Weight ≥ 45 kg: 28 mcg/day
 - Weight < 45 kg: 15 mcg/m²/day, not to exceed 28 mcg/day
- Days 29–42: 14-day treatment-free interval

Consolidation Cycles 6–9

- Days 1–28
 - Weight ≥ 45 kg: 28 mcg/day
 - Weight < 45 kg: 15 mcg/m²/day, not to exceed 28 mcg/day
- Days 29–84: 56-day treatment-free interval

Duration of authorization: 12 months

Version Effective Date: 11/04/2024

Title: Botulinum Toxin Agents

MEDICALLY NECESSARY:

BOTULINUM TOXIN A

OnabotulinumtoxinA (Botox), AbobotulinumtoxinA (Dysport), IncobotulinumtoxinA (Xeomin), DaxibotulinumtoxinA-lanm (Daxxify)

OnabotulinumtoxinA (Botox), abobotulinumtoxinA (Dysport), incobotulinumtoxinA (Xeomin), and daxibotulinumtoxinA-lanm (Daxxify) are considered medically necessary and, therefore, covered in adult individuals for the following indications:

- Achalasia and cardiospasm when at least one of the following criteria is met:
 - The individual whose condition has failed to respond to conventional therapy (e.g., sitting upright after eating, use of achalasia wedge for positioning, use of protein pump inhibitors or calcium channel blockers) or has a contraindication to such therapy.
 - The individual is at high risk of complications from pneumatic dilation or surgical myotomy.
 - The individual whose condition has failed to respond to prior myotomy or dilation.
 - The individual has prior dilation-induced esophageal perforation.
 - The individual has an epiphrenic diverticulum or hiatal hernia.
 - The individual is a poor surgical candidate.
- Blepharospasm in individuals 12 years of age and older
- Cervical dystonia (spasmodic torticollis)
- Chronic anal fissure with anal spasm (proctalgia fugax) with documentation that the individual has been unresponsive to one of the following:
 - Conservative treatments (e.g., sitz baths, topical anesthetics and steroids, topical glyceryl trinitrate [nitroglycerin])
 - Lateral sphincterotomy
- Prevention of chronic migraine headache or probable migraine headache occurring at least 15 days per month for at least 3 months when the duration of untreated headache on average is at least 4 hours per day. Initial treatment for botulinum toxin A is medically necessary when all of the following criteria are met:
 - A neurologist, headache specialist (headache specialist is a physician certified by the United Council for Neurologic Subspecialties [UCNS]), or pain specialist has established a diagnosis of either of the following:
 - Chronic migraine headache **OR**
 - Chronic probable migraine headache when the individual has experienced either of any two of the following pain criteria:
 - Moderate-to-severe headache pain intensity
 - Unilateral headache pain
 1. Pain aggravated by movement or pain that prohibits movement

2. Throbbing headache pain

OR

- One of the above pain criteria and one of the following associated symptoms:
 1. Nausea
 2. Sensitivity to light (photophobia) and sound (phonophobia)
- Prevention of chronic migraine headache or probable migraine headache with continued treatment will be medically necessary every 12 weeks when all of the following criteria are met:
 - The provider reports a clinically significant decrease in the frequency of headache days from the reported baseline of frequency prior to the initiation of the first series of botulinum toxin injections.
 - The re-treatment is based on continued, sustained improvement.
- Essential hand tremor in an individual whose condition has failed to respond to treatment with oral agent(s) (e.g., propranolol [Inderal], primidone [Mysoline])
- Focal dystonia or spastic dystonia: to relieve pain; to assist in posturing and walking; to increase range of motion; to assist in the outcome of physical therapy; and/or to reduce spasm, thus allowing adequate perineal hygiene after the failure of conventional treatment methods (e.g., trihexyphenidyl [Artane], tetrabenazine [Xenazine]) or if a contraindication to such treatments exist
- Hemifacial spasm
- Interstitial cystitis, as a fourth-line treatment option, after documented failure, intolerability, or contraindication to medical therapy (e.g., behavior/diet modification, pharmacologic therapy, pelvic floor physical therapy, intravesical instillations, hydrodistention)
- Isolated oromandibular dystonia
- Plantar-palmar hyperhidrosis refractory to conventional treatment options, including both topical and systemic pharmacotherapy (e.g., topical: astringents, iontophoresis; systemic: anticholinergic drugs; psychotherapy), unless clinically contraindicated AND one of the following:
 - The condition is significantly interfering with the ability to perform activities of daily living.
 - The condition is causing persistent or chronic cutaneous complications, such as skin maceration, dermatitis, secondary fungal, and microbial infections.
- Severe primary axillary hyperhidrosis that is inadequately managed by topical agents in individuals, who manifest focal, visible, severe sweating beyond physiological needs for at least 6 months without apparent cause when at least two of the following criteria are met:
 - Age of onset is younger than 25 years of age
 - Focal sweating is bilateral and relatively symmetric
 - Focal sweating does not occur during sleep
 - Family history is positive for severe primary focal hyperhidrosis

- Hyperhidrosis significantly impairs the individual's ability to participate in daily activities
- Sialorrhea (excessive drooling) due to disabling conditions such as motor neuron disease or Parkinson disease in individuals whose condition has failed to respond to a reasonable trial of traditional therapies (i.e., anticholinergics, speech therapy, surgical therapy) or who have a contraindication to such therapy
- Spasmodic dysphonia/laryngeal dystonia (e.g., abductor dysphonia, adductor dysphonia)
- Spasticity of upper and lower limbs in adult individuals, related to any of the following conditions:
 - Cerebral palsy (CP), including use for treatment of equinus foot deformity
 - Demyelinating diseases of the central nervous system
 - Brain injury
 - Hemiplegia or paraplegia
 - Multiple sclerosis
 - Spinal cord injury
 - Stroke
- Botherome simple motor tics (e.g., eye blinking, nose movement, head jerks) in individuals 10 years of age and older and when the benefits of treatment outweigh the risks
- Severely disabling or aggressive vocal tics in individuals 10 years of age and older when the benefits of treatment outweigh the risks
- Tourette disorder with chronic motor or vocal tics in individuals 10 years of age and older
- Urinary incontinence due to neurogenic bladder after documented failure, intolerability, or contraindication to medical therapy (e.g., pelvic floor exercises, diet/fluid management, anticholinergics, intermittent catheterization)
- Urinary incontinence due to overactive bladder with symptoms of urge urinary incontinence, urgency, and frequency
 - The individual has a documented failure, intolerability, or contraindication to one of the following:
 - Anticholinergic medication (e.g., darifenacin [Enablex], trospium [Trosec])
 - Beta-3 adrenergic agonist (e.g., Myrbetriq or one generic alternative [solifenacin, oxybutynin tabs/tab ER/syrup, tolterodine, etc.])

OnabotulinumtoxinA (Botox), abobotulinumtoxinA (Dysport), incobotulinumtoxinA (Xeomin), and daxibotulinumtoxinA-lanm (Daxxify) are considered medically necessary and, therefore, covered in pediatric individuals for the following indications:

- Spasticity of upper limbs, in pediatric individuals who are 2 years or older, related to CP or stroke when all of the following criteria are met:
 - Body weight 10 kg or over
 - Modified Ashworth Scale (MAS*) score of 2 or more in affected elbow or wrist flexors
- Spasticity of lower limbs related to CP in pediatric individuals who are 2 years or older, when all of the following criteria are met:

- Body weight 10 kg or over
 - CP with dynamic muscle contracture of the ankle
- Strabismus in visually mature individuals (≥12 years of age) who have vision in both eyes, are unable to maintain fusion of image, and have at least one of the following:
 - Diplopia
 - Abnormal head turn
 - Asthenopia
 - Impairment of peripheral vision due to esotropia
- Chronic sialorrhea in individuals 2 years of age or older when any of the following criteria are met:
 - The individual diagnosed with a neurological disorder (e.g., CP or traumatic brain injury) and/or intellectual disability (ID) associated with chronic troublesome sialorrhea for at least 3 months.
 - The individual has an ID without neurological disorders, and the diagnosis of ID was established by a specialist, e.g., pediatrician, or by a center for developmental medicine.
 - The individual has severe drooling (modified Teachers Drooling Scale [mTDS] ≥6; clothing occasionally becomes damp)
- Neurogenic detrusor overactivity (NDO) in pediatric individuals 5 years of age and older when all of the following criteria are met:
 - The individual had an inadequate response to or was intolerant of at least one anticholinergic agent (e.g., oxybutynin [Ditropan XL, Oxytrol], tolterodine [Detrol]).
 - The individual is regularly using clean intermittent catheterization to empty the bladder
 - The individual does not have any of the following:
 - Surgery of the spinal cord within 6 months
 - Diagnosis of CP
 - Use of an indwelling catheter for urinary incontinence
 - Myasthenia gravis, Eaton-Lambert syndrome, or amyotrophic lateral sclerosis

BOTULINUM TOXIN B

RimabotulinumtoxinB (Myobloc)

RimabotulinumtoxinB (Myobloc) is considered medically necessary and, therefore, covered in adult individuals for the following indications:

- Cervical dystonia (spasmodic torticollis)
- Sialorrhea (excessive drooling) due to disabling conditions such as motor neuron disease or Parkinson disease in individuals whose condition has failed to respond to a reasonable trial of traditional therapies (i.e., anticholinergics, speech therapy, surgical therapy) or who have a contraindication to such therapy

Duration of authorization: 12 months

Version Effective Date: 04/21/2025

Title: Botulinum Toxin Agents

MEDICALLY NECESSARY

BOTOX (ONABOTULINUMTOXINA), DYSPORT (ABOBOTULINUMTOXINA), XEOMIN (INCOBOTULINUMTOXINA), AND DAXXIFY (DAXIBOTULINUMTOXINA-LANM) ARE CONSIDERED MEDICALLY NECESSARY FOR THE FOLLOWING INDICATIONS:

F95.1 Chronic motor or vocal tic disorder
F95.2 Tourette's disorder
G04.1 Tropical spastic paraplegia
G11.4 Hereditary spastic paraplegia
G24.09 Other drug induced dystonia
G24.1 Genetic torsion dystonia
G24.2 Idiopathic nonfamilial dystonia
G24.3 Spasmodic torticollis
G24.4 Idiopathic orofacial dystonia
G24.5 Blepharospasm
G24.8 Other dystonia
G24.9 Dystonia, unspecified
G25.0 Essential tremor
G25.89 Other specified extrapyramidal and movement disorders
G43.001 Migraine without aura, not intractable, with status migrainosus
G43.009 Migraine without aura, not intractable, without status migrainosus
G43.011 Migraine without aura, intractable, with status migrainosus
G43.019 Migraine without aura, intractable, without status migrainosus
G43.101 Migraine with aura, not intractable, with status migrainosus
G43.109 Migraine with aura, not intractable, without status migrainosus
G43.111 Migraine with aura, intractable, with status migrainosus
G43.119 Migraine with aura, intractable, without status migrainosus
G43.401 Hemiplegic migraine, not intractable, with status migrainosus
G43.409 Hemiplegic migraine, not intractable, without status migrainosus
G43.411 Hemiplegic migraine, intractable, with status migrainosus
G43.419 Hemiplegic migraine, intractable, without status migrainosus
G43.501 Persistent migraine aura without cerebral infarction, not intractable, with status migrainosus
G43.509 Persistent migraine aura without cerebral infarction, not intractable, without status migrainosus
G43.511 Persistent migraine aura without cerebral infarction, intractable, with status migrainosus
G43.519 Persistent migraine aura without cerebral infarction, intractable, without status migrainosus
G43.601 Persistent migraine aura with cerebral infarction, not intractable, with status migrainosus

G43.609 Persistent migraine aura with cerebral infarction, not intractable, without status migrainosus
G43.611 Persistent migraine aura with cerebral infarction, intractable, with status migrainosus
G43.619 Persistent migraine aura with cerebral infarction, intractable, without status migrainosus
G43.701 Chronic migraine without aura, not intractable, with status migrainosus
G43.709 Chronic migraine without aura, not intractable, without status migrainosus
G43.711 Chronic migraine without aura, intractable, with status migrainosus
G43.719 Chronic migraine without aura, intractable, without status migrainosus
G43.801 Other migraine, not intractable, with status migrainosus
G43.809 Other migraine, not intractable, without status migrainosus
G43.811 Other migraine, intractable, with status migrainosus
G43.819 Other migraine, intractable, without status migrainosus
G43.901 Migraine, unspecified, not intractable, with status migrainosus
G43.909 Migraine, unspecified, not intractable, without status migrainosus
G43.911 Migraine, unspecified, intractable, with status migrainosus
G43.919 Migraine, unspecified, intractable, without status migrainosus
G43.B0 Ophthalmoplegic migraine, not intractable
G43.B1 Ophthalmoplegic migraine, intractable
G43.E01 Chronic migraine with aura, not intractable, with status migrainosus
G43.E09 Chronic migraine with aura, not intractable, without status migrainosus
G43.E11 Chronic migraine with aura, intractable, with status migrainosus
G43.E19 Chronic migraine with aura, intractable, without status migrainosus
G51.2 Melkersson's syndrome
G51.31 Clonic hemifacial spasm, right
G51.32 Clonic hemifacial spasm, left
G51.33 Clonic hemifacial spasm, bilateral
G51.8 Other disorders of facial nerve
G61.0 Guillain-Barre syndrome
G80.0 Spastic quadriplegic cerebral palsy
G80.1 Spastic diplegic cerebral palsy
G80.2 Spastic hemiplegic cerebral palsy
G81.11 Spastic hemiplegia affecting right dominant side
G81.12 Spastic hemiplegia affecting left dominant side
G81.13 Spastic hemiplegia affecting right nondominant side
G81.14 Spastic hemiplegia affecting left nondominant side
G82.50 Quadriplegia, unspecified
G82.51 Quadriplegia, C1-C4 complete
G82.52 Quadriplegia, C1-C4 incomplete
G82.53 Quadriplegia, C5-C7 complete
G82.54 Quadriplegia, C5-C7 incomplete
G83.0 Diplegia of upper limbs
G83.11 Monoplegia of lower limb affecting right dominant side
G83.12 Monoplegia of lower limb affecting left dominant side

G83.13 Monoplegia of lower limb affecting right nondominant side
G83.14 Monoplegia of lower limb affecting left nondominant side
G83.21 Monoplegia of upper limb affecting right dominant side
G83.22 Monoplegia of upper limb affecting left dominant side
G83.23 Monoplegia of upper limb affecting right nondominant side
G83.24 Monoplegia of upper limb affecting left nondominant side
G83.31 Monoplegia, unspecified affecting right dominant side
G83.32 Monoplegia, unspecified affecting left dominant side
G83.33 Monoplegia, unspecified affecting right nondominant side
G83.34 Monoplegia, unspecified affecting left nondominant side
G83.81 Brown-Sequard syndrome
G83.82 Anterior cord syndrome
G83.83 Posterior cord syndrome
G83.84 Todd's paralysis (postepileptic)
G83.89 Other specified paralytic syndromes
G83.9 Paralytic syndrome, unspecified
G90.3 Multi-system degeneration of the autonomic nervous system
H49.01 Third [oculomotor] nerve palsy, right eye
H49.02 Third [oculomotor] nerve palsy, left eye
H49.03 Third [oculomotor] nerve palsy, bilateral
H49.11 Fourth [trochlear] nerve palsy, right eye
H49.12 Fourth [trochlear] nerve palsy, left eye
H49.13 Fourth [trochlear] nerve palsy, bilateral
H49.21 Sixth [abducent] nerve palsy, right eye
H49.22 Sixth [abducent] nerve palsy, left eye
H49.23 Sixth [abducent] nerve palsy, bilateral
H49.31 Total (external) ophthalmoplegia, right eye
H49.32 Total (external) ophthalmoplegia, left eye
H49.33 Total (external) ophthalmoplegia, bilateral
H49.41 Progressive external ophthalmoplegia, right eye
H49.42 Progressive external ophthalmoplegia, left eye
H49.43 Progressive external ophthalmoplegia, bilateral
H49.881 Other paralytic strabismus, right eye
H49.882 Other paralytic strabismus, left eye
H49.883 Other paralytic strabismus, bilateral
H49.9 Unspecified paralytic strabismus
H50.00 Unspecified esotropia
H50.011 Monocular esotropia, right eye
H50.012 Monocular esotropia, left eye
H50.021 Monocular esotropia with A pattern, right eye
H50.022 Monocular esotropia with A pattern, left eye
H50.031 Monocular esotropia with V pattern, right eye
H50.032 Monocular esotropia with V pattern, left eye
H50.041 Monocular esotropia with other noncomitancies, right eye

H50.042 Monocular esotropia with other noncomitancies, left eye
H50.05 Alternating esotropia
H50.06 Alternating esotropia with A pattern
H50.07 Alternating esotropia with V pattern
H50.08 Alternating esotropia with other noncomitancies
H50.10 Unspecified exotropia
H50.111 Monocular exotropia, right eye
H50.112 Monocular exotropia, left eye
H50.121 Monocular exotropia with A pattern, right eye
H50.122 Monocular exotropia with A pattern, left eye
H50.131 Monocular exotropia with V pattern, right eye
H50.132 Monocular exotropia with V pattern, left eye
H50.141 Monocular exotropia with other noncomitancies, right eye
H50.142 Monocular exotropia with other noncomitancies, left eye
H50.15 Alternating exotropia
H50.16 Alternating exotropia with A pattern
H50.17 Alternating exotropia with V pattern
H50.18 Alternating exotropia with other noncomitancies
H50.21 Vertical strabismus, right eye
H50.22 Vertical strabismus, left eye
H50.30 Unspecified intermittent heterotropia
H50.311 Intermittent monocular esotropia, right eye
H50.312 Intermittent monocular esotropia, left eye
H50.32 Intermittent alternating esotropia
H50.331 Intermittent monocular exotropia, right eye
H50.332 Intermittent monocular exotropia, left eye
H50.34 Intermittent alternating exotropia
H50.40 Unspecified heterotropia
H50.411 Cyclotropia, right eye
H50.412 Cyclotropia, left eye
H50.42 Monofixation syndrome
H50.43 Accommodative component in esotropia
H50.50 Unspecified heterophoria
H50.51 Esophoria
H50.52 Exophoria
H50.53 Vertical heterophoria
H50.54 Cyclophoria
H50.55 Alternating heterophoria
H50.60 Mechanical strabismus, unspecified
H50.611 Brown's sheath syndrome, right eye
H50.612 Brown's sheath syndrome, left eye
H50.69 Other mechanical strabismus
H50.811 Duane's syndrome, right eye
H50.812 Duane's syndrome, left eye

H50.89 Other specified strabismus
H50.9 Unspecified strabismus
H51.0 Palsy (spasm) of conjugate gaze
H51.11 Convergence insufficiency
H51.12 Convergence excess
H51.21 Internuclear ophthalmoplegia, right eye
H51.22 Internuclear ophthalmoplegia, left eye
H51.23 Internuclear ophthalmoplegia, bilateral
H51.8 Other specified disorders of binocular movement
H51.9 Unspecified disorder of binocular movement
H53.031 Strabismic amblyopia, right eye
H53.032 Strabismic amblyopia, left eye
H53.033 Strabismic amblyopia, bilateral
I69.031 Monoplegia of upper limb following nontraumatic subarachnoid hemorrhage affecting right dominant side
I69.032 Monoplegia of upper limb following nontraumatic subarachnoid hemorrhage affecting left dominant side
I69.033 Monoplegia of upper limb following nontraumatic subarachnoid hemorrhage affecting right non-dominant side
I69.034 Monoplegia of upper limb following nontraumatic subarachnoid hemorrhage affecting left non-dominant side
I69.041 Monoplegia of lower limb following nontraumatic subarachnoid hemorrhage affecting right dominant side
I69.042 Monoplegia of lower limb following nontraumatic subarachnoid hemorrhage affecting left dominant side
I69.043 Monoplegia of lower limb following nontraumatic subarachnoid hemorrhage affecting right non-dominant side
I69.044 Monoplegia of lower limb following nontraumatic subarachnoid hemorrhage affecting left non-dominant side
I69.061 Other paralytic syndrome following nontraumatic subarachnoid hemorrhage affecting right dominant side
I69.062 Other paralytic syndrome following nontraumatic subarachnoid hemorrhage affecting left dominant side
I69.063 Other paralytic syndrome following nontraumatic subarachnoid hemorrhage affecting right non-dominant side
I69.064 Other paralytic syndrome following nontraumatic subarachnoid hemorrhage affecting left non-dominant side
I69.065 Other paralytic syndrome following nontraumatic subarachnoid hemorrhage, bilateral
I69.131 Monoplegia of upper limb following nontraumatic intracerebral hemorrhage affecting right dominant side
I69.132 Monoplegia of upper limb following nontraumatic intracerebral hemorrhage affecting left dominant side
I69.133 Monoplegia of upper limb following nontraumatic intracerebral hemorrhage affecting right non-dominant side

I69.134 Monoplegia of upper limb following nontraumatic intracerebral hemorrhage affecting left non-dominant side

I69.141 Monoplegia of lower limb following nontraumatic intracerebral hemorrhage affecting right dominant side

I69.142 Monoplegia of lower limb following nontraumatic intracerebral hemorrhage affecting left dominant side

I69.143 Monoplegia of lower limb following nontraumatic intracerebral hemorrhage affecting right non-dominant side

I69.144 Monoplegia of lower limb following nontraumatic intracerebral hemorrhage affecting left non-dominant side

I69.151 Hemiplegia and hemiparesis following nontraumatic intracerebral hemorrhage affecting right dominant side

I69.152 Hemiplegia and hemiparesis following nontraumatic intracerebral hemorrhage affecting left dominant side

I69.153 Hemiplegia and hemiparesis following nontraumatic intracerebral hemorrhage affecting right non-dominant side

I69.154 Hemiplegia and hemiparesis following nontraumatic intracerebral hemorrhage affecting left non-dominant side

I69.161 Other paralytic syndrome following nontraumatic intracerebral hemorrhage affecting right dominant side

I69.162 Other paralytic syndrome following nontraumatic intracerebral hemorrhage affecting left dominant side

I69.163 Other paralytic syndrome following nontraumatic intracerebral hemorrhage affecting right non-dominant side

I69.164 Other paralytic syndrome following nontraumatic intracerebral hemorrhage affecting left non-dominant side

I69.165 Other paralytic syndrome following nontraumatic intracerebral hemorrhage, bilateral

I69.231 Monoplegia of upper limb following other nontraumatic intracranial hemorrhage affecting right dominant side

I69.232 Monoplegia of upper limb following other nontraumatic intracranial hemorrhage affecting left dominant side

I69.233 Monoplegia of upper limb following other nontraumatic intracranial hemorrhage affecting right non-dominant side

I69.234 Monoplegia of upper limb following other nontraumatic intracranial hemorrhage affecting left non-dominant side

I69.241 Monoplegia of lower limb following other nontraumatic intracranial hemorrhage affecting right dominant side

I69.242 Monoplegia of lower limb following other nontraumatic intracranial hemorrhage affecting left dominant side

I69.243 Monoplegia of lower limb following other nontraumatic intracranial hemorrhage affecting right non-dominant side

I69.244 Monoplegia of lower limb following other nontraumatic intracranial hemorrhage affecting left non-dominant side

I69.261 Other paralytic syndrome following other nontraumatic intracranial hemorrhage affecting right dominant side

I69.262 Other paralytic syndrome following other nontraumatic intracranial hemorrhage affecting left dominant side

I69.263 Other paralytic syndrome following other nontraumatic intracranial hemorrhage affecting right non-dominant side

I69.264 Other paralytic syndrome following other nontraumatic intracranial hemorrhage affecting left non-dominant side

I69.265 Other paralytic syndrome following other nontraumatic intracranial hemorrhage, bilateral

I69.331 Monoplegia of upper limb following cerebral infarction affecting right dominant side

I69.332 Monoplegia of upper limb following cerebral infarction affecting left dominant side

I69.333 Monoplegia of upper limb following cerebral infarction affecting right non-dominant side

I69.334 Monoplegia of upper limb following cerebral infarction affecting left non-dominant side

I69.341 Monoplegia of lower limb following cerebral infarction affecting right dominant side

I69.342 Monoplegia of lower limb following cerebral infarction affecting left dominant side

I69.343 Monoplegia of lower limb following cerebral infarction affecting right non-dominant side

I69.344 Monoplegia of lower limb following cerebral infarction affecting left non-dominant side

I69.398 Other sequelae of cerebral infarction

I69.361 Other paralytic syndrome following cerebral infarction affecting right dominant side

I69.362 Other paralytic syndrome following cerebral infarction affecting left dominant side

I69.363 Other paralytic syndrome following cerebral infarction affecting right non-dominant side

I69.364 Other paralytic syndrome following cerebral infarction affecting left non-dominant side

I69.365 Other paralytic syndrome following cerebral infarction, bilateral

I69.831 Monoplegia of upper limb following other cerebrovascular disease affecting right dominant side

I69.832 Monoplegia of upper limb following other cerebrovascular disease affecting left dominant side

I69.833 Monoplegia of upper limb following other cerebrovascular disease affecting right non-dominant side

I69.834 Monoplegia of upper limb following other cerebrovascular disease affecting left non-dominant side

I69.841 Monoplegia of lower limb following other cerebrovascular disease affecting right dominant side

I69.842 Monoplegia of lower limb following other cerebrovascular disease affecting left dominant side

I69.843 Monoplegia of lower limb following other cerebrovascular disease affecting right non-dominant side

I69.844 Monoplegia of lower limb following other cerebrovascular disease affecting left non-dominant side

I69.931 Monoplegia of upper limb following unspecified cerebrovascular disease affecting right dominant side
I69.932 Monoplegia of upper limb following unspecified cerebrovascular disease affecting left dominant side
I69.933 Monoplegia of upper limb following unspecified cerebrovascular disease affecting right non-dominant side
I69.934 Monoplegia of upper limb following unspecified cerebrovascular disease affecting left non-dominant side
I69.941 Monoplegia of lower limb following unspecified cerebrovascular disease affecting right dominant side
I69.942 Monoplegia of lower limb following unspecified cerebrovascular disease affecting left dominant side
I69.943 Monoplegia of lower limb following unspecified cerebrovascular disease affecting right non-dominant side
I69.944 Monoplegia of lower limb following unspecified cerebrovascular disease affecting left non-dominant side
J38.3 Other diseases of vocal cords
J38.5 Laryngeal spasm
J38.7 Other diseases of larynx
K11.20 Sialoadenitis, unspecified
K11.21 Acute sialoadenitis
K11.22 Acute recurrent sialoadenitis
K11.23 Chronic sialoadenitis
K11.7 Disturbances of salivary secretion
K22.0 Achalasia of cardia
K59.4 Anal spasm
K60.1 Chronic anal fissure
L74.510 Primary focal hyperhidrosis, axilla
L74.512 Primary focal hyperhidrosis, palms
L74.513 Primary focal hyperhidrosis, soles
L74.519 Primary focal hyperhidrosis, unspecified
M43.6 Torticollis
N30.10 Interstitial cystitis (chronic) without hematuria
N30.11 Interstitial cystitis (chronic) with hematuria
N31.0 Uninhibited neuropathic bladder, not elsewhere classified
N31.1 Reflex neuropathic bladder, not elsewhere classified
N31.8 Other neuromuscular dysfunction of bladder
N31.9 Neuromuscular dysfunction of bladder, unspecified
N32.81 Overactive bladder
N39.41 Urge incontinence
N39.42 Incontinence without sensory awareness
N39.46 Mixed incontinence
N39.498 Other specified urinary incontinence
Q39.5 Congenital dilatation of esophagus

Q40.0 Congenital hypertrophic pyloric stenosis
R32 Unspecified urinary incontinence
R49.0 Dysphonia
R49.8 Other voice and resonance disorders
R68.2 Dry mouth, unspecified

BOTOX (ONABOTULINUMTOXINA), DYSPORT (ABOBOTULINUMTOXINA), XEOMIN (INCOBOTULINUMTOXINA), AND DAXXIFY (DAXIBOTULINUMTOXINA-LANM) ARE MEDICALLY NECESSARY WHEN REPORTED FOR THE FOLLOWING INDICATIONS:

For spasticity of limbs, multiple diagnoses are required:

M62.838 Other muscle spasm

AND at least one of the following:

G23.8 Other specified degenerative diseases of basal ganglia
G23.9 Degenerative disease of basal ganglia, unspecified
G35 Multiple sclerosis
G36.0 Neuromyelitis optica [Devic]
G36.1 Acute and subacute hemorrhagic leukoencephalitis [Hurst]
G36.8 Other specified acute disseminated demyelination
G36.9 Acute disseminated demyelination, unspecified
G37.0 Diffuse sclerosis of central nervous system
G37.1 Central demyelination of corpus callosum
G37.2 Central pontine myelinolysis
G37.3 Acute transverse myelitis in demyelinating disease of central nervous system
G37.4 Subacute necrotizing myelitis of central nervous system
G37.5 Concentric sclerosis [Balo] of central nervous system
G37.9 Demyelinating disease of central nervous system, unspecified
G37.81 Myelin oligodendrocyte glycoprotein antibody disease
G37.89 Other specified demyelinating diseases of central nervous system
G51.4 Facial myokymia
G61.81 Chronic inflammatory demyelinating polyneuritis
G80.3 Athetoid cerebral palsy
G80.4 Ataxic cerebral palsy
G80.8 Other cerebral palsy
G80.9 Cerebral palsy, unspecified
G82.20 Paraplegia, unspecified
G82.21 Paraplegia, complete
G82.22 Paraplegia, incomplete
I69.051 Hemiplegia and hemiparesis following nontraumatic subarachnoid hemorrhage affecting right dominant side

I69.052 Hemiplegia and hemiparesis following nontraumatic subarachnoid hemorrhage affecting left dominant side

I69.053 Hemiplegia and hemiparesis following nontraumatic subarachnoid hemorrhage affecting right non-dominant side

I69.054 Hemiplegia and hemiparesis following nontraumatic subarachnoid hemorrhage affecting left non-dominant side

I69.151 Hemiplegia and hemiparesis following nontraumatic intracerebral hemorrhage affecting right dominant side

I69.152 Hemiplegia and hemiparesis following nontraumatic intracerebral hemorrhage affecting left dominant side

I69.153 Hemiplegia and hemiparesis following nontraumatic intracerebral hemorrhage affecting right non-dominant side

I69.154 Hemiplegia and hemiparesis following nontraumatic intracerebral hemorrhage affecting left non-dominant side

I69.251 Hemiplegia and hemiparesis following other nontraumatic intracranial hemorrhage affecting right dominant side

I69.252 Hemiplegia and hemiparesis following other nontraumatic intracranial hemorrhage affecting left dominant side

I69.253 Hemiplegia and hemiparesis following other nontraumatic intracranial hemorrhage affecting right non-dominant side

I69.254 Hemiplegia and hemiparesis following other nontraumatic intracranial hemorrhage affecting left non-dominant side

I69.351 Hemiplegia and hemiparesis following cerebral infarction affecting right dominant side

I69.352 Hemiplegia and hemiparesis following cerebral infarction affecting left dominant side

I69.353 Hemiplegia and hemiparesis following cerebral infarction affecting right non-dominant side

I69.354 Hemiplegia and hemiparesis following cerebral infarction affecting left non-dominant side

I69.398 Other sequelae of cerebral infarction

I69.851 Hemiplegia and hemiparesis following other cerebrovascular disease affecting right dominant side

I69.852 Hemiplegia and hemiparesis following other cerebrovascular disease affecting left dominant side

I69.853 Hemiplegia and hemiparesis following other cerebrovascular disease affecting right non-dominant side

I69.854 Hemiplegia and hemiparesis following other cerebrovascular disease affecting left non-dominant side

I69.861 Other paralytic syndrome following other cerebrovascular disease affecting right dominant side

I69.862 Other paralytic syndrome following other cerebrovascular disease affecting left dominant side

I69.863 Other paralytic syndrome following other cerebrovascular disease affecting right non-dominant side

I69.864 Other paralytic syndrome following other cerebrovascular disease affecting left non-dominant side

I69.865 Other paralytic syndrome following other cerebrovascular disease, bilateral

I69.951 Hemiplegia and hemiparesis following unspecified cerebrovascular disease affecting right dominant side

I69.952 Hemiplegia and hemiparesis following unspecified cerebrovascular disease affecting left dominant side

I69.953 Hemiplegia and hemiparesis following unspecified cerebrovascular disease affecting right non-dominant side

I69.954 Hemiplegia and hemiparesis following unspecified cerebrovascular disease affecting left non-dominant side

I69.961 Other paralytic syndrome following unspecified cerebrovascular disease affecting right dominant side

I69.962 Other paralytic syndrome following unspecified cerebrovascular disease affecting left dominant side

I69.963 Other paralytic syndrome following unspecified cerebrovascular disease affecting right non-dominant side

I69.964 Other paralytic syndrome following unspecified cerebrovascular disease affecting left non-dominant side

I69.965 Other paralytic syndrome following unspecified cerebrovascular disease, bilateral

S01.90XA Unspecified open wound of unspecified part of head, initial encounter

S01.90XD Unspecified open wound of unspecified part of head, subsequent encounter

S01.90XS Unspecified open wound of unspecified part of head, sequela

S06.0X0A Concussion without loss of consciousness, initial encounter

S06.0X0D Concussion without loss of consciousness, subsequent encounter

S06.0X0S Concussion without loss of consciousness, sequela

S06.0XAA Concussion with loss of consciousness status unknown, initial encounter

S06.0XAD Concussion with loss of consciousness status unknown, subsequent encounter

S06.0XAS Concussion with loss of consciousness status unknown, sequela

S06.1XAA Traumatic cerebral edema with loss of consciousness status unknown, initial encounter

S06.1XAD Traumatic cerebral edema with loss of consciousness status unknown, subsequent encounter

S06.1XAS Traumatic cerebral edema with loss of consciousness status unknown, sequela

S06.2XAA Diffuse traumatic brain injury with loss of consciousness status unknown, initial encounter

S06.2XAD Diffuse traumatic brain injury with loss of consciousness status unknown, subsequent encounter

S06.2XAS Diffuse traumatic brain injury with loss of consciousness status unknown, sequela

S06.30AA Unspecified focal traumatic brain injury with loss of consciousness status unknown, initial encounter

S06.30AD Unspecified focal traumatic brain injury with loss of consciousness status unknown, subsequent encounter

S06.30AS Unspecified focal traumatic brain injury with loss of consciousness status unknown, sequela

S06.81AA Injury of right internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness status unknown, initial encounter

S06.81AD Injury of right internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness status unknown, subsequent encounter

S06.81AS Injury of right internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness status unknown, sequela

S06.82AA Injury of left internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness status unknown, initial encounter

S06.82AD Injury of left internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness status unknown, subsequent encounter

S06.82AS Injury of left internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness status unknown, sequela

S06.89AA Other specified intracranial injury with loss of consciousness status unknown, initial encounter

S06.89AD Other specified intracranial injury with loss of consciousness status unknown, subsequent encounter

S06.89AS Other specified intracranial injury with loss of consciousness status unknown, sequela

S06.8A0A Primary blast injury of brain, not elsewhere classified without loss of consciousness, initial encounter

S06.8A0D Primary blast injury of brain, not elsewhere classified without loss of consciousness, subsequent encounter

S06.8A0S Primary blast injury of brain, not elsewhere classified without loss of consciousness, sequela

S06.8A1A Primary blast injury of brain, not elsewhere classified with loss of consciousness of 30 minutes or less, initial encounter

S06.8A1D Primary blast injury of brain, not elsewhere classified with loss of consciousness of 30 minutes or less, subsequent encounter

S06.8A1S Primary blast injury of brain, not elsewhere classified with loss of consciousness of 30 minutes or less, sequela

S06.8A2A Primary blast injury of brain, not elsewhere classified with loss of consciousness of 31 minutes to 59 minutes, initial encounter

S06.8A2D Primary blast injury of brain, not elsewhere classified with loss of consciousness of 31 minutes to 59 minutes, subsequent encounter

S06.8A2S Primary blast injury of brain, not elsewhere classified with loss of consciousness of 31 minutes to 59 minutes, sequela

S06.8A3A Primary blast injury of brain, not elsewhere classified with loss of consciousness of 1 hour to 5 hours 59 minutes, initial encounter

S06.8A3D Primary blast injury of brain, not elsewhere classified with loss of consciousness of 1 hour to 5 hours 59 minutes, subsequent encounter

S06.8A3S Primary blast injury of brain, not elsewhere classified with loss of consciousness of 1 hour to 5 hours 59 minutes, sequela

S06.8A4A Primary blast injury of brain, not elsewhere classified with loss of consciousness of 6 hours to 24 hours, initial encounter

S06.8A4D Primary blast injury of brain, not elsewhere classified with loss of consciousness of 6 hours to 24 hours, subsequent encounter

S06.8A4S Primary blast injury of brain, not elsewhere classified with loss of consciousness of 6 hours to 24 hours, sequela

S06.8A5A Primary blast injury of brain, not elsewhere classified with loss of consciousness greater than 24 hours with return to pre-existing conscious level, initial encounter

S06.8A5D Primary blast injury of brain, not elsewhere classified with loss of consciousness greater than 24 hours with return to pre-existing conscious level, subsequent encounter

S06.8A5S Primary blast injury of brain, not elsewhere classified with loss of consciousness greater than 24 hours with return to pre-existing conscious level, sequela

S06.8A6A Primary blast injury of brain, not elsewhere classified with loss of consciousness greater than 24 hours without return to pre-existing conscious level with patient surviving, initial encounter

S06.8A6D Primary blast injury of brain, not elsewhere classified with loss of consciousness greater than 24 hours without return to pre-existing conscious level with patient surviving, subsequent encounter

S06.8A6S Primary blast injury of brain, not elsewhere classified with loss of consciousness greater than 24 hours without return to pre-existing conscious level with patient surviving, sequela

S06.8A7A Primary blast injury of brain, not elsewhere classified with loss of consciousness of any duration with death due to brain injury prior to regaining consciousness, initial encounter

S06.8A8A Primary blast injury of brain, not elsewhere classified with loss of consciousness of any duration with death due to other cause prior to regaining consciousness, initial encounter

S06.8A9A Primary blast injury of brain, not elsewhere classified with loss of consciousness of unspecified duration, initial encounter

S06.8A9D Primary blast injury of brain, not elsewhere classified with loss of consciousness of unspecified duration, subsequent encounter

S06.8A9S Primary blast injury of brain, not elsewhere classified with loss of consciousness of unspecified duration, sequela

S06.8AAA Primary blast injury of brain, not elsewhere classified with loss of consciousness status unknown, initial encounter

S06.8AAD Primary blast injury of brain, not elsewhere classified with loss of consciousness status unknown, subsequent encounter

S06.8AAS Primary blast injury of brain, not elsewhere classified with loss of consciousness status unknown, sequela

S06.9XAA Unspecified intracranial injury with loss of consciousness status unknown, initial encounter

S06.9XAD Unspecified intracranial injury with loss of consciousness status unknown, subsequent encounter

S06.9XAS Unspecified intracranial injury with loss of consciousness status unknown, sequela

S06.1X0A Traumatic cerebral edema without loss of consciousness, initial encounter

S06.1X0D Traumatic cerebral edema without loss of consciousness, subsequent encounter

S06.1X0S Traumatic cerebral edema without loss of consciousness, sequela
S06.1X1A Traumatic cerebral edema with loss of consciousness of 30 minutes or less, initial encounter
S06.1X1D Traumatic cerebral edema with loss of consciousness of 30 minutes or less, subsequent encounter
S06.1X1S Traumatic cerebral edema with loss of consciousness of 30 minutes or less, sequela
S06.1X2A Traumatic cerebral edema with loss of consciousness of 31 minutes to 59 minutes, initial encounter
S06.1X2D Traumatic cerebral edema with loss of consciousness of 31 minutes to 59 minutes, subsequent encounter
S06.1X2S Traumatic cerebral edema with loss of consciousness of 31 minutes to 59 minutes, sequela
S06.1X3A Traumatic cerebral edema with loss of consciousness of 1 hour to 5 hours 59 minutes, initial encounter
S06.1X3D Traumatic cerebral edema with loss of consciousness of 1 hour to 5 hours 59 minutes, subsequent encounter
S06.1X3S Traumatic cerebral edema with loss of consciousness of 1 hour to 5 hours 59 minutes, sequela
S06.1X4A Traumatic cerebral edema with loss of consciousness of 6 hours to 24 hours, initial encounter
S06.1X4D Traumatic cerebral edema with loss of consciousness of 6 hours to 24 hours, subsequent encounter
S06.1X4S Traumatic cerebral edema with loss of consciousness of 6 hours to 24 hours, sequela
S06.1X5A Traumatic cerebral edema with loss of consciousness greater than 24 hours with return to pre-existing conscious level, initial encounter
S06.1X5D Traumatic cerebral edema with loss of consciousness greater than 24 hours with return to pre-existing conscious level, subsequent encounter
S06.1X5S Traumatic cerebral edema with loss of consciousness greater than 24 hours with return to pre-existing conscious level, sequela
S06.1X6A Traumatic cerebral edema with loss of consciousness greater than 24 hours without return to pre-existing conscious level with patient surviving, initial encounter
S06.1X6D Traumatic cerebral edema with loss of consciousness greater than 24 hours without return to pre-existing conscious level with patient surviving, subsequent encounter
S06.1X6S Traumatic cerebral edema with loss of consciousness greater than 24 hours without return to pre-existing conscious level with patient surviving, sequela
S06.1X7A Traumatic cerebral edema with loss of consciousness of any duration with death due to brain injury prior to regaining consciousness, initial encounter
S06.1X8A Traumatic cerebral edema with loss of consciousness of any duration with death due to other cause prior to regaining consciousness, initial encounter
S06.1X9A Traumatic cerebral edema with loss of consciousness of unspecified duration, initial encounter
S06.1X9D Traumatic cerebral edema with loss of consciousness of unspecified duration, subsequent encounter
S06.1X9S Traumatic cerebral edema with loss of consciousness of unspecified duration, sequela

S06.2X0A Diffuse traumatic brain injury without loss of consciousness, initial encounter
S06.2X0D Diffuse traumatic brain injury without loss of consciousness, subsequent encounter
S06.2X0S Diffuse traumatic brain injury without loss of consciousness, sequela
S06.2X1A Diffuse traumatic brain injury with loss of consciousness of 30 minutes or less, initial encounter
S06.2X1D Diffuse traumatic brain injury with loss of consciousness of 30 minutes or less, subsequent encounter
S06.2X1S Diffuse traumatic brain injury with loss of consciousness of 30 minutes or less, sequela
S06.2X2A Diffuse traumatic brain injury with loss of consciousness of 31 minutes to 59 minutes, initial encounter
S06.2X2D Diffuse traumatic brain injury with loss of consciousness of 31 minutes to 59 minutes, subsequent encounter
S06.2X2S Diffuse traumatic brain injury with loss of consciousness of 31 minutes to 59 minutes, sequela
S06.2X3A Diffuse traumatic brain injury with loss of consciousness of 1 hour to 5 hours 59 minutes, initial encounter
S06.2X3D Diffuse traumatic brain injury with loss of consciousness of 1 hour to 5 hours 59 minutes, subsequent encounter
S06.2X3S Diffuse traumatic brain injury with loss of consciousness of 1 hour to 5 hours 59 minutes, sequela
S06.2X4A Diffuse traumatic brain injury with loss of consciousness of 6 hours to 24 hours, initial encounter
S06.2X4D Diffuse traumatic brain injury with loss of consciousness of 6 hours to 24 hours, subsequent encounter
S06.2X4S Diffuse traumatic brain injury with loss of consciousness of 6 hours to 24 hours, sequela
S06.2X5A Diffuse traumatic brain injury with loss of consciousness greater than 24 hours with return to pre-existing conscious levels, initial encounter
S06.2X5D Diffuse traumatic brain injury with loss of consciousness greater than 24 hours with return to pre-existing conscious levels, subsequent encounter
S06.2X5S Diffuse traumatic brain injury with loss of consciousness greater than 24 hours with return to pre-existing conscious levels, sequela
S06.2X6A Diffuse traumatic brain injury with loss of consciousness greater than 24 hours without return to pre-existing conscious level with patient surviving, initial encounter
S06.2X6D Diffuse traumatic brain injury with loss of consciousness greater than 24 hours without return to pre-existing conscious level with patient surviving, subsequent encounter
S06.2X6S Diffuse traumatic brain injury with loss of consciousness greater than 24 hours without return to pre-existing conscious level with patient surviving, sequela
S06.2X7A Diffuse traumatic brain injury with loss of consciousness of any duration with death due to brain injury prior to regaining consciousness, initial encounter
S06.2X8A Diffuse traumatic brain injury with loss of consciousness of any duration with death due to other cause prior to regaining consciousness, initial encounter

S06.2X9A Diffuse traumatic brain injury with loss of consciousness of unspecified duration, initial encounter

S06.2X9D Diffuse traumatic brain injury with loss of consciousness of unspecified duration, subsequent encounter

S06.2X9S Diffuse traumatic brain injury with loss of consciousness of unspecified duration, sequela

S06.300A Unspecified focal traumatic brain injury without loss of consciousness, initial encounter

S06.300D Unspecified focal traumatic brain injury without loss of consciousness, subsequent encounter

S06.300S Unspecified focal traumatic brain injury without loss of consciousness, sequela

S06.301A Unspecified focal traumatic brain injury with loss of consciousness of 30 minutes or less, initial encounter

S06.301D Unspecified focal traumatic brain injury with loss of consciousness of 30 minutes or less, subsequent encounter

S06.301S Unspecified focal traumatic brain injury with loss of consciousness of 30 minutes or less, sequela

S06.302A Unspecified focal traumatic brain injury with loss of consciousness of 31 minutes to 59 minutes, initial encounter

S06.302D Unspecified focal traumatic brain injury with loss of consciousness of 31 minutes to 59 minutes, subsequent encounter

S06.302S Unspecified focal traumatic brain injury with loss of consciousness of 31 minutes to 59 minutes, sequela

S06.303A Unspecified focal traumatic brain injury with loss of consciousness of 1 hour to 5 hours 59 minutes, initial encounter

S06.303D Unspecified focal traumatic brain injury with loss of consciousness of 1 hour to 5 hours 59 minutes, subsequent encounter

S06.303S Unspecified focal traumatic brain injury with loss of consciousness of 1 hour to 5 hours 59 minutes, sequela

S06.304A Unspecified focal traumatic brain injury with loss of consciousness of 6 hours to 24 hours, initial encounter

S06.304D Unspecified focal traumatic brain injury with loss of consciousness of 6 hours to 24 hours, subsequent encounter

S06.304S Unspecified focal traumatic brain injury with loss of consciousness of 6 hours to 24 hours, sequela

S06.305A Unspecified focal traumatic brain injury with loss of consciousness greater than 24 hours with return to pre-existing conscious level, initial encounter

S06.305D Unspecified focal traumatic brain injury with loss of consciousness greater than 24 hours with return to pre-existing conscious level, subsequent encounter

S06.305S Unspecified focal traumatic brain injury with loss of consciousness greater than 24 hours with return to pre-existing conscious level, sequela

S06.306A Unspecified focal traumatic brain injury with loss of consciousness greater than 24 hours without return to pre-existing conscious level with patient surviving, initial encounter

S06.306D Unspecified focal traumatic brain injury with loss of consciousness greater than 24 hours without return to pre-existing conscious level with patient surviving, subsequent encounter

S06.306S Unspecified focal traumatic brain injury with loss of consciousness greater than 24 hours without return to pre-existing conscious level with patient surviving, sequela

S06.307A Unspecified focal traumatic brain injury with loss of consciousness of any duration with death due to brain injury prior to regaining consciousness, initial encounter

S06.308A Unspecified focal traumatic brain injury with loss of consciousness of any duration with death due to other cause prior to regaining consciousness, initial encounter

S06.309A Unspecified focal traumatic brain injury with loss of consciousness of unspecified duration, initial encounter

S06.309D Unspecified focal traumatic brain injury with loss of consciousness of unspecified duration, subsequent encounter

S06.309S Unspecified focal traumatic brain injury with loss of consciousness of unspecified duration, sequela

S06.810A Injury of right internal carotid artery, intracranial portion, not elsewhere classified without loss of consciousness, initial encounter

S06.810D Injury of right internal carotid artery, intracranial portion, not elsewhere classified without loss of consciousness, subsequent encounter

S06.810S Injury of right internal carotid artery, intracranial portion, not elsewhere classified without loss of consciousness, sequela

S06.811A Injury of right internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness of 30 minutes or less, initial encounter

S06.811D Injury of right internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness of 30 minutes or less, subsequent encounter

S06.811S Injury of right internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness of 30 minutes or less, sequela

S06.812A Injury of right internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness of 31 minutes to 59 minutes, initial encounter

S06.812D Injury of right internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness of 31 minutes to 59 minutes, subsequent encounter

S06.812S Injury of right internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness of 31 minutes to 59 minutes, sequela

S06.813A Injury of right internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness of 1 hour to 5 hours 59 minutes, initial encounter

S06.813D Injury of right internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness of 1 hour to 5 hours 59 minutes, subsequent encounter

S06.813S Injury of right internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness of 1 hour to 5 hours 59 minutes, sequela

S06.814A Injury of right internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness of 6 hours to 24 hours, initial encounter

S06.814D Injury of right internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness of 6 hours to 24 hours, subsequent encounter

S06.814S Injury of right internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness of 6 hours to 24 hours, sequela

S06.815A Injury of right internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness greater than 24 hours with return to pre-existing conscious level, initial encounter

S06.815D Injury of right internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness greater than 24 hours with return to pre-existing conscious level, subsequent encounter

S06.815S Injury of right internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness greater than 24 hours with return to pre-existing conscious level, sequela

S06.816A Injury of right internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness greater than 24 hours without return to pre-existing conscious level with patient surviving, initial encounter

S06.816D Injury of right internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness greater than 24 hours without return to pre-existing conscious level with patient surviving, subsequent encounter

S06.816S Injury of right internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness greater than 24 hours without return to pre-existing conscious level with patient surviving, sequela

S06.817A Injury of right internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness of any duration with death due to brain injury prior to regaining consciousness, initial encounter

S06.818A Injury of right internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness of any duration with death due to other cause prior to regaining consciousness, initial encounter

S06.819A Injury of right internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness of unspecified duration, initial encounter

S06.819D Injury of right internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness of unspecified duration, subsequent encounter

S06.819S Injury of right internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness of unspecified duration, sequela

S06.820A Injury of left internal carotid artery, intracranial portion, not elsewhere classified without loss of consciousness, initial encounter

S06.820D Injury of left internal carotid artery, intracranial portion, not elsewhere classified without loss of consciousness, subsequent encounter

S06.820S Injury of left internal carotid artery, intracranial portion, not elsewhere classified without loss of consciousness, sequela

S06.821A Injury of left internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness of 30 minutes or less, initial encounter

S06.821D Injury of left internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness of 30 minutes or less, subsequent encounter

S06.821S Injury of left internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness of 30 minutes or less, sequela

S06.822A Injury of left internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness of 31 minutes to 59 minutes, initial encounter

S06.822D Injury of left internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness of 31 minutes to 59 minutes, subsequent encounter

S06.822S Injury of left internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness of 31 minutes to 59 minutes, sequela

S06.823A Injury of left internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness of 1 hour to 5 hours 59 minutes, initial encounter

S06.823D Injury of left internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness of 1 hour to 5 hours 59 minutes, subsequent encounter

S06.823S Injury of left internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness of 1 hour to 5 hours 59 minutes, sequela

S06.824A Injury of left internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness of 6 hours to 24 hours, initial encounter

S06.824D Injury of left internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness of 6 hours to 24 hours, subsequent encounter

S06.824S Injury of left internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness of 6 hours to 24 hours, sequela

S06.825A Injury of left internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness greater than 24 hours with return to pre-existing conscious level, initial encounter

S06.825D Injury of left internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness greater than 24 hours with return to pre-existing conscious level, subsequent encounter

S06.825S Injury of left internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness greater than 24 hours with return to pre-existing conscious level, sequela

S06.826A Injury of left internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness greater than 24 hours without return to pre-existing conscious level with patient surviving, initial encounter

S06.826D Injury of left internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness greater than 24 hours without return to pre-existing conscious level with patient surviving, subsequent encounter

S06.826S Injury of left internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness greater than 24 hours without return to pre-existing conscious level with patient surviving, sequela

S06.827A Injury of left internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness of any duration with death due to brain injury prior to regaining consciousness, initial encounter

S06.828A Injury of left internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness of any duration with death due to other cause prior to regaining consciousness, initial encounter

S06.829A Injury of left internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness of unspecified duration, initial encounter

S06.829D Injury of left internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness of unspecified duration, subsequent encounter

S06.829S Injury of left internal carotid artery, intracranial portion, not elsewhere classified with loss of consciousness of unspecified duration, sequela

S06.890A Other specified intracranial injury without loss of consciousness, initial encounter

S06.890D Other specified intracranial injury without loss of consciousness, subsequent encounter

S06.890S Other specified intracranial injury without loss of consciousness, sequela

S06.891A Other specified intracranial injury with loss of consciousness of 30 minutes or less, initial encounter

S06.891D Other specified intracranial injury with loss of consciousness of 30 minutes or less, subsequent encounter

S06.891S Other specified intracranial injury with loss of consciousness of 30 minutes or less, sequela

S06.892A Other specified intracranial injury with loss of consciousness of 31 minutes to 59 minutes, initial encounter

S06.892D Other specified intracranial injury with loss of consciousness of 31 minutes to 59 minutes, subsequent encounter

S06.892S Other specified intracranial injury with loss of consciousness of 31 minutes to 59 minutes, sequela

S06.893A Other specified intracranial injury with loss of consciousness of 1 hour to 5 hours 59 minutes, initial encounter

S06.893D Other specified intracranial injury with loss of consciousness of 1 hour to 5 hours 59 minutes, subsequent encounter

S06.893S Other specified intracranial injury with loss of consciousness of 1 hour to 5 hours 59 minutes, sequela

S06.894A Other specified intracranial injury with loss of consciousness of 6 hours to 24 hours, initial encounter

S06.894D Other specified intracranial injury with loss of consciousness of 6 hours to 24 hours, subsequent encounter

S06.894S Other specified intracranial injury with loss of consciousness of 6 hours to 24 hours, sequela

S06.895A Other specified intracranial injury with loss of consciousness greater than 24 hours with return to pre-existing conscious level, initial encounter

S06.895D Other specified intracranial injury with loss of consciousness greater than 24 hours with return to pre-existing conscious level, subsequent encounter

S06.895S Other specified intracranial injury with loss of consciousness greater than 24 hours with return to pre-existing conscious level, sequela

S06.896A Other specified intracranial injury with loss of consciousness greater than 24 hours without return to pre-existing conscious level with patient surviving, initial encounter

S06.896D Other specified intracranial injury with loss of consciousness greater than 24 hours without return to pre-existing conscious level with patient surviving, subsequent encounter

S06.896S Other specified intracranial injury with loss of consciousness greater than 24 hours without return to pre-existing conscious level with patient surviving, sequela

S06.897A Other specified intracranial injury with loss of consciousness of any duration with death due to brain injury prior to regaining consciousness, initial encounter

S06.898A Other specified intracranial injury with loss of consciousness of any duration with death due to other cause prior to regaining consciousness, initial encounter

S06.899A Other specified intracranial injury with loss of consciousness of unspecified duration, initial encounter

S06.899D Other specified intracranial injury with loss of consciousness of unspecified duration, subsequent encounter

S06.899S Other specified intracranial injury with loss of consciousness of unspecified duration, sequela

S06.9X0A Unspecified intracranial injury without loss of consciousness, initial encounter

S06.9X0D Unspecified intracranial injury without loss of consciousness, subsequent encounter

S06.9X0S Unspecified intracranial injury without loss of consciousness, sequela

S06.9X1A Unspecified intracranial injury with loss of consciousness of 30 minutes or less, initial encounter

S06.9X1D Unspecified intracranial injury with loss of consciousness of 30 minutes or less, subsequent encounter

S06.9X1S Unspecified intracranial injury with loss of consciousness of 30 minutes or less, sequela

S06.9X2A Unspecified intracranial injury with loss of consciousness of 31 minutes to 59 minutes, initial encounter

S06.9X2D Unspecified intracranial injury with loss of consciousness of 31 minutes to 59 minutes, subsequent encounter

S06.9X2S Unspecified intracranial injury with loss of consciousness of 31 minutes to 59 minutes, sequela

S06.9X3A Unspecified intracranial injury with loss of consciousness of 1 hour to 5 hours 59 minutes, initial encounter

S06.9X3D Unspecified intracranial injury with loss of consciousness of 1 hour to 5 hours 59 minutes, subsequent encounter

S06.9X3S Unspecified intracranial injury with loss of consciousness of 1 hour to 5 hours 59 minutes, sequela

S06.9X4A Unspecified intracranial injury with loss of consciousness of 6 hours to 24 hours, initial encounter

S06.9X4D Unspecified intracranial injury with loss of consciousness of 6 hours to 24 hours, subsequent encounter

S06.9X4S Unspecified intracranial injury with loss of consciousness of 6 hours to 24 hours, sequela

S06.9X5A Unspecified intracranial injury with loss of consciousness greater than 24 hours with return to pre-existing conscious level, initial encounter

S06.9X5D Unspecified intracranial injury with loss of consciousness greater than 24 hours with return to pre-existing conscious level, subsequent encounter

S06.9X5S Unspecified intracranial injury with loss of consciousness greater than 24 hours with return to pre-existing conscious level, sequela

S06.9X6A Unspecified intracranial injury with loss of consciousness greater than 24 hours without return to pre-existing conscious level with patient surviving, initial encounter
S06.9X6D Unspecified intracranial injury with loss of consciousness greater than 24 hours without return to pre-existing conscious level with patient surviving, subsequent encounter
S06.9X6S Unspecified intracranial injury with loss of consciousness greater than 24 hours without return to pre-existing conscious level with patient surviving, sequela
S06.9X7A Unspecified intracranial injury with loss of consciousness of any duration with death due to brain injury prior to regaining consciousness, initial encounter
S06.9X8A Unspecified intracranial injury with loss of consciousness of any duration with death due to other cause prior to regaining consciousness, initial encounter
S06.9X9A Unspecified intracranial injury with loss of consciousness of unspecified duration, initial encounter
S06.9X9D Unspecified intracranial injury with loss of consciousness of unspecified duration, subsequent encounter
S06.9X9S Unspecified intracranial injury with loss of consciousness of unspecified duration, sequela
S14.0XXA Concussion and edema of cervical spinal cord, initial encounter
S14.0XXD Concussion and edema of cervical spinal cord, subsequent encounter
S14.0XXS Concussion and edema of cervical spinal cord, sequela
S14.101A Unspecified injury at C1 level of cervical spinal cord, initial encounter
S14.101D Unspecified injury at C1 level of cervical spinal cord, subsequent encounter
S14.101S Unspecified injury at C1 level of cervical spinal cord, sequela
S14.102A Unspecified injury at C2 level of cervical spinal cord, initial encounter
S14.102D Unspecified injury at C2 level of cervical spinal cord, subsequent encounter
S14.102S Unspecified injury at C2 level of cervical spinal cord, sequela
S14.103A Unspecified injury at C3 level of cervical spinal cord, initial encounter
S14.103D Unspecified injury at C3 level of cervical spinal cord, subsequent encounter
S14.103S Unspecified injury at C3 level of cervical spinal cord, sequela
S14.104A Unspecified injury at C4 level of cervical spinal cord, initial encounter
S14.104D Unspecified injury at C4 level of cervical spinal cord, subsequent encounter
S14.104S Unspecified injury at C4 level of cervical spinal cord, sequela
S14.105A Unspecified injury at C5 level of cervical spinal cord, initial encounter
S14.105D Unspecified injury at C5 level of cervical spinal cord, subsequent encounter
S14.105S Unspecified injury at C5 level of cervical spinal cord, sequela
S14.106A Unspecified injury at C6 level of cervical spinal cord, initial encounter
S14.106D Unspecified injury at C6 level of cervical spinal cord, subsequent encounter
S14.106S Unspecified injury at C6 level of cervical spinal cord, sequela
S14.107A Unspecified injury at C7 level of cervical spinal cord, initial encounter
S14.107D Unspecified injury at C7 level of cervical spinal cord, subsequent encounter
S14.107S Unspecified injury at C7 level of cervical spinal cord, sequela
S14.108A Unspecified injury at C8 level of cervical spinal cord, initial encounter
S14.108D Unspecified injury at C8 level of cervical spinal cord, subsequent encounter
S14.108S Unspecified injury at C8 level of cervical spinal cord, sequela
S14.109A Unspecified injury at unspecified level of cervical spinal cord, initial encounter

S14.109D Unspecified injury at unspecified level of cervical spinal cord, subsequent encounter
S14.109S Unspecified injury at unspecified level of cervical spinal cord, sequela
S14.111A Complete lesion at C1 level of cervical spinal cord, initial encounter
S14.111D Complete lesion at C1 level of cervical spinal cord, subsequent encounter
S14.111S Complete lesion at C1 level of cervical spinal cord, sequela
S14.112A Complete lesion at C2 level of cervical spinal cord, initial encounter
S14.112D Complete lesion at C2 level of cervical spinal cord, subsequent encounter
S14.112S Complete lesion at C2 level of cervical spinal cord, sequela
S14.113A Complete lesion at C3 level of cervical spinal cord, initial encounter
S14.113D Complete lesion at C3 level of cervical spinal cord, subsequent encounter
S14.113S Complete lesion at C3 level of cervical spinal cord, sequela
S14.114A Complete lesion at C4 level of cervical spinal cord, initial encounter
S14.114D Complete lesion at C4 level of cervical spinal cord, subsequent encounter
S14.114S Complete lesion at C4 level of cervical spinal cord, sequela
S14.115A Complete lesion at C5 level of cervical spinal cord, initial encounter
S14.115D Complete lesion at C5 level of cervical spinal cord, subsequent encounter
S14.115S Complete lesion at C5 level of cervical spinal cord, sequela
S14.116A Complete lesion at C6 level of cervical spinal cord, initial encounter
S14.116D Complete lesion at C6 level of cervical spinal cord, subsequent encounter
S14.116S Complete lesion at C6 level of cervical spinal cord, sequela
S14.117A Complete lesion at C7 level of cervical spinal cord, initial encounter
S14.117D Complete lesion at C7 level of cervical spinal cord, subsequent encounter
S14.117S Complete lesion at C7 level of cervical spinal cord, sequela
S14.118A Complete lesion at C8 level of cervical spinal cord, initial encounter
S14.118D Complete lesion at C8 level of cervical spinal cord, subsequent encounter
S14.118S Complete lesion at C8 level of cervical spinal cord, sequela
S14.119A Complete lesion at unspecified level of cervical spinal cord, initial encounter
S14.119D Complete lesion at unspecified level of cervical spinal cord, subsequent encounter
S14.119S Complete lesion at unspecified level of cervical spinal cord, sequela
S14.121A Central cord syndrome at C1 level of cervical spinal cord, initial encounter
S14.121D Central cord syndrome at C1 level of cervical spinal cord, subsequent encounter
S14.121S Central cord syndrome at C1 level of cervical spinal cord, sequela
S14.122A Central cord syndrome at C2 level of cervical spinal cord, initial encounter
S14.122D Central cord syndrome at C2 level of cervical spinal cord, subsequent encounter
S14.122S Central cord syndrome at C2 level of cervical spinal cord, sequela
S14.123A Central cord syndrome at C3 level of cervical spinal cord, initial encounter
S14.123D Central cord syndrome at C3 level of cervical spinal cord, subsequent encounter
S14.123S Central cord syndrome at C3 level of cervical spinal cord, sequela
S14.124A Central cord syndrome at C4 level of cervical spinal cord, initial encounter
S14.124D Central cord syndrome at C4 level of cervical spinal cord, subsequent encounter
S14.124S Central cord syndrome at C4 level of cervical spinal cord, sequela
S14.125A Central cord syndrome at C5 level of cervical spinal cord, initial encounter
S14.125D Central cord syndrome at C5 level of cervical spinal cord, subsequent encounter
S14.125S Central cord syndrome at C5 level of cervical spinal cord, sequela

S14.126A Central cord syndrome at C6 level of cervical spinal cord, initial encounter
S14.126D Central cord syndrome at C6 level of cervical spinal cord, subsequent encounter
S14.126S Central cord syndrome at C6 level of cervical spinal cord, sequela
S14.127A Central cord syndrome at C7 level of cervical spinal cord, initial encounter
S14.127D Central cord syndrome at C7 level of cervical spinal cord, subsequent encounter
S14.127S Central cord syndrome at C7 level of cervical spinal cord, sequela
S14.128A Central cord syndrome at C8 level of cervical spinal cord, initial encounter
S14.128D Central cord syndrome at C8 level of cervical spinal cord, subsequent encounter
S14.128S Central cord syndrome at C8 level of cervical spinal cord, sequela
S14.129A Central cord syndrome at unspecified level of cervical spinal cord, initial encounter
S14.129D Central cord syndrome at unspecified level of cervical spinal cord, subsequent encounter
S14.129S Central cord syndrome at unspecified level of cervical spinal cord, sequela
S14.131A Anterior cord syndrome at C1 level of cervical spinal cord, initial encounter
S14.131D Anterior cord syndrome at C1 level of cervical spinal cord, subsequent encounter
S14.131S Anterior cord syndrome at C1 level of cervical spinal cord, sequela
S14.132A Anterior cord syndrome at C2 level of cervical spinal cord, initial encounter
S14.132D Anterior cord syndrome at C2 level of cervical spinal cord, subsequent encounter
S14.132S Anterior cord syndrome at C2 level of cervical spinal cord, sequela
S14.133A Anterior cord syndrome at C3 level of cervical spinal cord, initial encounter
S14.133D Anterior cord syndrome at C3 level of cervical spinal cord, subsequent encounter
S14.133S Anterior cord syndrome at C3 level of cervical spinal cord, sequela
S14.134A Anterior cord syndrome at C4 level of cervical spinal cord, initial encounter
S14.134D Anterior cord syndrome at C4 level of cervical spinal cord, subsequent encounter
S14.134S Anterior cord syndrome at C4 level of cervical spinal cord, sequela
S14.135A Anterior cord syndrome at C5 level of cervical spinal cord, initial encounter
S14.135D Anterior cord syndrome at C5 level of cervical spinal cord, subsequent encounter
S14.135S Anterior cord syndrome at C5 level of cervical spinal cord, sequela
S14.136A Anterior cord syndrome at C6 level of cervical spinal cord, initial encounter
S14.136D Anterior cord syndrome at C6 level of cervical spinal cord, subsequent encounter
S14.136S Anterior cord syndrome at C6 level of cervical spinal cord, sequela
S14.137A Anterior cord syndrome at C7 level of cervical spinal cord, initial encounter
S14.137D Anterior cord syndrome at C7 level of cervical spinal cord, subsequent encounter
S14.137S Anterior cord syndrome at C7 level of cervical spinal cord, sequela
S14.138A Anterior cord syndrome at C8 level of cervical spinal cord, initial encounter
S14.138D Anterior cord syndrome at C8 level of cervical spinal cord, subsequent encounter
S14.138S Anterior cord syndrome at C8 level of cervical spinal cord, sequela
S14.139A Anterior cord syndrome at unspecified level of cervical spinal cord, initial encounter
S14.139D Anterior cord syndrome at unspecified level of cervical spinal cord, subsequent encounter
S14.139S Anterior cord syndrome at unspecified level of cervical spinal cord, sequela
S14.141A Brown-Sequard syndrome at C1 level of cervical spinal cord, initial encounter
S14.141D Brown-Sequard syndrome at C1 level of cervical spinal cord, subsequent encounter
S14.141S Brown-Sequard syndrome at C1 level of cervical spinal cord, sequela

S14.142A Brown-Sequard syndrome at C2 level of cervical spinal cord, initial encounter
S14.142D Brown-Sequard syndrome at C2 level of cervical spinal cord, subsequent encounter
S14.142S Brown-Sequard syndrome at C2 level of cervical spinal cord, sequela
S14.143A Brown-Sequard syndrome at C3 level of cervical spinal cord, initial encounter
S14.143D Brown-Sequard syndrome at C3 level of cervical spinal cord, subsequent encounter
S14.143S Brown-Sequard syndrome at C3 level of cervical spinal cord, sequela
S14.144A Brown-Sequard syndrome at C4 level of cervical spinal cord, initial encounter
S14.144D Brown-Sequard syndrome at C4 level of cervical spinal cord, subsequent encounter
S14.144S Brown-Sequard syndrome at C4 level of cervical spinal cord, sequela
S14.145A Brown-Sequard syndrome at C5 level of cervical spinal cord, initial encounter
S14.145D Brown-Sequard syndrome at C5 level of cervical spinal cord, subsequent encounter
S14.145S Brown-Sequard syndrome at C5 level of cervical spinal cord, sequela
S14.146A Brown-Sequard syndrome at C6 level of cervical spinal cord, initial encounter
S14.146D Brown-Sequard syndrome at C6 level of cervical spinal cord, subsequent encounter
S14.146S Brown-Sequard syndrome at C6 level of cervical spinal cord, sequela
S14.147A Brown-Sequard syndrome at C7 level of cervical spinal cord, initial encounter
S14.147D Brown-Sequard syndrome at C7 level of cervical spinal cord, subsequent encounter
S14.147S Brown-Sequard syndrome at C7 level of cervical spinal cord, sequela
S14.148A Brown-Sequard syndrome at C8 level of cervical spinal cord, initial encounter
S14.148D Brown-Sequard syndrome at C8 level of cervical spinal cord, subsequent encounter
S14.148S Brown-Sequard syndrome at C8 level of cervical spinal cord, sequela
S14.149A Brown-Sequard syndrome at unspecified level of cervical spinal cord, initial encounter
S14.149D Brown-Sequard syndrome at unspecified level of cervical spinal cord, subsequent encounter
S14.149S Brown-Sequard syndrome at unspecified level of cervical spinal cord, sequela
S14.151A Other incomplete lesion at C1 level of cervical spinal cord, initial encounter
S14.151D Other incomplete lesion at C1 level of cervical spinal cord, subsequent encounter
S14.151S Other incomplete lesion at C1 level of cervical spinal cord, sequela
S14.152A Other incomplete lesion at C2 level of cervical spinal cord, initial encounter
S14.152D Other incomplete lesion at C2 level of cervical spinal cord, subsequent encounter
S14.152S Other incomplete lesion at C2 level of cervical spinal cord, sequela
S14.153A Other incomplete lesion at C3 level of cervical spinal cord, initial encounter
S14.153D Other incomplete lesion at C3 level of cervical spinal cord, subsequent encounter
S14.153S Other incomplete lesion at C3 level of cervical spinal cord, sequela
S14.154A Other incomplete lesion at C4 level of cervical spinal cord, initial encounter
S14.154D Other incomplete lesion at C4 level of cervical spinal cord, subsequent encounter
S14.154S Other incomplete lesion at C4 level of cervical spinal cord, sequela
S14.155A Other incomplete lesion at C5 level of cervical spinal cord, initial encounter
S14.155D Other incomplete lesion at C5 level of cervical spinal cord, subsequent encounter
S14.155S Other incomplete lesion at C5 level of cervical spinal cord, sequela
S14.156A Other incomplete lesion at C6 level of cervical spinal cord, initial encounter
S14.156D Other incomplete lesion at C6 level of cervical spinal cord, subsequent encounter
S14.156S Other incomplete lesion at C6 level of cervical spinal cord, sequela
S14.157A Other incomplete lesion at C7 level of cervical spinal cord, initial encounter

S14.157D Other incomplete lesion at C7 level of cervical spinal cord, subsequent encounter
S14.157S Other incomplete lesion at C7 level of cervical spinal cord, sequela
S14.158A Other incomplete lesion at C8 level of cervical spinal cord, initial encounter
S14.158D Other incomplete lesion at C8 level of cervical spinal cord, subsequent encounter
S14.158S Other incomplete lesion at C8 level of cervical spinal cord, sequela
S14.159A Other incomplete lesion at unspecified level of cervical spinal cord, initial encounter
S14.159D Other incomplete lesion at unspecified level of cervical spinal cord, subsequent encounter
S14.159S Other incomplete lesion at unspecified level of cervical spinal cord, sequela
S24.0XXA Concussion and edema of thoracic spinal cord, initial encounter
S24.0XXD Concussion and edema of thoracic spinal cord, subsequent encounter
S24.0XXS Concussion and edema of thoracic spinal cord, sequela
S24.101A Unspecified injury at T1 level of thoracic spinal cord, initial encounter
S24.101D Unspecified injury at T1 level of thoracic spinal cord, subsequent encounter
S24.101S Unspecified injury at T1 level of thoracic spinal cord, sequela
S24.102A Unspecified injury at T2-T6 level of thoracic spinal cord, initial encounter
S24.102D Unspecified injury at T2-T6 level of thoracic spinal cord, subsequent encounter
S24.102S Unspecified injury at T2-T6 level of thoracic spinal cord, sequela
S24.103A Unspecified injury at T7-T10 level of thoracic spinal cord, initial encounter
S24.103D Unspecified injury at T7-T10 level of thoracic spinal cord, subsequent encounter
S24.103S Unspecified injury at T7-T10 level of thoracic spinal cord, sequela
S24.104A Unspecified injury at T11-T12 level of thoracic spinal cord, initial encounter
S24.104D Unspecified injury at T11-T12 level of thoracic spinal cord, subsequent encounter
S24.104S Unspecified injury at T11-T12 level of thoracic spinal cord, sequela
S24.109A Unspecified injury at unspecified level of thoracic spinal cord, initial encounter
S24.109D Unspecified injury at unspecified level of thoracic spinal cord, subsequent encounter
S24.109S Unspecified injury at unspecified level of thoracic spinal cord, sequela
S24.111A Complete lesion at T1 level of thoracic spinal cord, initial encounter
S24.111D Complete lesion at T1 level of thoracic spinal cord, subsequent encounter
S24.111S Complete lesion at T1 level of thoracic spinal cord, sequela
S24.112A Complete lesion at T2-T6 level of thoracic spinal cord, initial encounter
S24.112D Complete lesion at T2-T6 level of thoracic spinal cord, subsequent encounter
S24.112S Complete lesion at T2-T6 level of thoracic spinal cord, sequela
S24.113A Complete lesion at T7-T10 level of thoracic spinal cord, initial encounter
S24.113D Complete lesion at T7-T10 level of thoracic spinal cord, subsequent encounter
S24.113S Complete lesion at T7-T10 level of thoracic spinal cord, sequela
S24.114A Complete lesion at T11-T12 level of thoracic spinal cord, initial encounter
S24.114D Complete lesion at T11-T12 level of thoracic spinal cord, subsequent encounter
S24.114S Complete lesion at T11-T12 level of thoracic spinal cord, sequela
S24.119A Complete lesion at unspecified level of thoracic spinal cord, initial encounter
S24.119D Complete lesion at unspecified level of thoracic spinal cord, subsequent encounter
S24.119S Complete lesion at unspecified level of thoracic spinal cord, sequela
S24.131A Anterior cord syndrome at T1 level of thoracic spinal cord, initial encounter
S24.131D Anterior cord syndrome at T1 level of thoracic spinal cord, subsequent encounter

S24.131S Anterior cord syndrome at T1 level of thoracic spinal cord, sequela
S24.132A Anterior cord syndrome at T2-T6 level of thoracic spinal cord, initial encounter
S24.132D Anterior cord syndrome at T2-T6 level of thoracic spinal cord, subsequent encounter
S24.132S Anterior cord syndrome at T2-T6 level of thoracic spinal cord, sequela
S24.133A Anterior cord syndrome at T7-T10 level of thoracic spinal cord, initial encounter
S24.133D Anterior cord syndrome at T7-T10 level of thoracic spinal cord, subsequent encounter
S24.133S Anterior cord syndrome at T7-T10 level of thoracic spinal cord, sequela
S24.134A Anterior cord syndrome at T11-T12 level of thoracic spinal cord, initial encounter
S24.134D Anterior cord syndrome at T11-T12 level of thoracic spinal cord, subsequent encounter
S24.134S Anterior cord syndrome at T11-T12 level of thoracic spinal cord, sequela
S24.139A Anterior cord syndrome at unspecified level of thoracic spinal cord, initial encounter
S24.139D Anterior cord syndrome at unspecified level of thoracic spinal cord, subsequent encounter
S24.139S Anterior cord syndrome at unspecified level of thoracic spinal cord, sequela
S24.141A Brown-Sequard syndrome at T1 level of thoracic spinal cord, initial encounter
S24.141D Brown-Sequard syndrome at T1 level of thoracic spinal cord, subsequent encounter
S24.141S Brown-Sequard syndrome at T1 level of thoracic spinal cord, sequela
S24.142A Brown-Sequard syndrome at T2-T6 level of thoracic spinal cord, initial encounter
S24.142D Brown-Sequard syndrome at T2-T6 level of thoracic spinal cord, subsequent encounter
S24.142S Brown-Sequard syndrome at T2-T6 level of thoracic spinal cord, sequela
S24.143A Brown-Sequard syndrome at T7-T10 level of thoracic spinal cord, initial encounter
S24.143D Brown-Sequard syndrome at T7-T10 level of thoracic spinal cord, subsequent encounter
S24.143S Brown-Sequard syndrome at T7-T10 level of thoracic spinal cord, sequela
S24.144A Brown-Sequard syndrome at T11-T12 level of thoracic spinal cord, initial encounter
S24.144D Brown-Sequard syndrome at T11-T12 level of thoracic spinal cord, subsequent encounter
S24.144S Brown-Sequard syndrome at T11-T12 level of thoracic spinal cord, sequela
S24.149A Brown-Sequard syndrome at unspecified level of thoracic spinal cord, initial encounter
S24.149D Brown-Sequard syndrome at unspecified level of thoracic spinal cord, subsequent encounter
S24.149S Brown-Sequard syndrome at unspecified level of thoracic spinal cord, sequela
S24.151A Other incomplete lesion at T1 level of thoracic spinal cord, initial encounter
S24.151D Other incomplete lesion at T1 level of thoracic spinal cord, subsequent encounter
S24.151S Other incomplete lesion at T1 level of thoracic spinal cord, sequela
S24.152A Other incomplete lesion at T2-T6 level of thoracic spinal cord, initial encounter
S24.152D Other incomplete lesion at T2-T6 level of thoracic spinal cord, subsequent encounter
S24.152S Other incomplete lesion at T2-T6 level of thoracic spinal cord, sequela
S24.153A Other incomplete lesion at T7-T10 level of thoracic spinal cord, initial encounter
S24.153D Other incomplete lesion at T7-T10 level of thoracic spinal cord, subsequent encounter
S24.153S Other incomplete lesion at T7-T10 level of thoracic spinal cord, sequela

S24.154A Other incomplete lesion at T11-T12 level of thoracic spinal cord, initial encounter
S24.154D Other incomplete lesion at T11-T12 level of thoracic spinal cord, subsequent encounter
S24.154S Other incomplete lesion at T11-T12 level of thoracic spinal cord, sequela
S24.159A Other incomplete lesion at unspecified level of thoracic spinal cord, initial encounter
S24.159D Other incomplete lesion at unspecified level of thoracic spinal cord, subsequent encounter
S24.159S Other incomplete lesion at unspecified level of thoracic spinal cord, sequela
S34.01XA Concussion and edema of lumbar spinal cord, initial encounter
S34.01XD Concussion and edema of lumbar spinal cord, subsequent encounter
S34.01XS Concussion and edema of lumbar spinal cord, sequela
S34.02XA Concussion and edema of sacral spinal cord, initial encounter
S34.02XD Concussion and edema of sacral spinal cord, subsequent encounter
S34.02XS Concussion and edema of sacral spinal cord, sequela
S34.101A Unspecified injury to L1 level of lumbar spinal cord, initial encounter
S34.101D Unspecified injury to L1 level of lumbar spinal cord, subsequent encounter
S34.101S Unspecified injury to L1 level of lumbar spinal cord, sequela
S34.102A Unspecified injury to L2 level of lumbar spinal cord, initial encounter
S34.102D Unspecified injury to L2 level of lumbar spinal cord, subsequent encounter
S34.102S Unspecified injury to L2 level of lumbar spinal cord, sequela
S34.103A Unspecified injury to L3 level of lumbar spinal cord, initial encounter
S34.103D Unspecified injury to L3 level of lumbar spinal cord, subsequent encounter
S34.103S Unspecified injury to L3 level of lumbar spinal cord, sequela
S34.104A Unspecified injury to L4 level of lumbar spinal cord, initial encounter
S34.104D Unspecified injury to L4 level of lumbar spinal cord, subsequent encounter
S34.104S Unspecified injury to L4 level of lumbar spinal cord, sequela
S34.105A Unspecified injury to L5 level of lumbar spinal cord, initial encounter
S34.105D Unspecified injury to L5 level of lumbar spinal cord, subsequent encounter
S34.105S Unspecified injury to L5 level of lumbar spinal cord, sequela
S34.109A Unspecified injury to unspecified level of lumbar spinal cord, initial encounter
S34.109D Unspecified injury to unspecified level of lumbar spinal cord, subsequent encounter
S34.109S Unspecified injury to unspecified level of lumbar spinal cord, sequela
S34.111A Complete lesion of L1 level of lumbar spinal cord, initial encounter
S34.111D Complete lesion of L1 level of lumbar spinal cord, subsequent encounter
S34.111S Complete lesion of L1 level of lumbar spinal cord, sequela
S34.112A Complete lesion of L2 level of lumbar spinal cord, initial encounter
S34.112D Complete lesion of L2 level of lumbar spinal cord, subsequent encounter
S34.112S Complete lesion of L2 level of lumbar spinal cord, sequela
S34.113A Complete lesion of L3 level of lumbar spinal cord, initial encounter
S34.113D Complete lesion of L3 level of lumbar spinal cord, subsequent encounter
S34.113S Complete lesion of L3 level of lumbar spinal cord, sequela
S34.114A Complete lesion of L4 level of lumbar spinal cord, initial encounter
S34.114D Complete lesion of L4 level of lumbar spinal cord, subsequent encounter
S34.114S Complete lesion of L4 level of lumbar spinal cord, sequela

S34.115A Complete lesion of L5 level of lumbar spinal cord, initial encounter
S34.115D Complete lesion of L5 level of lumbar spinal cord, subsequent encounter
S34.115S Complete lesion of L5 level of lumbar spinal cord, sequela
S34.119A Complete lesion of unspecified level of lumbar spinal cord, initial encounter
S34.119D Complete lesion of unspecified level of lumbar spinal cord, subsequent encounter
S34.119S Complete lesion of unspecified level of lumbar spinal cord, sequela
S34.121A Incomplete lesion of L1 level of lumbar spinal cord, initial encounter
S34.121D Incomplete lesion of L1 level of lumbar spinal cord, subsequent encounter
S34.121S Incomplete lesion of L1 level of lumbar spinal cord, sequela
S34.122A Incomplete lesion of L2 level of lumbar spinal cord, initial encounter
S34.122D Incomplete lesion of L2 level of lumbar spinal cord, subsequent encounter
S34.122S Incomplete lesion of L2 level of lumbar spinal cord, sequela
S34.123A Incomplete lesion of L3 level of lumbar spinal cord, initial encounter
S34.123D Incomplete lesion of L3 level of lumbar spinal cord, subsequent encounter
S34.123S Incomplete lesion of L3 level of lumbar spinal cord, sequela
S34.124A Incomplete lesion of L4 level of lumbar spinal cord, initial encounter
S34.124D Incomplete lesion of L4 level of lumbar spinal cord, subsequent encounter
S34.124S Incomplete lesion of L4 level of lumbar spinal cord, sequela
S34.125A Incomplete lesion of L5 level of lumbar spinal cord, initial encounter
S34.125D Incomplete lesion of L5 level of lumbar spinal cord, subsequent encounter
S34.125S Incomplete lesion of L5 level of lumbar spinal cord, sequela
S34.129A Incomplete lesion of unspecified level of lumbar spinal cord, initial encounter
S34.129D Incomplete lesion of unspecified level of lumbar spinal cord, subsequent encounter
S34.129S Incomplete lesion of unspecified level of lumbar spinal cord, sequela
S34.131A Complete lesion of sacral spinal cord, initial encounter
S34.131D Complete lesion of sacral spinal cord, subsequent encounter
S34.131S Complete lesion of sacral spinal cord, sequela
S34.132A Incomplete lesion of sacral spinal cord, initial encounter
S34.132D Incomplete lesion of sacral spinal cord, subsequent encounter
S34.132S Incomplete lesion of sacral spinal cord, sequela
S34.139A Unspecified injury to sacral spinal cord, initial encounter
S34.139D Unspecified injury to sacral spinal cord, subsequent encounter
S34.139S Unspecified injury to sacral spinal cord, sequela
S34.3XXA Injury of cauda equina, initial encounter
S34.3XXD Injury of cauda equina, subsequent encounter
S34.3XXS Injury of cauda equina, sequela

MYOBLOC (RIMABOTULINUMTOXINB) IS CONSIDERED MEDICALLY NECESSARY FOR THE FOLLOWING INDICATIONS:

G24.3 Spasmodic torticollis
K11.20 Sialoadenitis, unspecified
K11.21 Acute sialoadenitis
K11.22 Acute recurrent sialoadenitis
K11.23 Chronic sialoadenitis

K11.7 Disturbances of salivary secretion
BENEFIT CONTRACT EXCLUSION

BOTOX and BOTOX COSMETIC (ONABOTULINUMTOXINA), MYOBLOC (RIMABOTULINUMTOXINB), DYSPORT (ABOBOTULINUMTOXINA), XEOMIN (INCOBOTULINUMTOXINA), OR DAXXIFY (DAXIBOTULINUMTOXINA-LANM) ARE COSMETIC WHEN REPORTED WITH THE FOLLOWING DIAGNOSIS CODES:

L57.2 Cutis rhomboidalis nuchae

L57.4 Cutis laxa senilis

L57.8 Other skin changes due to chronic exposure to nonionizing radiation

L90.8 Other atrophic disorders of skin

L90.9 Atrophic disorder of skin, unspecified

L91.8 Other hypertrophic disorders of the skin

L91.9 Hypertrophic disorder of the skin, unspecified

L98.8 Other specified disorders of the skin and subcutaneous tissue

R23.8 Other skin changes

R23.9 Unspecified skin changes

Duration of authorization: 12 months

Version Effective Date: 04/21/2025

Title: Brentuximab Vedotin (Adcetris®)

MEDICALLY NECESSARY:

Brentuximab vedotin (Adcetris®) is considered medically necessary and, therefore, covered for any of the following indications:

B-CELL LYMPHOMAS

Diffuse Large B-Cell Lymphoma

- As treatment for CD30+ disease as second-line and subsequent therapy if no intention to proceed to transplant for any of the following conditions:
 - For relapsed or refractory disease >12 months after completion of first-line therapy
 - For primary refractory disease (partial response, no response, or progression) or relapsed disease <12 months after completion of first-line therapy if no intention to proceed to Chimeric antigen receptor (CAR) T-cell therapy
 - As alternative systemic therapy (if not previously used) for relapsed/refractory disease if no intention to proceed to CAR T-cell therapy

High-Grade B-Cell Lymphomas

- For the treatment of individuals as a second-line or subsequent therapy for CD30+ disease if no intention to proceed to transplant, for any of the following conditions:
 - For relapsed or refractory disease >12 months after completion of first-line therapy
 - For primary refractory disease (partial response, no response, or progression) or relapsed disease <12 months after completion of first-line therapy if no intention to proceed to CAR T-cell therapy
 - As alternative systemic therapy (if not previously used) for relapsed/refractory disease if no intention to proceed to CAR T-cell therapy

B-Cell Lymphomas Post-Transplant Lymphoproliferative Disorders (PTLD)

- Second-line and subsequent therapy for the treatment of individuals with CD30+ monomorphic PTLD (B-cell type) if no intention to proceed to transplant for any of the following conditions:
 - For relapsed disease >12 months after completion of initial treatment with chemoimmunotherapy
 - For primary refractory disease (partial response, no response, or progression) or relapsed disease <12 months after completion of initial treatment with chemoimmunotherapy if no intention to proceed to CAR T-cell therapy

- As alternative systemic therapy (if not previously used) for relapsed/refractory disease if no intention to proceed to CAR T-cell therapy

HIV-Related B-Cell Lymphomas

- For the treatment of individuals as a second-line or subsequent therapy for of CD30+ human immunodeficiency virus (HIV)-related diffuse large B-cell lymphoma, primary effusion lymphoma, and human herpesvirus-8 (HHV8)-positive diffuse large B-cell lymphoma, not otherwise specified (NOS) if no intention to proceed to transplant for any of the following conditions:
 - For relapsed disease >12 months after completion of first-line therapy
 - For primary refractory disease (partial response, no response, or progression) or relapsed disease <12 months after completion of first-line therapy if no intention to proceed to CAR T-cell therapy
 - As alternative systemic therapy (if not previously used) for relapsed/refractory disease if no intention to proceed to CAR T-cell therapy

PEDIATRIC AGGRESSIVE MATURE B-CELL LYMPHOMAS

- National Comprehensive Cancer Network (NCCN)-preferred consolidation/additional therapy for Pediatric Aggressive Mature B-Cell Lymphomas for Primary Mediastinal Large B-Cell Lymphoma if partial response achieved after therapy for relapsed or refractory disease
 - In combination with nivolumab (Opdivo)
 - In combination with pembrolizumab (Keytruda)

CLASSIC HODGKIN LYMPHOMA

For individuals 18 to 60 years old with any of the following therapeutic approaches:

- As a maintenance therapy following high-dose therapy and autologous stem cell rescue (HDT/ASCR) for relapsed or refractory disease for individuals with a high risk* of relapse if Deauville score is 1 to 4 prior to transplant

*NCCN note: Individuals with two or more of the following risk factors are considered high risk: remission duration less than 1 year; extranodal involvement; PET+ response at the time of transplant; B-cell lymphoma symptoms; and/or >1 salvage/subsequent therapy regimen.

- As second-line or subsequent systemic therapy for relapsed or refractory disease for any of the following:
 - As a single agent
 - In combination with bendamustine
 - In combination with ICE (ifosfamide, carboplatin, etoposide)

- Second-line or subsequent systemic therapy (if not previously used) for relapsed or refractory disease in combination with nivolumab for any of the following conditions:
 - disease that has relapsed or progressed after HDT/ASCR ± brentuximab vedotin
 - individuals with relapsed/refractory disease who are transplant-ineligible based on comorbidity or failure of second-line chemotherapy
 - post-allogeneic transplant
- Second-line systemic therapy for relapsed or refractory disease in combination with nivolumab
- Subsequent systemic therapy (if not previously used) for relapsed or refractory disease (only if Deauville score is 4 or 5 following restaging with FDG-PET/CT):
 - In combination with nivolumab
 - As a single agent
 - In combination with bendamustine
 - In combination with ICE (ifosfamide, carboplatin, etoposide)
- As primary treatment in combination with AVD (doxorubicin, vinblastine, dacarbazine) for stage III to IV disease (use with caution in individuals >60 years old; contraindicated in those with neuropathy) (NCCN-preferred regimen)
- As primary treatment in combination as a component of BrECADD (brentuximab vedotin, etoposide, cyclophosphamide, doxorubicin, dacarbazine, dexamethasone) for stage III to IV disease

For individuals older than 60 years of age with either of the following therapeutic approaches:

- As primary treatment as a component of brentuximab vedotin followed by AVD (doxorubicin, vinblastine, dacarbazine) regimen conditionally followed by brentuximab vedotin in responding individuals with complete or partial response for stage I to II unfavorable or stage III to IV disease
- As primary treatment in combination with dacarbazine with low ejection fraction
- As a single agent part of palliative therapy for relapsed or refractory disease

For individuals 18 years or younger with either of the following therapeutic approaches:

- Primary treatment for high risk disease as a component of one of the following:
 - Bv-AVE-PC (brentuximab vedotin, doxorubicin, vincristine, etoposide, prednisone, cyclophosphamide) regimen (preferred)
 - AEPA (brentuximab vedotin, etoposide, prednisone, doxorubicin) regimen
- Additional treatment for high-risk disease as a component of CAPDAC (cyclophosphamide, brentuximab vedotin, prednisone, dacarbazine) regimen following primary treatment with AEPA regimen

- Re-induction therapy in combination with ISRT for relapsed or refractory disease (only in highly favorable individuals*) in individuals heavily pretreated (with platinum or anthracycline-based chemotherapy) or if a decrease in cardiac function observed, in combination with any of the following:
 - bendamustine
 - nivolumab
 - gemcitabine

*NCCN note: Recommended for those who may avoid ASCR: initial stage other than IIIB or IVB, no prior exposure to RT, duration of CR1 more than 1 year, absence of extranodal disease or B symptoms at relapse.

- Re-induction therapy or subsequent therapy (if not previously used) for relapsed or refractory disease as a consideration in individuals heavily pretreated (with platinum or anthracycline-based chemotherapy) or if a decrease in cardiac function observed, in combination with any of the following:
 - bendamustine
 - nivolumab
 - gemcitabine
- Maintenance therapy following high-dose therapy and autologous stem cell rescue (HDT/ASCR) for relapsed or refractory disease for select high-risk individuals*

*NCCN note: Any individuals with progressive disease, refractory disease, or relapse within 1 year of the original diagnosis

- Pediatric individuals 2 years and older with previously untreated high-risk classic Hodgkin lymphoma (cHL), in combination with doxorubicin, vincristine, etoposide, prednisone, and cyclophosphamide

Previously Untreated Stage III or IV Classic Hodgkin Lymphoma

- For the treatment of adult individuals in combination with AVD (doxorubicin, vinblastine, dacarbazine)

Classic Hodgkin Lymphoma Consolidation

- For the treatment of adult individuals with classic Hodgkin lymphoma at high risk of relapse or progression as post-autologous hematopoietic stem cell transplantation (auto-HSCT) consolidation
- For the treatment of adult individuals with classic Hodgkin lymphoma after failure of auto-HSCT or after failure of at least two prior multiagent chemotherapy regimens in individuals who are not auto-HSCT candidates

T-CELL LYMPHOMAS

Anaplastic Large Cell Lymphoma Lymphomas

- For the treatment of adult individuals with previously untreated systemic anaplastic large cell lymphoma (sALCL) or other CD30-expressing peripheral T-cell lymphomas (PTCL), including angioimmunoblastic T-cell lymphoma and PTCL not otherwise specified, in combination with cyclophosphamide, doxorubicin, and prednisone (CHP)
- For the treatment of adult individuals with systemic sALCL after failure of at least one prior multiagent chemotherapy regimen
- For the treatment of adult individuals with pcALCL or CD30-expressing mycosis fungoides (MF) who have received prior systemic therapy

Peripheral T-Cell Lymphomas

- As first-line therapy as a component of brentuximab vedotin + CHP (cyclophosphamide, doxorubicin, prednisone) regimen (NCCN-preferred therapy) for any of the following:
 - CD30+ stage I–IV peripheral T-cell lymphoma not otherwise specified (PTCL-NOS)
 - Angioimmunoblastic T-cell lymphoma (AITL)
 - Enteropathy-associated T-cell lymphoma (EATL)
 - Monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL)
 - Nodal peripheral T-cell lymphoma with TFH phenotype (PTCL, TFH)
 - Follicular T-cell lymphoma (FTCL)
 - Stage III, IV ALK-positive ALCL or stage I–IV ALK-negative ALCL (NCCN-preferred therapy)
 - Stage I, II ALK-positive ALCL as a component of brentuximab vedotin + CHP (cyclophosphamide, doxorubicin, prednisone) for six cycles ± involved-site radiation therapy (ISRT) (NCCN-preferred therapy)
- As second-line or initial palliative intent therapy and subsequent therapy (NCCN preferred) as a single agent for any of the following conditions:
 - Relapsed/refractory ALCL CD30+ peripheral T-cell lymphoma (PTCL)
 - CD30+ angioimmunoblastic T-cell lymphoma (AITL)
 - ALCL
 - Systemic sALCL after failure of at least one prior multiagent chemotherapy regimen

T-Cell Lymphomas—Breast Implant–Associated ALCL

- As NCCN-preferred adjuvant systemic therapy for the localized disease to capsule/implant/breast following incomplete excision or partial capsulectomy with the

residual disease if node-positive or radiation therapy is not feasible, or consider for extended disease (stage II–IV)

- As a single agent
- As a component of brentuximab vedotin + CHP (cyclophosphamide, doxorubicin, prednisone)
- As a second-line and subsequent therapy for relapsed/refractory disease, as a single agent (NCCN preferred)

Adult T-Cell Leukemia/Lymphoma

- As NCCN-preferred second-line or subsequent therapy as a single agent for nonresponders to first-line therapy for chronic high risk, acute or lymphoma subtypes (for CD30+ cases)
- As a component of brentuximab vedotin + CHP (cyclophosphamide, doxorubicin, prednisone) regimen for CD30+ individuals (NCCN preferred):
 - As additional therapy in nonresponders to first-line therapy for chronic low risk/smoldering symptomatic subtype
 - First-line therapy for chronic high-risk subtype
 - As additional therapy in nonresponders to first-line therapy with zidovudine and interferon for chronic high-risk subtype
 - As first-line therapy for acute subtype
 - As continued treatment in responders to first-line therapy for acute subtype
 - As additional therapy in nonresponders to first-line therapy for acute subtype (if not used in first-line therapy)
 - First-line therapy for lymphoma subtype
 - Continued treatment in responders to first-line therapy for lymphoma subtype

Hepatosplenic T-Cell Lymphoma

- As a single agent for CD30+ refractory disease after two first-line therapy regimens (NCCN preferred)

Extranodal NK/T-Cell Lymphoma, Nasal Type

- As a single agent for CD30+ relapsed/refractory disease following additional therapy with an alternate combination chemotherapy regimen (asparaginase-based) not previously used

PRIMARY CUTANEOUS LYMPHOMAS

Primary Cutaneous CD30+ T-Cell Lymphoproliferative Disorders

- For the treatment of primary cutaneous ALCL with multifocal lesions, or cutaneous ALCL with regional node (N1) (excludes systemic ALCL) as a single agent for one of the following:
 - Primary treatment (NCCN preferred)
 - Relapsed/refractory disease
- For the treatment of cutaneous ALCL with regional node (N1) (excludes systemic ALCL):
 - As a component of brentuximab vedotin + CHP (cyclophosphamide, doxorubicin, prednisone) for one of the following:
 - Primary treatment (NCCN preferred)
 - Relapsed/refractory disease
- Therapy for lymphomatoid papulosis (LyP) with extensive lesions as a single agent for relapsed/refractory disease following clinical trial, observation, retreatment with primary treatment, or treatment with an alternative regimen not used for primary treatment
- For the treatment of adult individuals with pcALCL or CD30-expressing mycosis fungoides (MF) who have received prior systemic therapy

Mycosis Fungoides (MF)/Sézary Syndrome (SS)

- NCCN-preferred systemic therapy as a single agent primary treatment for one of the following:
 - Stage IB-IIA MF in combination with skin-directed therapy in selected cases**
 - Stage IIB MF with limited tumor lesions, with or without local radiation therapy
 - Stage IIB MF with generalized tumor lesions, with or without in combination with skin-directed therapy
 - Stage III MF, in combination with skin-directed therapy
 - Stage IVA1 or IVA2 SS in combination with skin-directed therapy
 - Stage IVA2 non-Sézary or stage IVB visceral disease (solid organ), with or without radiation therapy for local control
 - Generalized cutaneous or extracutaneous lesions with large cell transformation (LCT), in combination with systemic therapy

**NCCN note: Systemic therapies should be considered for individuals with extensive skin involvement, higher skin disease burden, predominantly plaque disease, blood involvement, and/or inadequate response to skin-directed therapy

- Systemic therapy in combination with bendamustine as primary treatment for one of the following:
 - Stage IVA2 non-Sézary or stage IVB visceral disease (solid organ), with or without radiation therapy for local control

- Generalized cutaneous or extracutaneous lesions with LCT, in combination with skin-directed therapy (NCCN-preferred)
- NCCN-preferred systemic therapy as a single agent subsequent treatment for one of the following:
 - Stage IA MF refractory to multiple previous therapies, in combination with skin-directed therapy in selected cases**
 - Relapsed stage IB-IIA MF with a lower skin disease burden (e.g., predominantly patch disease), in combination with skin-directed therapy in selected cases**
 - Stage IB-IIA MF with a higher skin disease burden (e.g., predominantly plaque disease) that is relapsed or persistent with T1-T2 disease, with or without skin-directed therapy that is relapsed or persistent with T1-T2 disease, in combination with skin-directed therapy in selected cases**
 - Stage IB-IIA MF that is refractory to multiple previous therapies, in combination with skin-directed therapy
 - Relapsed stage IIB MF with T1-2 limited tumor lesions, in combination with skin-directed therapy in selected cases**
 - Relapsed stage IIB MF with T3 limited extent lesions, with or without local radiation therapy
 - Persistent stage IIB MF with T1-3 limited tumor lesions, with or without local radiation therapy
 - Stage IIB MF with limited tumor lesions that are refractory to multiple previous therapies, in combination with skin-directed therapy
 - Relapsed stage IIB MF with T1-2 generalized tumor lesions, in combination with skin-directed therapy in selected cases** refractory to multiple previous therapies
 - Relapsed stage IIB MF with T3 generalized tumor lesions, in combination with skin-directed therapy
 - Persistent stage IIB MF with T1-3 generalized tumor lesions, in combination with skin-directed therapy
 - Stage IIB MF with generalized tumor lesions that are refractory to multiple previous therapies, in combination with skin-directed therapy
 - Stage III MF relapsed or persistent in combination with or without skin-directed therapy
 - Stage III MF that is refractory to multiple previous therapies, in combination with skin-directed therapy

- Stage IVA1 or IVA2 relapsed or persistent Sézary syndrome, in combination with skin-directed therapy
- Stage IVA2 non-Sézary or stage IVB visceral relapsed or persistent disease (solid organ), with or without radiation therapy for local control
- Limited cutaneous lesions with LCT that is refractory to multiple previous therapies, in combination with skin-directed therapy
- Relapsed or persistent generalized cutaneous or extracutaneous lesions with LCT, in combination with skin-directed therapy

**** (NCCN) Note:** Systemic therapies should be considered for individuals with extensive skin involvement, higher skin disease burden, predominantly plaque disease, blood involvement, and/or inadequate response to skin-directed therapy

- Systemic therapy in combination with bendamustine as subsequent treatment for one of the following:
 - Stage IIB MF with generalized tumor lesions that is refractory to multiple previous therapies, in combination with skin-directed therapy (NCCN-preferred)
 - Stage III MF that is refractory to multiple previous therapies, in combination with skin-directed therapy (NCCN-preferred)
 - Relapsed or persistent stage IVA2 non-Sézary or stage IVB visceral disease (solid organ), with or without radiation therapy for local control
 - Limited cutaneous lesions with LCT that is refractory to multiple previous therapies, in combination with skin-directed therapy (NCCN-preferred)
 - Relapsed or persistent LCT with generalized cutaneous or extracutaneous lesions, in combination with skin-directed therapy (NCCN-preferred)

Duration of authorization: 12 months

Version Effective Date: 11/18/2024

Title: Brentuximab Vedotin (Adcetris®)

MEDICALLY NECESSARY:

C81.10 Nodular sclerosis Hodgkin lymphoma, unspecified site
C81.11 Nodular sclerosis Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.12 Nodular sclerosis Hodgkin lymphoma, intrathoracic lymph nodes
C81.13 Nodular sclerosis Hodgkin lymphoma, intra-abdominal lymph nodes
C81.14 Nodular sclerosis Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.15 Nodular sclerosis Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.16 Nodular sclerosis Hodgkin lymphoma, intrapelvic lymph nodes
C81.17 Nodular sclerosis Hodgkin lymphoma, spleen
C81.18 Nodular sclerosis Hodgkin lymphoma, lymph nodes of multiple sites
C81.19 Nodular sclerosis Hodgkin lymphoma, extranodal and solid organ sites
C81.20 Mixed cellularity Hodgkin lymphoma, unspecified site
C81.21 Mixed cellularity Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.22 Mixed cellularity Hodgkin lymphoma, intrathoracic lymph nodes
C81.23 Mixed cellularity Hodgkin lymphoma, intra-abdominal lymph nodes
C81.24 Mixed cellularity Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.25 Mixed cellularity Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.26 Mixed cellularity Hodgkin lymphoma, intrapelvic lymph nodes
C81.27 Mixed cellularity Hodgkin lymphoma, spleen
C81.28 Mixed cellularity Hodgkin lymphoma, lymph nodes of multiple sites
C81.29 Mixed cellularity Hodgkin lymphoma, extranodal and solid organ sites
C81.30 Lymphocyte depleted Hodgkin lymphoma, unspecified site
C81.31 Lymphocyte depleted Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.32 Lymphocyte depleted Hodgkin lymphoma, intrathoracic lymph nodes
C81.33 Lymphocyte depleted Hodgkin lymphoma, intra-abdominal lymph nodes
C81.34 Lymphocyte depleted Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.35 Lymphocyte depleted Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.36 Lymphocyte depleted Hodgkin lymphoma, intrapelvic lymph nodes
C81.37 Lymphocyte depleted Hodgkin lymphoma, spleen
C81.38 Lymphocyte depleted Hodgkin lymphoma, lymph nodes of multiple sites
C81.39 Lymphocyte depleted Hodgkin lymphoma, extranodal and solid organ sites
C81.40 Lymphocyte-rich Hodgkin lymphoma, unspecified site
C81.41 Lymphocyte-rich Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.42 Lymphocyte-rich Hodgkin lymphoma, intrathoracic lymph nodes
C81.43 Lymphocyte-rich Hodgkin lymphoma, intra-abdominal lymph nodes
C81.44 Lymphocyte-rich Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.45 Lymphocyte-rich Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.46 Lymphocyte-rich Hodgkin lymphoma, intrapelvic lymph nodes
C81.47 Lymphocyte-rich Hodgkin lymphoma, spleen
C81.48 Lymphocyte-rich Hodgkin lymphoma, lymph nodes of multiple sites

C81.49 Lymphocyte-rich Hodgkin lymphoma, extranodal and solid organ sites
C81.70 Other Hodgkin lymphoma, unspecified site
C81.71 Other Hodgkin lymphoma, lymph nodes of head, face, and neck
C81.72 Other Hodgkin lymphoma, intrathoracic lymph nodes
C81.73 Other Hodgkin lymphoma, intra-abdominal lymph nodes
C81.74 Other Hodgkin lymphoma, lymph nodes of axilla and upper limb
C81.75 Other Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C81.76 Other Hodgkin lymphoma, intrapelvic lymph nodes
C81.77 Other Hodgkin lymphoma, spleen
C81.78 Other Hodgkin lymphoma, lymph nodes of multiple sites
C81.79 Other Hodgkin lymphoma, extranodal and solid organ sites
C81.90 Hodgkin lymphoma, unspecified, unspecified site
C81.91 Hodgkin lymphoma, unspecified, lymph nodes of head, face, and neck
C81.92 Hodgkin lymphoma, unspecified, intrathoracic lymph nodes
C81.93 Hodgkin lymphoma, unspecified, intra-abdominal lymph nodes
C81.94 Hodgkin lymphoma, unspecified, lymph nodes of axilla and upper limb
C81.95 Hodgkin lymphoma, unspecified, lymph nodes of inguinal region and lower limb
C81.96 Hodgkin lymphoma, unspecified, intrapelvic lymph nodes
C81.97 Hodgkin lymphoma, unspecified, spleen
C81.98 Hodgkin lymphoma, unspecified, lymph nodes of multiple sites
C81.99 Hodgkin lymphoma, unspecified, extranodal and solid organ sites
C82.00 Follicular lymphoma grade I, unspecified site
C82.01 Follicular lymphoma grade I, lymph nodes of head, face, and neck
C82.02 Follicular lymphoma grade I, intrathoracic lymph nodes
C82.03 Follicular lymphoma grade I, intra-abdominal lymph nodes
C82.04 Follicular lymphoma grade I, lymph nodes of axilla and upper limb
C82.05 Follicular lymphoma grade I, lymph nodes of inguinal region and lower limb
C82.06 Follicular lymphoma grade I, intrapelvic lymph nodes
C82.07 Follicular lymphoma grade I, spleen
C82.08 Follicular lymphoma grade I, lymph nodes of multiple sites
C82.09 Follicular lymphoma grade I, extranodal and solid organ sites
C82.10 Follicular lymphoma grade II, unspecified site
C82.11 Follicular lymphoma grade II, lymph nodes of head, face, and neck
C82.12 Follicular lymphoma grade II, intrathoracic lymph nodes
C82.13 Follicular lymphoma grade II, intra-abdominal lymph nodes
C82.14 Follicular lymphoma grade II, lymph nodes of axilla and upper limb
C82.15 Follicular lymphoma grade II, lymph nodes of inguinal region and lower limb
C82.16 Follicular lymphoma grade II, intrapelvic lymph nodes
C82.17 Follicular lymphoma grade II, spleen
C82.18 Follicular lymphoma grade II, lymph nodes of multiple sites
C82.19 Follicular lymphoma grade II, extranodal and solid organ sites
C82.20 Follicular lymphoma grade III, unspecified, unspecified site
C82.21 Follicular lymphoma grade III, unspecified, lymph nodes of head, face, and neck
C82.22 Follicular lymphoma grade III, unspecified, intrathoracic lymph nodes

C82.23 Follicular lymphoma grade III, unspecified, intra-abdominal lymph nodes
C82.24 Follicular lymphoma grade III, unspecified, lymph nodes of axilla and upper limb
C82.25 Follicular lymphoma grade III, unspecified, lymph nodes of inguinal region and lower limb
C82.26 Follicular lymphoma grade III, unspecified, intrapelvic lymph nodes
C82.27 Follicular lymphoma grade III, unspecified, spleen
C82.28 Follicular lymphoma grade III, unspecified, lymph nodes of multiple sites
C82.29 Follicular lymphoma grade III, unspecified, extranodal and solid organ sites
C82.30 Follicular lymphoma grade IIIa, unspecified site
C82.31 Follicular lymphoma grade IIIa, lymph nodes of head, face, and neck
C82.32 Follicular lymphoma grade IIIa, intrathoracic lymph nodes
C82.33 Follicular lymphoma grade IIIa, intra-abdominal lymph nodes
C82.34 Follicular lymphoma grade IIIa, lymph nodes of axilla and upper limb
C82.35 Follicular lymphoma grade IIIa, lymph nodes of inguinal region and lower limb
C82.36 Follicular lymphoma grade IIIa, intrapelvic lymph nodes
C82.37 Follicular lymphoma grade IIIa, spleen
C82.38 Follicular lymphoma grade IIIa, lymph nodes of multiple sites
C82.39 Follicular lymphoma grade IIIa, extranodal and solid organ sites
C82.40 Follicular lymphoma grade IIIb, unspecified site
C82.41 Follicular lymphoma grade IIIb, lymph nodes of head, face, and neck
C82.42 Follicular lymphoma grade IIIb, intrathoracic lymph nodes
C82.43 Follicular lymphoma grade IIIb, intra-abdominal lymph nodes
C82.44 Follicular lymphoma grade IIIb, lymph nodes of axilla and upper limb
C82.45 Follicular lymphoma grade IIIb, lymph nodes of inguinal region and lower limb
C82.46 Follicular lymphoma grade IIIb, intrapelvic lymph nodes
C82.47 Follicular lymphoma grade IIIb, spleen
C82.48 Follicular lymphoma grade IIIb, lymph nodes of multiple sites
C82.49 Follicular lymphoma grade IIIb, extranodal and solid organ sites
C82.50 Diffuse follicle center lymphoma, unspecified site
C82.51 Diffuse follicle center lymphoma, lymph nodes of head, face, and neck
C82.52 Diffuse follicle center lymphoma, intrathoracic lymph nodes
C82.53 Diffuse follicle center lymphoma, intra-abdominal lymph nodes
C82.54 Diffuse follicle center lymphoma, lymph nodes of axilla and upper limb
C82.55 Diffuse follicle center lymphoma, lymph nodes of inguinal region and lower limb
C82.56 Diffuse follicle center lymphoma, intrapelvic lymph nodes
C82.57 Diffuse follicle center lymphoma, spleen
C82.58 Diffuse follicle center lymphoma, lymph nodes of multiple sites
C82.59 Diffuse follicle center lymphoma, extranodal and solid organ sites
C82.60 Cutaneous follicle center lymphoma, unspecified site
C82.61 Cutaneous follicle center lymphoma, lymph nodes of head, face, and neck
C82.62 Cutaneous follicle center lymphoma, intrathoracic lymph nodes
C82.63 Cutaneous follicle center lymphoma, intra-abdominal lymph nodes
C82.64 Cutaneous follicle center lymphoma, lymph nodes of axilla and upper limb
C82.65 Cutaneous follicle center lymphoma, lymph nodes of inguinal region and lower limb

C82.66 Cutaneous follicle center lymphoma, intrapelvic lymph nodes
C82.67 Cutaneous follicle center lymphoma, spleen
C82.68 Cutaneous follicle center lymphoma, lymph nodes of multiple sites
C82.69 Cutaneous follicle center lymphoma, extranodal and solid organ sites
C82.80 Other types of follicular lymphoma, unspecified site
C82.81 Other types of follicular lymphoma, lymph nodes of head, face, and neck
C82.82 Other types of follicular lymphoma, intrathoracic lymph nodes
C82.83 Other types of follicular lymphoma, intra-abdominal lymph nodes
C82.84 Other types of follicular lymphoma, lymph nodes of axilla and upper limb
C82.85 Other types of follicular lymphoma, lymph nodes of inguinal region and lower limb
C82.86 Other types of follicular lymphoma, intrapelvic lymph nodes
C82.87 Other types of follicular lymphoma, spleen
C82.88 Other types of follicular lymphoma, lymph nodes of multiple sites
C82.89 Other types of follicular lymphoma, extranodal and solid organ sites
C82.90 Follicular lymphoma, unspecified, unspecified site
C82.91 Follicular lymphoma, unspecified, lymph nodes of head, face, and neck
C82.92 Follicular lymphoma, unspecified, intrathoracic lymph nodes
C82.93 Follicular lymphoma, unspecified, intra-abdominal lymph nodes
C82.94 Follicular lymphoma, unspecified, lymph nodes of axilla and upper limb
C82.95 Follicular lymphoma, unspecified, lymph nodes of inguinal region and lower limb
C82.96 Follicular lymphoma, unspecified, intrapelvic lymph nodes
C82.97 Follicular lymphoma, unspecified, spleen
C82.98 Follicular lymphoma, unspecified, lymph nodes of multiple sites
C82.99 Follicular lymphoma, unspecified, extranodal and solid organ sites
C83.30 Diffuse large B-cell lymphoma, unspecified site
C83.31 Diffuse large B-cell lymphoma, lymph nodes of head, face, and neck
C83.32 Diffuse large B-cell lymphoma, intrathoracic lymph nodes
C83.33 Diffuse large B-cell lymphoma, intra-abdominal lymph nodes
C83.34 Diffuse large B-cell lymphoma, lymph nodes of axilla and upper limb
C83.35 Diffuse large B-cell lymphoma, lymph nodes of inguinal region and lower limb
C83.36 Diffuse large B-cell lymphoma, intrapelvic lymph nodes
C83.37 Diffuse large B-cell lymphoma, spleen
C83.38 Diffuse large B-cell lymphoma, lymph nodes of multiple sites
C83.398 Diffuse large B-cell lymphoma of other extranodal and solid organ sites
C83.50 Lymphoblastic (diffuse) lymphoma, unspecified site
C83.51 Lymphoblastic (diffuse) lymphoma, lymph nodes of head, face, and neck
C83.52 Lymphoblastic (diffuse) lymphoma, intrathoracic lymph nodes
C83.53 Lymphoblastic (diffuse) lymphoma, intra-abdominal lymph nodes
C83.54 Lymphoblastic (diffuse) lymphoma, lymph nodes of axilla and upper limb
C83.55 Lymphoblastic (diffuse) lymphoma, lymph nodes of inguinal region and lower limb
C83.56 Lymphoblastic (diffuse) lymphoma, intrapelvic lymph nodes
C83.57 Lymphoblastic (diffuse) lymphoma, spleen
C83.58 Lymphoblastic (diffuse) lymphoma, lymph nodes of multiple sites
C83.59 Lymphoblastic (diffuse) lymphoma, extranodal and solid organ sites

C83.80 Other non-follicular lymphoma, unspecified site
C83.81 Other non-follicular lymphoma, lymph nodes of head, face, and neck
C83.82 Other non-follicular lymphoma, intrathoracic lymph nodes
C83.83 Other non-follicular lymphoma, intra-abdominal lymph nodes
C83.84 Other non-follicular lymphoma, lymph nodes of axilla and upper limb
C83.85 Other non-follicular lymphoma, lymph nodes of inguinal region and lower limb
C83.86 Other non-follicular lymphoma, intrapelvic lymph nodes
C83.87 Other non-follicular lymphoma, spleen
C83.88 Other non-follicular lymphoma, lymph nodes of multiple sites
C83.89 Other non-follicular lymphoma, extranodal and solid organ sites
C83.90 Non-follicular (diffuse) lymphoma, unspecified, unspecified site
C83.91 Non-follicular (diffuse) lymphoma, unspecified, lymph nodes of head, face, and neck
C83.92 Non-follicular (diffuse) lymphoma, unspecified, intrathoracic lymph nodes
C83.93 Non-follicular (diffuse) lymphoma, unspecified, intra-abdominal lymph nodes
C83.94 Non-follicular (diffuse) lymphoma, unspecified, lymph nodes of axilla and upper limb
C83.95 Non-follicular (diffuse) lymphoma, unspecified, lymph nodes of inguinal region and lower limb
C83.96 Non-follicular (diffuse) lymphoma, unspecified, intrapelvic lymph nodes
C83.97 Non-follicular (diffuse) lymphoma, unspecified, spleen
C83.98 Non-follicular (diffuse) lymphoma, unspecified, lymph nodes of multiple sites
C83.99 Non-follicular (diffuse) lymphoma, unspecified, extranodal and solid organ sites
C84.00 Mycosis fungoides, unspecified site
C84.01 Mycosis fungoides, lymph nodes of head, face, and neck
C84.02 Mycosis fungoides, intrathoracic lymph nodes
C84.03 Mycosis fungoides, intra-abdominal lymph nodes
C84.04 Mycosis fungoides, lymph nodes of axilla and upper limb
C84.05 Mycosis fungoides, lymph nodes of inguinal region and lower limb
C84.06 Mycosis fungoides, intrapelvic lymph nodes
C84.07 Mycosis fungoides, spleen
C84.08 Mycosis fungoides, lymph nodes of multiple sites
C84.09 Mycosis fungoides, extranodal and solid organ sites
C84.10 Sezary disease, unspecified site
C84.11 Sezary disease, lymph nodes of head, face, and neck
C84.12 Sezary disease, intrathoracic lymph nodes
C84.13 Sezary disease, intra-abdominal lymph nodes
C84.14 Sezary disease, lymph nodes of axilla and upper limb
C84.15 Sezary disease, lymph nodes of inguinal region and lower limb
C84.16 Sezary disease, intrapelvic lymph nodes
C84.17 Sezary disease, spleen
C84.18 Sezary disease, lymph nodes of multiple sites
C84.19 Sezary disease, extranodal and solid organ sites
C84.40 Peripheral T-cell lymphoma, not elsewhere classified, unspecified site
C84.41 Peripheral T-cell lymphoma, not elsewhere classified, lymph nodes of head, face, and neck

C84.42 Peripheral T-cell lymphoma, not elsewhere classified, intrathoracic lymph nodes
C84.43 Peripheral T-cell lymphoma, not elsewhere classified, intra-abdominal lymph nodes
C84.44 Peripheral T-cell lymphoma, not elsewhere classified, lymph nodes of axilla and upper limb
C84.45 Peripheral T-cell lymphoma, not elsewhere classified, lymph nodes of inguinal region and lower limb
C84.46 Peripheral T-cell lymphoma, not elsewhere classified, intrapelvic lymph nodes
C84.47 Peripheral T-cell lymphoma, not elsewhere classified, spleen
C84.48 Peripheral T-cell lymphoma, not elsewhere classified, lymph nodes of multiple sites
C84.49 Peripheral T-cell lymphoma, not elsewhere classified, extranodal and solid organ sites
C84.60 Anaplastic large cell lymphoma, ALK-positive, unspecified site
C84.61 Anaplastic large cell lymphoma, ALK-positive, lymph nodes of head, face, and neck
C84.62 Anaplastic large cell lymphoma, ALK-positive, intrathoracic lymph nodes
C84.63 Anaplastic large cell lymphoma, ALK-positive, intra-abdominal lymph nodes
C84.64 Anaplastic large cell lymphoma, ALK-positive, lymph nodes of axilla and upper limb
C84.65 Anaplastic large cell lymphoma, ALK-positive, lymph nodes of inguinal region and lower limb
C84.66 Anaplastic large cell lymphoma, ALK-positive, intrapelvic lymph nodes
C84.67 Anaplastic large cell lymphoma, ALK-positive, spleen
C84.68 Anaplastic large cell lymphoma, ALK-positive, lymph nodes of multiple sites
C84.69 Anaplastic large cell lymphoma, ALK-positive, extranodal and solid organ sites
C84.70 Anaplastic large cell lymphoma, ALK-negative, unspecified site
C84.71 Anaplastic large cell lymphoma, ALK-negative, lymph nodes of head, face, and neck
C84.72 Anaplastic large cell lymphoma, ALK-negative, intrathoracic lymph nodes
C84.73 Anaplastic large cell lymphoma, ALK-negative, intra-abdominal lymph nodes
C84.74 Anaplastic large cell lymphoma, ALK-negative, lymph nodes of axilla and upper limb
C84.75 Anaplastic large cell lymphoma, ALK-negative, lymph nodes of inguinal region and lower limb
C84.76 Anaplastic large cell lymphoma, ALK-negative, intrapelvic lymph nodes
C84.77 Anaplastic large cell lymphoma, ALK-negative, spleen
C84.78 Anaplastic large cell lymphoma, ALK-negative, lymph nodes of multiple sites
C84.79 Anaplastic large cell lymphoma, ALK-negative, extranodal and solid organ sites
C84.7A Anaplastic large cell lymphoma, ALK-negative, breast
C84.90 Mature T/NK-cell lymphomas, unspecified, unspecified site
C84.91 Mature T/NK-cell lymphomas, unspecified, lymph nodes of head, face, and neck
C84.92 Mature T/NK-cell lymphomas, unspecified, intrathoracic lymph nodes
C84.93 Mature T/NK-cell lymphomas, unspecified, intra-abdominal lymph nodes
C84.94 Mature T/NK-cell lymphomas, unspecified, lymph nodes of axilla and upper limb
C84.95 Mature T/NK-cell lymphomas, unspecified, lymph nodes of inguinal region and lower limb
C84.96 Mature T/NK-cell lymphomas, unspecified, intrapelvic lymph nodes
C84.97 Mature T/NK-cell lymphomas, unspecified, spleen
C84.98 Mature T/NK-cell lymphomas, unspecified, lymph nodes of multiple sites
C84.99 Mature T/NK-cell lymphomas, unspecified, extranodal and solid organ sites

C84.A0 Cutaneous T-cell lymphoma, unspecified, unspecified site
C84.A1 Cutaneous T-cell lymphoma, unspecified lymph nodes of head, face, and neck
C84.A2 Cutaneous T-cell lymphoma, unspecified, intrathoracic lymph nodes
C84.A3 Cutaneous T-cell lymphoma, unspecified, intra-abdominal lymph nodes
C84.A4 Cutaneous T-cell lymphoma, unspecified, lymph nodes of axilla and upper limb
C84.A5 Cutaneous T-cell lymphoma, unspecified, lymph nodes of inguinal region and lower limb
C84.A6 Cutaneous T-cell lymphoma, unspecified, intrapelvic lymph nodes
C84.A7 Cutaneous T-cell lymphoma, unspecified, spleen
C84.A8 Cutaneous T-cell lymphoma, unspecified, lymph nodes of multiple sites
C84.A9 Cutaneous T-cell lymphoma, unspecified, extranodal and solid organ sites
C84.Z0 Other mature T/NK-cell lymphomas, unspecified site
C84.Z1 Other mature T/NK-cell lymphomas, lymph nodes of head, face, and neck
C84.Z2 Other mature T/NK-cell lymphomas, intrathoracic lymph nodes
C84.Z3 Other mature T/NK-cell lymphomas, intra-abdominal lymph nodes
C84.Z4 Other mature T/NK-cell lymphomas, lymph nodes of axilla and upper limb
C84.Z5 Other mature T/NK-cell lymphomas, lymph nodes of inguinal region and lower limb
C84.Z6 Other mature T/NK-cell lymphomas, intrapelvic lymph nodes
C84.Z7 Other mature T/NK-cell lymphomas, spleen
C84.Z8 Other mature T/NK-cell lymphomas, lymph nodes of multiple sites
C84.Z9 Other mature T/NK-cell lymphomas, extranodal and solid organ sites
C85.10 Unspecified B-cell lymphoma, unspecified site
C85.11 Unspecified B-cell lymphoma, lymph nodes of head, face, and neck
C85.12 Unspecified B-cell lymphoma, intrathoracic lymph nodes
C85.13 Unspecified B-cell lymphoma, intra-abdominal lymph nodes
C85.14 Unspecified B-cell lymphoma, lymph nodes of axilla and upper limb
C85.15 Unspecified B-cell lymphoma, lymph nodes of inguinal region and lower limb
C85.16 Unspecified B-cell lymphoma, intrapelvic lymph nodes
C85.17 Unspecified B-cell lymphoma, spleen
C85.18 Unspecified B-cell lymphoma, lymph nodes of multiple sites
C85.19 Unspecified B-cell lymphoma, extranodal and solid organ sites
C85.20 Mediastinal (thymic) large B-cell lymphoma, unspecified site
C85.21 Mediastinal (thymic) large B-cell lymphoma, lymph nodes of head, face, and neck
C85.22 Mediastinal (thymic) large B-cell lymphoma, intrathoracic lymph nodes
C85.23 Mediastinal (thymic) large B-cell lymphoma, intra-abdominal lymph nodes
C85.24 Mediastinal (thymic) large B-cell lymphoma, lymph nodes of axilla and upper limb
C85.25 Mediastinal (thymic) large B-cell lymphoma, lymph nodes of inguinal region and lower limb
C85.26 Mediastinal (thymic) large B-cell lymphoma, intrapelvic lymph nodes
C85.27 Mediastinal (thymic) large B-cell lymphoma, spleen
C85.28 Mediastinal (thymic) large B-cell lymphoma, lymph nodes of multiple sites
C85.29 Mediastinal (thymic) large B-cell lymphoma, extranodal and solid organ sites
C85.80 Other specified types of non-Hodgkin lymphoma, unspecified site
C85.81 Other specified types of non-Hodgkin lymphoma, lymph nodes of head, face, and neck
C85.82 Other specified types of non-Hodgkin lymphoma, intrathoracic lymph nodes

C85.83 Other specified types of non-Hodgkin lymphoma, intrathoracic lymph nodes
C85.84 Other specified types of non-Hodgkin lymphoma, lymph nodes of axilla and upper limb
C85.85 Other specified types of non-Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C85.86 Other specified types of non-Hodgkin lymphoma, intrapelvic lymph nodes
C85.87 Other specified types of non-Hodgkin lymphoma, spleen
C85.88 Other specified types of non-Hodgkin lymphoma, lymph nodes of multiple sites
C85.89 Other specified types of non-Hodgkin lymphoma, extranodal and solid organ sites
C86.00 Extranodal NK/T-cell lymphoma, nasal type not having achieved remission
C86.10 Hepatosplenic T-cell lymphoma not having achieved remission
C86.20 Enteropathy-type (intestinal) T-cell lymphoma not having achieved remission
C86.50 Angioimmunoblastic T-cell lymphoma not having achieved remission
C86.60 Primary cutaneous CD30-positive T-cell proliferations not having achieved remission
C91.50 Adult T-cell lymphoma/leukemia (HTLV-1-associated) not having achieved remission
C91.51 Adult T-cell lymphoma/leukemia (HTLV-1-associated), in remission
C91.52 Adult T-cell lymphoma/leukemia (HTLV-1-associated), in relapse
D47.Z1 Post -transplant lymphoproliferative disorder (PTLD)

Duration of authorization: 12 months

Version Effective Date: 11/18/2024

Title: Burosumab-twza (Crysvita®)

MEDICALLY NECESSARY:

INITIAL THERAPY

Burosumab-twza (Crysvita®) is considered medically necessary and, therefore, covered for:

1. Individuals at least 6 months of age and older with X-linked hypophosphatemia (XLH)
2. Individuals at least 2 years of age and older with tumor-induced osteomalacia (TIO) associated with phosphaturic mesenchymal tumors (PMT) that cannot be curatively resected or localized

when all of the following criteria listed below are met:

- Diagnosis of XLH or TIO associated with PMT supported by one of the following:
 - For XLH: Documented PHEX pathogenic (i.e., disease-causing) mutation in either the individual or in a directly related family member with appropriate x-linked inheritance
 - For TIO: Documented evidence of TIO associated with PMT
 - Serum fibroblast growth factor 23 FGF23 (FGF23) level > 30 pg/mL
- Documentation of classic clinical features of disease (e.g., rickets, growth abnormalities [short stature or lower extremity bowing], bone pain, bone fractures)
- Fasting serum phosphorus is below the normal range for age
- Does not have renal impairment or end stage renal disease defined as a glomerular filtration rate < 30 mL/min
- Individual has or is willing to discontinue use of oral phosphate and active vitamin D analogs within one week prior to treatment initiation

CONTINUATION THERAPY

Burosumab-twza (Crysvita®) is considered medically necessary and, therefore, covered during continuation therapy for individuals at least 6 months of age and older with XLH and individuals at least 2 years of age and older with TIO associated with phosphaturic mesenchymal tumors that cannot be curatively resected or localized when all of the following criteria listed below are met:

- Normalized serum phosphate during therapy, and the absence of hyperphosphatemia
- Documented clinical improvement in the following:
 - Adult individuals --- (e.g., improvement in bone pain, enhanced mobility, radiographic evidence of improvement in osteomalacia/ fracture healing)
 - Pediatric individuals --- (e.g., enhanced height velocity, improvement in lower extremity bowing and associated abnormalities, improved walking ability, radiographic evidence of improvements of rickets/ osteomalacia/ epiphyseal healing)

Duration of authorization: 12 months

Version Effective Date: 05/28/2025

Title: Canakinumab (Ilaris®)

MEDICALLY NECESSARY:

The following indications will be addressed in this policy. Please see the specific criteria below for the Medical Necessity criteria:

- Gout flares
- Periodic fever syndromes:
 - Cryopyrin-associated periodic syndromes (CAPS) including: familial cold autoinflammatory syndrome (FCAS) and Muckle-Wells syndrome (MWS)
 - Tumor necrosis factor (TNF) receptor–associated periodic syndrome (TRAPS)
 - Hyperimmunoglobulin D (Hyper-IgD) syndrome (HIDS)/mevalonate kinase deficiency (MKD)
 - Familial Mediterranean fever (FMF)
- Still's disease: adult-onset Still disease (AOSD) and systemic juvenile idiopathic arthritis (SJIA)

GOUT FLARES

Initial Therapy

Canakinumab (Ilaris) is considered medically necessary and, therefore, covered for the treatment of gout flares in adults when the following criteria, including Dosing and Frequency Requirements, are met:

- Documentation of at least three gout flares in the previous 12 months
- Documentation of a contraindication, or inadequate response or intolerance to at least 3 months of therapy with all of the following: nonsteroidal anti-inflammatory drugs (NSAIDs), colchicine, corticosteroids
- Canakinumab (Ilaris) will not be used in combination with TNF inhibitors (e.g., adalimumab [Humira], etanercept [Enbrel], or infliximab [Remicade]) or other interleukin-1 [IL-1] blocking agents (e.g., rilonacept [Arcalyst] and anakinra [Kineret])
- Individual does not have chronic or active infection, including human immunodeficiency virus (HIV), hepatitis B, hepatitis C, or tuberculosis
- Dosing and frequency: 150 mg administered by subcutaneous injection for one dose

Continuation Therapy (after at least 12 weeks since initial therapy)

Canakinumab (Ilaris) is considered medically necessary and, therefore, covered for continuation therapy following at least 12 weeks since initial therapy when the individual meets all of the following criteria:

- Individual meets the dosing and frequency criteria outlined above
- Documented improvement in clinical signs and symptoms of gout (e.g, reduction joint pain/swelling) since the last dose, and gouty arthritis flare has recurred

PERIODIC FEVER SYNDROMES

Canakinumab (Ilaris) is considered medically necessary and, therefore, covered for any of the following indications when **all** of the corresponding criteria, including dosing and frequency requirements, are met:

Cryopyrin-Associated Periodic Syndromes (CAPS), Including Familial Cold Autoinflammatory Syndrome (FCAS), and Muckle-Wells Syndrome (MWS)

Initial Therapy

- Documented diagnosis of CAPS confirmed by molecular genetic testing that reveals pathogenic variation(s) in the *NLRP3* (also known as CIAS1) gene (e.g., variation of p.Leu353Pro or p.Leu305Pro for FCAS; variation of R260W or T348M for MWS)
- Documented presence of symptoms associated with CAPS (e.g., fever or chills, rash, joint or muscle pain, eye discomfort or redness, fatigue, headache)
- Individual is 4 years of age or older
- Canakinumab (Ilaris) will not be used in combination with TNF inhibitors (e.g., adalimumab [Humira], etanercept [Enbrel], or infliximab [Remicade]) or other IL-1–blocking agents (e.g., rilonacept [Arcalyst] and anakinra [Kineret]).
- Individual does not have chronic or active infection, including HIV, hepatitis B, hepatitis C, or tuberculosis
- Dosing and frequency: subcutaneous administration is every 8 weeks
 - For individuals with body weight greater than 40 kg, dose is 150 mg
 - For individuals with body weight 15 to 40 kg, dose is 2 mg/kg. If inadequate response, the dose may be increased to 3 mg/kg.

Continuation Therapy (After At Least 24 Weeks of Therapy)

Canakinumab (Ilaris) is considered medically necessary and, therefore, covered for continuation therapy following at least 24 weeks of therapy when the individual meets all of the following criteria:

- Individual meets the dosing and frequency criteria outlined above
- Documented reduction in total number of fever episodes and reduction in severity of other symptoms, compared to baseline

Tumor Necrosis Factor (TNF) Receptor–Associated Periodic Syndrome (TRAPS)

Initial Therapy

- Documented diagnosis of TRAPS confirmed by molecular genetic testing that reveals pathogenic variation(s) in the *TNFRSF1A* gene (e.g., R92Q, T50M, C29F, C30R/S, C33G/Y, Y38C, C52F, C55S, C70R/Y, C88R/Y)
- Documented presence of all of the following characteristics of TRAPS:
 - Chronic or recurrent disease (i.e., more than six fever episodes per year)
 - C-reactive protein (CRP) level of more than 10 mg/L
 - Physician’s global assessment (PGA) score of 2 or higher for fever, skin rash, musculoskeletal pain, abdominal pain, and eye manifestations
- Individual is 2 years of age or older

- Canakinumab (Ilaris) will not be used in combination with TNF inhibitors (e.g., adalimumab [Humira], etanercept [Enbrel], or infliximab [Remicade]) or other IL-1–blocking agents (e.g., rilonacept [Arcalyst] and anakinra [Kineret]).
- Individual does not have chronic or active infection, including HIV, hepatitis B, hepatitis C, or tuberculosis.
- Dosing and frequency by subcutaneous injection as follows:
 - For individuals with body weight less than or equal to 40 kg, dose is 2 mg/kg administered every 4 weeks. If inadequate response, the dose can be increased to 4 mg/kg every 4 weeks.
 - For individuals with body weight greater than 40 kg, the dose is 150 mg administered every 4 weeks. If inadequate response, the dose can be increased to 300 mg every 4 weeks.

Continuation Therapy (After At Least 16 Weeks of Therapy)

Canakinumab (Ilaris) is considered medically necessary and, therefore, covered for continuation therapy following at least 16 weeks of therapy when the individual meets all of the following criteria:

- Individual meets the dosing and frequency criteria outlined above
- PGA score less than 2 for fever, skin rash, musculoskeletal pain, abdominal pain, and eye manifestations
- Documented CRP level of 10 mg/L or less, or a reduction by 70% or more from baseline

Hyperimmunoglobulin D (Hyper-IgD) Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD)*

Initial Therapy

- Documented presence of all of the following characteristics of HIDS/MKD:
 - Documented history of at least three fever episodes in a 6-month period when not receiving prophylactic treatment
 - CRP level of more than 10 mg/L
 - PGA score of 2 or higher for fever, abdominal pain, lymphadenopathy, aphthous ulcers
- Individual is 2 years of age or older
- Canakinumab (Ilaris) will not be used in combination with TNF inhibitors (e.g., adalimumab [Humira], etanercept [Enbrel], or infliximab [Remicade]) or other IL-1 blocking agents (e.g., rilonacept [Arcalyst] and anakinra [Kineret])
- Individual does not have chronic or active infection, including HIV, hepatitis B, hepatitis C, or tuberculosis
- Dosing and frequency by subcutaneous injection as follows:
 - For individuals with body weight less than or equal to 40 kg, dose is 2 mg/kg administered every 4 weeks. If inadequate response, the dose can be increased to 4 mg/kg every 4 weeks.
 - For individuals with body weight greater than 40 kg, the dose is 150 mg administered every 4 weeks. If inadequate response, the dose can be increased to 300 mg every 4 weeks.

*If genetic variation(s) in the *MVK* gene is noted in documentation, the above clinical criteria must also be met.

Continuation Therapy (after at least 16 weeks of therapy)

Canakinumab (Ilaris) is considered medically necessary and, therefore, covered for continuation therapy following at least 16 weeks of therapy when the individual meets all of the following criteria:

- Individual meets the dosing and frequency criteria outlined above
- PGA score less than 2 for fever, skin rash, musculoskeletal pain, abdominal pain, and eye manifestations
- Documented CRP level of 10 mg/L or less, or a reduction by 70% or more from baseline

Familial Mediterranean Fever (FMF)**

Initial Therapy

- Documented presence of all of the following characteristics of FMF:
 - Documented history of at least one fever episode per month
 - CRP level of more than 10 mg/L
 - PGA score of 2 or higher for fever, abdominal pain, skin rash, chest pain, arthralgia, arthritis
 - Fulfillment of Tel HaShomer diagnostic criteria for FMF as follows: two or more major symptoms, or one major plus two minor symptoms, as listed below:
 - Major Symptoms
 - Recurrent febrile episodes with serositis (peritonitis, synovitis, or pleuritis)
 - Amyloidosis of AA type without a predisposing disease
 - Favorable response to regular colchicine treatment
 - Minor Symptoms
 - Recurrent febrile episodes
 - Erysipelas-like erythema
 - FMF in a first-degree relative
- Documented contraindication, failure, or intolerance to colchicine
- Individual is 2 years of age or older
- Canakinumab (Ilaris) will not be used in combination with TNF inhibitors (e.g., adalimumab [Humira], etanercept [Enbrel], or infliximab [Remicade]) or other IL-1 blocking agents (e.g., rilonacept [Arcalyst] and anakinra [Kineret])
- Individual does not have chronic or active infection, including HIV, hepatitis B, hepatitis C, or tuberculosis
- Dosing and frequency by subcutaneous injection as follows:
 - For individuals with body weight less than or equal to 40 kg, dose is 2 mg/kg administered every 4 weeks. If inadequate response, the dose can be increased to 4 mg/kg every 4 weeks.
 - For individuals with body weight greater than 40 kg, the dose is 150 mg administered every 4 weeks. If inadequate response, the dose can be increased to 300 mg every 4 weeks.

****If genetic variation(s) in the *MEFV* gene is noted in documentation, the above clinical criteria must also be met.**

Continuation Therapy (after at least 16 weeks of therapy)

Canakinumab (Ilaris) is considered medically necessary and, therefore, covered for continuation therapy following at least 16 weeks of therapy when the individual meets all of the following criteria:

- Individual meets the dosing and frequency criteria outlined above
- PGA score less than 2 for fever, skin rash, musculoskeletal pain, abdominal pain, and eye manifestations
- Documented CRP level of 10 mg/L or less, or a reduction by 70% or more from baseline STILL DISEASE (ADULT-ONSET STILL DISEASE [AOSD], SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS [SJIA])

Initial Therapy

Canakinumab (Ilaris) is considered medically necessary and, therefore, covered for the treatment of active Still disease, including AOSD or SJIA when the following criteria, including dosing and frequency requirements, are met:

- Documented diagnosis of moderate to severely active AOSD or SJIA characterized by all of the following symptoms:
 - Chronic arthritis with two or more active joints involved (for SJIA) or four or more active joints involved (for AOSD)
 - Daily, but intermittently, high spiking fever
 - Additionally, accompanied by one or more of the following: rash, hepatosplenomegaly, lymphadenopathy, serositis
- Individual is 2 years of age or older
- There is documentation of inadequate response, intolerance, or contraindication to at least one of the following: nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, other disease-modifying antirheumatic drugs (DMARDs) (e.g., anakinra, methotrexate, tocilizumab, TNF inhibitors)
- Canakinumab (Ilaris) will not be used in combination with NF inhibitors (e.g., adalimumab [Humira], etanercept [Enbrel], or infliximab [Remicade]) or other IL-1 blocking agents (e.g., rilonacept [Arcalyst] and anakinra [Kineret])
- Individual does not have chronic or active infection, including HIV, hepatitis B, hepatitis C, or tuberculosis
- Dosing and frequency: for individuals with body weight 7.5 kg or above, dose is 4 mg/kg (maximum of 300 mg) administered by subcutaneous injection every 4 weeks

Continuation Therapy (after at least 32 weeks of therapy)

Canakinumab (Ilaris) is considered medically necessary and, therefore, covered for continuation therapy following at least 32 weeks of therapy when the individual meets all of the following criteria:

- Individual meets the dosing and frequency criteria outlined above
- Documented improvement or stability of AOSD or SJIA (e.g., reduction in the signs and symptoms [including number of active joints involved], and reduction in corticosteroid dose)

Duration of authorization: 12 months

Version Effective Date: 05/28/2025

Title: Canakinumab (Ilaris®)

MEDICALLY NECESSARY:

ICD-10 CODES AND NARRATIVES

E85.0 Non-neuropathic hereditary amyloidosis

M04.1 Periodic fever syndromes

M04.2 Cryopyrin-associated periodic syndromes

M06.1 Adult-onset Still's disease

M08.20 Juvenile rheumatoid arthritis with systemic onset, unspecified site

M08.211 Juvenile rheumatoid arthritis with systemic onset, right shoulder

M08.212 Juvenile rheumatoid arthritis with systemic onset, left shoulder

M08.221 Juvenile rheumatoid arthritis with systemic onset, right elbow

M08.222 Juvenile rheumatoid arthritis with systemic onset, left elbow

M08.231 Juvenile rheumatoid arthritis with systemic onset, right wrist

M08.232 Juvenile rheumatoid arthritis with systemic onset, left wrist

M08.241 Juvenile rheumatoid arthritis with systemic onset, right hand

M08.242 Juvenile rheumatoid arthritis with systemic onset, left hand

M08.251 Juvenile rheumatoid arthritis with systemic onset, right hip

M08.252 Juvenile rheumatoid arthritis with systemic onset, left hip

M08.261 Juvenile rheumatoid arthritis with systemic onset, right knee

M08.262 Juvenile rheumatoid arthritis with systemic onset, left knee

M08.271 Juvenile rheumatoid arthritis with systemic onset, right ankle and foot

M08.272 Juvenile rheumatoid arthritis with systemic onset, left ankle and foot

M08.28 Juvenile rheumatoid arthritis with systemic onset, vertebrae

M08.29 Juvenile rheumatoid arthritis with systemic onset, multiple sites

M08.2A Juvenile rheumatoid arthritis with systemic onset, other specified site

M1A.00X0 Idiopathic chronic gout, unspecified site, without tophus (tophi)

M1A.00X1 Idiopathic chronic gout, unspecified site, with tophus (tophi)

M1A.0110 Idiopathic chronic gout, right shoulder, without tophus (tophi)

M1A.0111 Idiopathic chronic gout, right shoulder, with tophus (tophi)

M1A.0120 Idiopathic chronic gout, left shoulder, without tophus (tophi)

M1A.0121 Idiopathic chronic gout, left shoulder, with tophus (tophi)

M1A.0210 Idiopathic chronic gout, right elbow, without tophus (tophi)

M1A.0211 Idiopathic chronic gout, right elbow, with tophus (tophi)

M1A.0220 Idiopathic chronic gout, left elbow, without tophus (tophi)

M1A.0221 Idiopathic chronic gout, left elbow, with tophus (tophi)

M1A.0310 Idiopathic chronic gout, right wrist, without tophus (tophi)

M1A.0311 Idiopathic chronic gout, right wrist, with tophus (tophi)

M1A.0320 Idiopathic chronic gout, left wrist, without tophus (tophi)

M1A.0321 Idiopathic chronic gout, left wrist, with tophus (tophi)

M1A.0410 Idiopathic chronic gout, right hand, without tophus (tophi)

M1A.0411 Idiopathic chronic gout, right hand, with tophus (tophi)

M1A.0420	Idiopathic chronic gout, left hand, without tophus (tophi)
M1A.0421	Idiopathic chronic gout, left hand, with tophus (tophi)
M1A.0510	Idiopathic chronic gout, right hip, without tophus (tophi)
M1A.0511	Idiopathic chronic gout, right hip, with tophus (tophi)
M1A.0520	Idiopathic chronic gout, left hip, without tophus (tophi)
M1A.0521	Idiopathic chronic gout, left hip, with tophus (tophi)
M1A.0610	Idiopathic chronic gout, right knee, without tophus (tophi)
M1A.0611	Idiopathic chronic gout, right knee, with tophus (tophi)
M1A.0620	Idiopathic chronic gout, left knee, without tophus (tophi)
M1A.0621	Idiopathic chronic gout, left knee, with tophus (tophi)
M1A.0710	Idiopathic chronic gout, right ankle and foot, without tophus (tophi)
M1A.0711	Idiopathic chronic gout, right ankle and foot, with tophus (tophi)
M1A.0720	Idiopathic chronic gout, left ankle and foot, without tophus (tophi)
M1A.0721	Idiopathic chronic gout, left ankle and foot, with tophus (tophi)
M1A.08X0	Idiopathic chronic gout, vertebrae, without tophus (tophi)
M1A.08X1	Idiopathic chronic gout, vertebrae, with tophus (tophi)
M1A.09X0	Idiopathic chronic gout, multiple sites, without tophus (tophi)
M1A.09X1	Idiopathic chronic gout, multiple sites, with tophus (tophi)
M1A.10X0	Lead-induced chronic gout, unspecified site, without tophus (tophi)
M1A.10X1	Lead-induced chronic gout, unspecified site, with tophus (tophi)
M1A.1110	Lead-induced chronic gout, right shoulder, without tophus (tophi)
M1A.1111	Lead-induced chronic gout, right shoulder, with tophus (tophi)
M1A.1120	Lead-induced chronic gout, left shoulder, without tophus (tophi)
M1A.1121	Lead-induced chronic gout, left shoulder, with tophus (tophi)
M1A.1210	Lead-induced chronic gout, right elbow, without tophus (tophi)
M1A.1211	Lead-induced chronic gout, right elbow, with tophus (tophi)
M1A.1220	Lead-induced chronic gout, left elbow, without tophus (tophi)
M1A.1221	Lead-induced chronic gout, left elbow, with tophus (tophi)
M1A.1310	Lead-induced chronic gout, right wrist, without tophus (tophi)
M1A.1311	Lead-induced chronic gout, right wrist, with tophus (tophi)
M1A.1320	Lead-induced chronic gout, left wrist, without tophus (tophi)
M1A.1321	Lead-induced chronic gout, left wrist, with tophus (tophi)
M1A.1410	Lead-induced chronic gout, right hand, without tophus (tophi)
M1A.1411	Lead-induced chronic gout, right hand, with tophus (tophi)
M1A.1420	Lead-induced chronic gout, left hand, without tophus (tophi)
M1A.1421	Lead-induced chronic gout, left hand, with tophus (tophi)
M1A.1510	Lead-induced chronic gout, right hip, without tophus (tophi)
M1A.1511	Lead-induced chronic gout, right hip, with tophus (tophi)
M1A.1520	Lead-induced chronic gout, left hip, without tophus (tophi)
M1A.1521	Lead-induced chronic gout, left hip, with tophus (tophi)
M1A.1610	Lead-induced chronic gout, right knee, without tophus (tophi)
M1A.1611	Lead-induced chronic gout, right knee, with tophus (tophi)
M1A.1620	Lead-induced chronic gout, left knee, without tophus (tophi)
M1A.1621	Lead-induced chronic gout, left knee, with tophus (tophi)

M1A.1710	Lead-induced chronic gout, right ankle and foot, without tophus (tophi)
M1A.1711	Lead-induced chronic gout, right ankle and foot, with tophus (tophi)
M1A.1720	Lead-induced chronic gout, left ankle and foot, without tophus (tophi)
M1A.1721	Lead-induced chronic gout, left ankle and foot, with tophus (tophi)
M1A.18X0	Lead-induced chronic gout, vertebrae, without tophus (tophi)
M1A.18X1	Lead-induced chronic gout, vertebrae, with tophus (tophi)
M1A.19X0	Lead-induced chronic gout, multiple sites, without tophus (tophi)
M1A.19X1	Lead-induced chronic gout, multiple sites, with tophus (tophi)
M1A.20X0	Drug-induced chronic gout, unspecified site, without tophus (tophi)
M1A.20X1	Drug-induced chronic gout, unspecified site, with tophus (tophi)
M1A.2110	Drug-induced chronic gout, right shoulder, without tophus (tophi)
M1A.2111	Drug-induced chronic gout, right shoulder, with tophus (tophi)
M1A.2120	Drug-induced chronic gout, left shoulder, without tophus (tophi)
M1A.2121	Drug-induced chronic gout, left shoulder, with tophus (tophi)
M1A.2210	Drug-induced chronic gout, right elbow, without tophus (tophi)
M1A.2211	Drug-induced chronic gout, right elbow, with tophus (tophi)
M1A.2220	Drug-induced chronic gout, left elbow, without tophus (tophi)
M1A.2221	Drug-induced chronic gout, left elbow, with tophus (tophi)
M1A.2310	Drug-induced chronic gout, right wrist, without tophus (tophi)
M1A.2311	Drug-induced chronic gout, right wrist, with tophus (tophi)
M1A.2320	Drug-induced chronic gout, left wrist, without tophus (tophi)
M1A.2321	Drug-induced chronic gout, left wrist, with tophus (tophi)
M1A.2410	Drug-induced chronic gout, right hand, without tophus (tophi)
M1A.2411	Drug-induced chronic gout, right hand, with tophus (tophi)
M1A.2420	Drug-induced chronic gout, left hand, without tophus (tophi)
M1A.2421	Drug-induced chronic gout, left hand, with tophus (tophi)
M1A.2510	Drug-induced chronic gout, right hip, without tophus (tophi)
M1A.2511	Drug-induced chronic gout, right hip, with tophus (tophi)
M1A.2520	Drug-induced chronic gout, left hip, without tophus (tophi)
M1A.2521	Drug-induced chronic gout, left hip, with tophus (tophi)
M1A.2610	Drug-induced chronic gout, right knee, without tophus (tophi)
M1A.2611	Drug-induced chronic gout, right knee, with tophus (tophi)
M1A.2620	Drug-induced chronic gout, left knee, without tophus (tophi)
M1A.2621	Drug-induced chronic gout, left knee, with tophus (tophi)
M1A.2710	Drug-induced chronic gout, right ankle and foot, without tophus (tophi)
M1A.2711	Drug-induced chronic gout, right ankle and foot, with tophus (tophi)
M1A.2720	Drug-induced chronic gout, left ankle and foot, without tophus (tophi)
M1A.2721	Drug-induced chronic gout, left ankle and foot, with tophus (tophi)
M1A.28X0	Drug-induced chronic gout, vertebrae, without tophus (tophi)
M1A.28X1	Drug-induced chronic gout, vertebrae, with tophus (tophi)
M1A.29X0	Drug-induced chronic gout, multiple sites, without tophus (tophi)
M1A.29X1	Drug-induced chronic gout, multiple sites, with tophus (tophi)
M1A.30X0	Chronic gout due to renal impairment, unspecified site, without tophus (tophi)
M1A.30X1	Chronic gout due to renal impairment, unspecified site, with tophus (tophi)

M1A.3110	Chronic gout due to renal impairment, right shoulder, without tophus (tophi)
M1A.3111	Chronic gout due to renal impairment, right shoulder, with tophus (tophi)
M1A.3120	Chronic gout due to renal impairment, left shoulder, without tophus (tophi)
M1A.3121	Chronic gout due to renal impairment, left shoulder, with tophus (tophi)
M1A.3210	Chronic gout due to renal impairment, right elbow, without tophus (tophi)
M1A.3211	Chronic gout due to renal impairment, right elbow, with tophus (tophi)
M1A.3220	Chronic gout due to renal impairment, left elbow, without tophus (tophi)
M1A.3221	Chronic gout due to renal impairment, left elbow, with tophus (tophi)
M1A.3310	Chronic gout due to renal impairment, right wrist, without tophus (tophi)
M1A.3311	Chronic gout due to renal impairment, right wrist, with tophus (tophi)
M1A.3320	Chronic gout due to renal impairment, left wrist, without tophus (tophi)
M1A.3321	Chronic gout due to renal impairment, left wrist, with tophus (tophi)
M1A.3410	Chronic gout due to renal impairment, right hand, without tophus (tophi)
M1A.3411	Chronic gout due to renal impairment, right hand, with tophus (tophi)
M1A.3420	Chronic gout due to renal impairment, left hand, without tophus (tophi)
M1A.3421	Chronic gout due to renal impairment, left hand, with tophus (tophi)
M1A.3510	Chronic gout due to renal impairment, right hip, without tophus (tophi)
M1A.3511	Chronic gout due to renal impairment, right hip, with tophus (tophi)
M1A.3520	Chronic gout due to renal impairment, left hip, without tophus (tophi)
M1A.3521	Chronic gout due to renal impairment, left hip, with tophus (tophi)
M1A.3610	Chronic gout due to renal impairment, right knee, without tophus (tophi)
M1A.3611	Chronic gout due to renal impairment, right knee, with tophus (tophi)
M1A.3620	Chronic gout due to renal impairment, left knee, without tophus (tophi)
M1A.3621	Chronic gout due to renal impairment, left knee, with tophus (tophi)
M1A.3710	Chronic gout due to renal impairment, right ankle and foot, without tophus (tophi)
M1A.3711	Chronic gout due to renal impairment, right ankle and foot, with tophus (tophi)
M1A.3720	Chronic gout due to renal impairment, left ankle and foot, without tophus (tophi)
M1A.3721	Chronic gout due to renal impairment, left ankle and foot, with tophus (tophi)
M1A.38X0	Chronic gout due to renal impairment, vertebrae, without tophus (tophi)
M1A.38X1	Chronic gout due to renal impairment, vertebrae, with tophus (tophi)
M1A.39X1	Chronic gout due to renal impairment, multiple sites, with tophus (tophi)
M1A.40X0	Other secondary chronic gout, unspecified site, without tophus (tophi)
M1A.40X1	Other secondary chronic gout, unspecified site, with tophus (tophi)
M1A.4110	Other secondary chronic gout, right shoulder, without tophus (tophi)
M1A.4111	Other secondary chronic gout, right shoulder, with tophus (tophi)
M1A.4120	Other secondary chronic gout, left shoulder, without tophus (tophi)
M1A.4121	Other secondary chronic gout, left shoulder, with tophus (tophi)
M1A.4210	Other secondary chronic gout, right elbow, without tophus (tophi)
M1A.4211	Other secondary chronic gout, right elbow, with tophus (tophi)
M1A.4220	Other secondary chronic gout, left elbow, without tophus (tophi)
M1A.4221	Other secondary chronic gout, left elbow, with tophus (tophi)
M1A.4310	Other secondary chronic gout, right wrist, without tophus (tophi)
M1A.4311	Other secondary chronic gout, right wrist, with tophus (tophi)

M1A.4320	Other secondary chronic gout, left wrist, without tophus (tophi)
M1A.4321	Other secondary chronic gout, left wrist, with tophus (tophi)
M1A.4410	Other secondary chronic gout, right hand, without tophus (tophi)
M1A.4411	Other secondary chronic gout, right hand, with tophus (tophi)
M1A.4420	Other secondary chronic gout, left hand, without tophus (tophi)
M1A.4421	Other secondary chronic gout, left hand, with tophus (tophi)
M1A.4510	Other secondary chronic gout, right hip, without tophus (tophi)
M1A.4511	Other secondary chronic gout, right hip, with tophus (tophi)
M1A.4520	Other secondary chronic gout, left hip, without tophus (tophi)
M1A.4521	Other secondary chronic gout, left hip, with tophus (tophi)
M1A.4610	Other secondary chronic gout, right knee, without tophus (tophi)
M1A.4611	Other secondary chronic gout, right knee, with tophus (tophi)
M1A.4620	Other secondary chronic gout, left knee, without tophus (tophi)
M1A.4621	Other secondary chronic gout, left knee, with tophus (tophi)
M1A.4710	Other secondary chronic gout, right ankle and foot, without tophus (tophi)
M1A.4711	Other secondary chronic gout, right ankle and foot, with tophus (tophi)
M1A.4720	Other secondary chronic gout, left ankle and foot, without tophus (tophi)
M1A.4721	Other secondary chronic gout, left ankle and foot, with tophus (tophi)
M1A.48X0	Other secondary chronic gout, vertebrae, without tophus (tophi)
M1A.48X1	Other secondary chronic gout, vertebrae, with tophus (tophi)
M1A.49X0	Other secondary chronic gout, multiple sites, without tophus (tophi)
M1A.49X1	Other secondary chronic gout, multiple sites, with tophus (tophi)
M1A.9XX0	Chronic gout, unspecified, without tophus (tophi)
M1A.9XX1	Chronic gout, unspecified, with tophus (tophi)

Duration of authorization: 12 months

Version Effective Date: 05/28/2025

Title: Carfilzomib (Kyprolis®)

MEDICALLY NECESSARY:

Carfilzomib (Kyprolis) is considered medically necessary and, therefore, covered for the treatment of individuals with any of the following indications:

- Multiple myeloma
 - Primary therapy for symptomatic multiple myeloma for transplant candidates in combination with daratumumab, lenalidomide, and dexamethasone
 - Primary therapy for symptomatic myeloma or for disease relapse after 6 months following primary induction therapy with the same regimen
 - In combination with dexamethasone and lenalidomide (National Comprehensive Cancer Network [NCCN]-preferred regimen) when used in transplant candidates as primary therapy and in the relapse setting; other recommended regimen when used in nontransplant candidates as primary therapy (ixazomib may be substituted for carfilzomib in select individuals)
 - In combination with dexamethasone and cyclophosphamide (ixazomib may be substituted for carfilzomib in select individuals)
 - Maintenance therapy for symptomatic multiple myeloma in combination with lenalidomide for transplant candidates
 - After response to primary myeloma therapy
 - For response or stable disease following an autologous hematopoietic cell transplant (HCT)
 - For response or stable disease following a tandem autologous or allogeneic HCT for high-risk individuals under certain circumstances
 - Therapy for previously treated myeloma for relapse or progressive disease
 - As a single agent for the treatment of individuals with relapsed or refractory multiple myeloma who have received one or more lines of therapy (FDA)
 - In combination with dexamethasone, given once weekly or twice weekly
 - In combination with dexamethasone and lenalidomide if bortezomib-refractory
 - In combination with daratumumab and dexamethasone if bortezomib- or lenalidomide-refractory (NCCN-preferred regimen)
 - In combination with isatuximab-irfc and dexamethasone if bortezomib- or lenalidomide-refractory (NCCN-preferred regimen)
 - In combination with dexamethasone and cyclophosphamide
 - In combination with pomalidomide, and daratumumab and dexamethasone (NCCN-preferred regimen)
 - In combination with dexamethasone, cyclophosphamide, and thalidomide
 - In combination with selinexor and dexamethasone

- In combination with venetoclax and dexamethasone for patients with t(11:14)
 - Therapy for previously treated myeloma for relapsed/refractory disease after three prior lines of therapy in combination with bendamustine and dexamethasone
 - For the treatment of individuals with relapsed or refractory multiple myeloma who have received one to three prior therapies:
 - In combination with dexamethasone
 - In combination with lenalidomide and dexamethasone
 - In combination with daratumumab and dexamethasone
 - In combination with daratumumab and hyaluronidase-fihj and dexamethasone
 - In combination with isatuximab and dexamethasone
 - For the management of POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes) syndrome as a replacement for bortezomib in select patients
- Systemic Light Chain Amyloidosis
 - Treatment for newly diagnosed disease for all stages in combination with dexamethasone if significant neuropathy
 - Treatment for relapsed/refractory noncardiac disease
 - As a single agent
 - In combination with dexamethasone
- Waldenström macroglobulinemia/lymphoplasmacytic lymphoma
 - As a component of CaRD (carfilzomib, rituximab [Rituxan], and dexamethasone) regimen for the treatment of individuals with Waldenström macroglobulinemia/lymphoplasmacytic lymphoma as:
 - Primary therapy
 - Treatment after relapse if used as primary therapy that was well tolerated and elicited a prolonged response

Duration of authorization: 12 months

Version Effective Date: 11/18/2024

Title: Casgevy™ (exagamglogene autotemcel)

MEDICALLY NECESSARY:

Exagamglogene autotemcel (Casgevy) is considered medically necessary and, therefore, covered for the treatment of the following conditions in individuals aged 12 years and older when ALL of the associated criteria for them are met:

SEVERE SICKLE CELL DISEASE -- (must meet all):

- Individual has diagnosis of severe sickle cell disease (SCD) with one of the following genotypes as confirmed by genetic testing results [(a or b) [see GUIDELINES for additional note]:
 - a. β^S/β^S
 - b. β^S/β^0
- Documentation that the individual is a candidate for an allogeneic HSCT, but ineligible due to absence of an appropriate donor (i.e., individual does not have a human leukocyte antigen (HLA)-matched donor; or individual has an HLA-matched donor, but the potential donor is not able or is not willing to donate);
- Individual has not received a prior **allogeneic** hematopoietic stem cell transplant;
- Individual is eligible to receive an autologous hematopoietic stem cell transplant;
- Individual has been treated with at least ONE pharmacologic treatment for SCD (e.g., pharmacologic treatment for SCD including hydroxyurea, L-glutamine, Adakveo (crizanlizumab-tmca intravenous infusion), and Oxbryta [voxelotor tablets and tablets for oral suspension]);
- While receiving appropriate standard treatment for SCD, individual had at least four severe vaso-occlusive crises or events (VOCs/VOEs) in the previous 2 years, which can be defined by one or more of the following (i, ii, iii, iv, or v):
 - i. An episode of acute pain that resulted in a visit to a medical facility that required administration of at least ONE of the following (a or b):
 - a) Intravenous opioid; OR
 - b) Intravenous nonsteroidal anti-inflammatory drug;
 - ii. Acute chest syndrome (acute chest syndrome is defined by the presence of a new pulmonary infiltrate associated with pneumonia-like symptoms (e.g., chest pain, fever [$> 99.5^\circ\text{F}$], tachypnea, wheezing or cough, or findings upon lung auscultation);
 - iii. Acute hepatic sequestration (defined by a sudden increase in liver size associated with pain in the right upper quadrant, abnormal results of liver function test not due to biliary tract disease, and the reduction of hemoglobin concentration by ≥ 2 g/dL below the baseline value);
 - iv. Acute splenic sequestration (defined by an enlarged spleen, left upper quadrant pain, and an acute decrease in hemoglobin concentration of ≥ 2 g/dL below the baseline value);
 - v. Acute priapism lasting >2 hours and requiring a visit to a medical facility

- The gene therapy is prescribed by a hematologist or a stem cell transplant physician; AND
- Individual has not received any gene therapy and/or is not under consideration for treatment for another gene therapy for SCD.

TRANSFUSION-DEPENDENT β -THALASSEMIA

Treatment of transfusion-dependent β -thalassemia when ALL of the following criteria are met (must meet ALL):

- Individual has ONE of the following genotypes as confirmed by genetic testing (i or ii):
 - i. Non- β^0/β^0 genotype (e.g., β^0/β^+ , β^E/β^0 , and β^+/β^+); OR
 - ii. β^0/β^0 genotypes (other examples include $\beta^0/\beta^+(\text{IVS-I-110})$ and $\beta^+(\text{IVS-I-110})/\beta^+(\text{IVS-I-110})$);
 - Individual is transfusion-dependent, as defined by meeting ONE of the following (i or ii):
 - i. Receipt of transfusions of ≥ 100 mL per kg of body weight of packed red blood cells per year in the previous 2 years; OR
 - ii. Receipt of transfusions of ≥ 10 units of packed red blood cells per year in the previous 2 years;
- Documentation that the individual is a candidate for an allogeneic HSCT, but ineligible due to absence of an appropriate donor (i.e., individual does not have a Human Leukocyte Antigen (HLA)-matched donor; or individual has an HLA-matched donor, but the potential donor is not able or is not willing to donate);
- According to the prescribing physician, an autologous hematopoietic stem cell transplantation is appropriate for the individual;
- Individual has not received a previous allogeneic hematopoietic stem cell transplant; AND
- Individual has not received any gene therapy and/or is not under consideration for treatment for another gene therapy for beta thalassemia.

Duration of authorization: 12 months

Version Effective Date: 01/01/2025

Title: Cemiplimab-rwlc (Libtayo®)

MEDICALLY NECESSARY:

BASAL CELL CARCINOMA (BCC)

Cemiplimab-rwlc (Libtayo) is considered medically necessary and, therefore, covered as a single-agent therapy for the treatment of adult individuals (18 years or older) with BCC when **one** of the following indications are met:

- The treatment of individuals with locally advanced BCC (laBCC) previously treated with a hedgehog pathway inhibitor (HHI) (e.g., vismodegib, sonidegib) or for whom an HHI is not appropriate
- The treatment of individuals with metastatic BCC (mBCC) previously treated with an HHI or for whom an HHI is not appropriate
- The treatment of individuals with laBCC (extensive) disease where surgery and/or radiation therapy (RT) may not result in a cure or would possibly produce a significant functional limitation
- The treatment of individuals with:
 - nodal disease if surgery is not feasible
 - metastatic disease

CUTANEOUS SQUAMOUS CELL CARCINOMA (CSCC)

Cemiplimab-rwlc (Libtayo) is considered medically necessary and, therefore, covered as a National Comprehensive Cancer Network (NCCN)-preferred single-agent therapy for the treatment of adult individuals (18 years or older) with CSCC when **one** of the following indications are met:

- The individual has complicated locally advanced CSCC (laCSCC) (i.e., a cancer that has spread from the first site to nearby tissue), recurrent, or metastatic in which curative surgery and curative RT are not feasible
- As neoadjuvant therapy for:
 - unresectable, inoperable, or incompletely resected regional disease
 - very-high-risk cutaneous squamous cell carcinoma
 - locally advanced or unresectable disease

NON-SMALL CELL LUNG CANCER (NSCLC)

Cemiplimab-rwlc (Libtayo) is considered medically necessary and, therefore, covered for the treatment of adult individuals (18 years or older) with NSCLC, with no contraindications* to Programmed Death Receptor-1 (PD-1) or PD-L1 inhibitors, and with an Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0 to 2 when **one** of the following indications are met:

- The tumor is PD-L1 expression–positive (Tumor Proportion Score [TPS] 50 percent or higher) as determined by a U.S. Food and Drug Administration (FDA)-approved test and negative for actionable molecular biomarkers** (may be KRAS G12C mutation–positive) and **one** of the following:

- As a single agent as first-line treatment in an individual with **both** of the following:
 - locally advanced tumor
 - not a candidate for surgical resection or definitive chemoradiation
- As a single agent as first-line treatment in an individual whose tumor is metastatic
- As a single agent as first-line therapy (NCCN preferred) for individuals whose tumor is recurrent (including mediastinal lymph node recurrence with prior RT), advanced, or metastatic disease, but excluding locoregional recurrence or symptomatic local disease
- As a single agent as continuation maintenance therapy for individuals with **both** of the following:
 - The tumor is recurrent (including mediastinal lymph node recurrence with prior RT), advanced, or metastatic disease but excluding locoregional recurrence or symptomatic local disease
 - The tumor achieved a response or stable disease following first-line therapy with cemiplimab-rwlc as monotherapy, or as part of combination therapy
- The tumor is PD-L1 expression–positive (TPS 1 percent or higher) as determined by an FDA-approved test and negative for actionable molecular biomarkers** (may be KRAS G12C mutation positive) and **one** of the following:
 - As first-line treatment for individuals whose tumor is recurrent (including mediastinal lymph node recurrence with prior RT), advanced, or metastatic disease, but excluding locoregional recurrence or symptomatic local disease in **one** of the following regimens:
 - In combination with paclitaxel and either carboplatin or cisplatin (NCCN-preferred for squamous cell histology)
 - In combination with pemetrexed and either carboplatin or cisplatin for nonsquamous cell histology (NCCN-preferred for nonsquamous cell histology)
 - As continuation maintenance therapy in combination with pemetrexed for individuals with **both** of the following:
 - The tumor is recurrent (including mediastinal lymph node recurrence with prior RT), advanced, or metastatic disease but excluding locoregional recurrence or symptomatic local disease
 - The tumor achieved a response or stable disease following first-line therapy with cemiplimab-rwlc/pemetrexed/carboplatin or cisplatin for nonsquamous cell histology
- The tumor is PD-L1 expression–positive (TPS 1 to 49 percent) as determined by an FDA-approved test and negative for actionable molecular biomarkers** (may be KRAS G12C mutation positive) and **both** of the following:
 - As a single agent as continuation maintenance therapy for individuals whose tumor is recurrent (including mediastinal lymph node recurrence with prior RT),

- advanced, or metastatic disease, but excluding locoregional recurrence or symptomatic local disease
 - The tumor achieved a response or stable disease following first-line therapy with cemiplimab-rwlc combination therapy
- The tumor is PD-L1 expression–positive (**TPS less than 1 percent**) as determined by a FDA-approved test and negative for actionable molecular biomarkers** (may be KRAS G12C mutation positive) and **one** of the following:
 - As a single agent (if previously received first-line cemiplimab-rwlc combination therapy) as continuation maintenance therapy for individuals with **both** of the following:
 - The tumor is recurrent (including mediastinal lymph node recurrence with prior RT), advanced, or metastatic disease, but excluding locoregional recurrence or symptomatic local disease
 - The tumor achieved a response or stable disease following initial systemic therapy
 - In combination with pemetrexed (if previously received first-line cemiplimab-rwlc/pemetrexed/carboplatin or cisplatin) as continuation maintenance therapy for nonsquamous cell histology and **both** of the following:
 - The tumor is recurrent (including mediastinal lymph node recurrence with prior RT), advanced, or metastatic disease, but excluding locoregional recurrence or symptomatic local disease
 - The tumor achieved a response or stable disease following initial systemic therapy
- The tumor PD-L1 expression is **not specified** and **one** of the following:
 - In combination with platinum-based chemotherapy as first-line treatment in an individual with **all** of the following:
 - The tumor is locally advanced
 - The individual is not a candidate for surgical resection or definitive chemoradiation
 - The tumor is negative for actionable molecular biomarkers**
 - In combination with platinum-based chemotherapy as first-line treatment in an individual with **all** of the following:
 - The tumor is metastatic
 - The tumor is negative for actionable molecular biomarkers**

Cemiplimab-rwlc (Libtayo) is considered medically necessary and, therefore, covered for the initial systemic treatment of adult individuals (18 years or older) with NSCLC, with no contraindications* to PD-1 or PD-L1 inhibitors, with a PS of 0 to 1, a tumor with PD-L1 less than 1 percent and negative for any actionable biomarkers**(may be KRAS G12C mutation positive), and **both** of the following:

- The tumor is recurrent (including mediastinal lymph node recurrence with prior RT), advanced, or metastatic disease, but excluding locoregional recurrence or symptomatic local disease
- In combination with **one** of the following regimens:

- Paclitaxel and either carboplatin or cisplatin (NCCN-preferred for squamous cell histology)
- Pemetrexed and either carboplatin or cisplatin for nonsquamous cell histology (NCCN-preferred for nonsquamous cell histology)

Cemiplimab-rwlc (Libtayo) is considered medically necessary and, therefore, covered for the treatment of adult individuals (18 years or older) with NSCLC, with no contraindications* to PD-1 or PD-L1 inhibitors, with a PS of 0 to 1, and **all** of the following:

- The tumor is recurrent (including mediastinal lymph node recurrence with prior RT), advanced, or metastatic disease, but excluding locoregional recurrence or symptomatic local disease
- In combination with **one** of the following regimens:
 - Paclitaxel and either carboplatin or cisplatin
 - Pemetrexed and either carboplatin or cisplatin for nonsquamous cell histology
- The above regimens are used for **one** of the following:
 - First-line therapy for EGFR exon 20 mutation–positive tumors
 - First-line therapy for KRAS G12C mutation–positive tumors
 - First-line or subsequent therapy for BRAF V600E mutation–positive tumors
 - First-line or subsequent therapy for NTRK 1/2/3 gene fusion–positive tumors
 - First-line or subsequent therapy for MET exon 14 skipping mutation–positive tumors
 - First-line or subsequent therapy for RET rearrangement–positive tumors
 - First-line therapy for ERBB2 (HER2) mutation–positive tumors
 - Subsequent therapy for EGFR exon 19 deletion or exon 21 L858R tumors and prior erlotinib ± (ramucirumab or bevacizumab), afatinib, gefitinib, osimertinib, or dacomitinib therapy
 - Subsequent therapy for EGFR S768I, L861Q, and/or G719X mutation–positive tumors and prior afatinib, osimertinib, erlotinib, gefitinib, or dacomitinib therapy
 - Subsequent therapy for ALK rearrangement–positive tumors and prior crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib therapy
 - Subsequent therapy for ROS1 rearrangement–positive tumors and prior crizotinib, entrectinib, or ceritinib therapy

*Contraindications for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or current use of immunosuppressive agents, and some oncogenic drivers (i.e., EGFR exon 19 deletion or exon 21 L858R ALK rearrangements) have been shown to be associated with less benefit from PD-1/PD-L1 inhibitors

**If there is insufficient tissue to allow testing for all of epidermal growth factor receptor (EGFR), Kirsten rat sarcoma (KRAS), anaplastic lymphoma kinase (ALK), c-ros oncogene 1 (ROS1), B-Raf Proto-Oncogene (BRAF), neurotrophic tyrosine kinase receptor (NTRK) 1/2/3, mesenchymal-epithelial transition (MET), rearranged during transfection (RET), and erythroblastic oncogene B (ERBB2) human epidermal growth factor receptor 2 (HER2), repeat biopsy and/or plasma testing should be done. If these are not feasible, treatment is guided by

available results and, if unknown, these individuals are treated as though they do not have driver oncogenes.

CERVICAL AND VAGINAL CANCER

Cemiplimab-rwlc (Libtayo) is considered medically necessary and, therefore, covered as a single agent for the treatment of adult individuals with cervical and vaginal cancer as second-line (NCCN-preferred) or subsequent therapy for **either** of the following:

- Local/regional recurrence
- Stage IVB or recurrence with distant metastasis

VULVAR CANCER

Cemiplimab-rwlc (Libtayo) is considered medically necessary and, therefore, covered as a single agent for the treatment of adult individuals with vulvar cancer as second-line therapy for advanced or recurrent/metastatic disease.

Duration of authorization: 12 months

Version Effective Date: 11/18/2024

Title: Cerliponase alfa (Brineura®)

MEDICALLY NECESSARY:

INITIAL THERAPY

Cerliponase alfa (Brineura®) is considered medically necessary and, therefore, covered for pediatric individuals when all of the following criteria are met, including the dosing and frequency requirements listed in Attachment A:

- Diagnosis of late infantile neuronal ceroid lipofuscinosis type 2 (CLN2) disease is confirmed by either of the following:
 - TPP1 enzyme activity test indicating deficient activity in leukocytes or fibroblasts
 - Genetic test validating homozygous pathogenic variation for *TPP1*
- Individual is symptomatic (i.e., seizures, ataxia, language delay, vision loss, or symptoms characteristic of CLN2)
- Score of at least 1 in the motor domain on the CLN2 Clinical Rating Scale

CONTINUATION THERAPY

Cerliponase alfa (Brineura) is considered medically necessary and, therefore, covered for continuation therapy when the pediatric individual meets all of the following criteria:

- Individual is symptomatic (i.e., seizures, ataxia, language delay, vision loss, or symptoms characteristic of CLN2)
- Score of at least 1 in the motor domain on the CLN2 Clinical Rating Scale

Duration of authorization: 12 months

Version Effective Date: 12/02/2024

Title: Cerliponase alfa (Brineura®)

MEDICALLY NECESSARY:

Dosing and Frequency Requirements for Cerliponase alfa (Brineura®)

The Company reserves the right to modify the Dosing and Frequency Requirements listed in this policy to ensure consistency with the most recently published recommendations for the use of Cerliponase alfa (Brineura®). Changes to these guidelines are based on a consensus of information obtained from resources such as, but not limited to: the US Food and Drug Administration (FDA); Company-recognized authoritative pharmacology compendia; or published peer-reviewed clinical research. The professional provider must supply supporting documentation (i.e., published peer-reviewed literature) in order to request coverage for an amount of Cerliponase alfa (Brineura®) outside of the Dosing and Frequency Requirements listed in this policy. For a list of Company-recognized pharmacology compendia, view our policy on off-label coverage for prescription drugs and biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of this drug. If the member's dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider must submit those changes to the Company for a new approval based on those changes as part of the utilization management activities. The Company reserves the right to conduct post-payment review and audit procedures for any claims submitted for cerliponase alfa (Brineura®).

Age Groups	BRINEURA Dose (Every Other Week)	Volume of BRINEURA Solution	Infusion Rate
Birth to < 6 months	100 mg	3.3 mL	1.25 mL/hr
6 months to < 1 year	150 mg	5 mL	2.5 mL/hr
1 year to < 2 years	200 mg (first 4 doses)	6.7 mL (first 4 doses)	2.5 mL/hr
	300 mg (subsequent doses)	10 mL (subsequent doses)	
2 years and older	300 mg	10 mL	2.5 mL/hr

The FDA does not recommend dosing in pediatric individuals less than 37 weeks post-menstrual age (gestational age plus post-natal age) or those weighing less than 2.5kg.

Duration of authorization: 12 months

Version Effective Date: 12/02/2024

Title: Cetuximab (Erbix[®])

MEDICALLY NECESSARY:

COLORECTAL CANCER

Cetuximab (Erbix) for the treatment of colorectal cancer is considered medically necessary and, therefore, covered when the dosing and frequency requirements listed in Attachment A and **any** of the following are met:

Metastatic Colorectal Cancer (mCRC)

Cetuximab (Erbix) used for the treatment of metastatic colorectal cancer (mCRC) that is Kirsten rat sarcoma (K-Ras) wild-type, epidermal growth factor receptor (EGFR)-expressing, in **any** of the following:

- In combination with FOLFIRI (5-fluorouracil [5-FU], leucovorin [LV], and irinotecan) or FOLFOX (5-fluorouracil [5-FU], leucovorin [LV], and oxaliplatin) as first-line treatment
- In combination with irinotecan in individuals who are refractory to irinotecan-based chemotherapy (i.e., the tumor response rate was poor/progression was not halted)
- As a single agent in individuals who are intolerant to irinotecan or after failure of both irinotecan-based and oxaliplatin-based chemotherapy (i.e., the tumor response rate was poor/progression was not halted)

Colon Cancer

- Cetuximab (Erbix) used in combination with FOLFIRI, CapeOX (capecitabine and oxaliplatin), or FOLFOX for therapy for KRAS/neuroblastoma-ras (NRAS)/b-rapidly accelerated fibrosarcoma (BRAF) wild-type gene and left-sided only tumors (proficient mismatch repair/microsatellite-stable [pMMR/MSS] or ineligible for or progression on checkpoint inhibitor immunotherapy for deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H]) in individuals appropriate for intensive therapy, in **any** of the following:
 - As primary therapy for locally unresectable or medically inoperable disease
 - As primary treatment for synchronous abdominal/peritoneal metastases that are nonobstructing, or following local therapy for individuals with imminent or existing obstruction
 - For synchronous unresectable metastases of other sites
 - As initial treatment for unresectable metachronous metastases in individuals who have not received previous FOLFOX or CapeOX within the past 12 months, who have received previous 5-FU/LV or capecitabine therapy, or who have not received any previous chemotherapy
 - For individuals who progressed on nonintensive therapy, except if received previous fluoropyrimidine, with improvement in functional status
- Cetuximab (Erbix) used as primary treatment for unresectable synchronous liver and/or lung metastases (KRAS/NRAS/BRAF wild-type gene and left-sided tumors only) (pMMR/MSS only or dMMR/MSI-H and individual is not a candidate for immunotherapy) in combination with FOLFOX or FOLFIRI regimens

- Cetuximab (Erbix) used in combination with irinotecan or FOLFIRI as initial treatment in individuals with unresectable metachronous metastases (KRAS/NRAS/BRAF wild-type gene and left-sided tumors only) (pMMR/MSS only) and previous FOLFOX or CapeOX within the past 12 months
- Cetuximab (Erbix) used as initial treatment in combination with encorafenib for individuals with unresectable metachronous metastases (BRAF V600E mutation positive) (pMMR/MSS only) and previous FOLFOX or CapeOX within the past 12 months
- Cetuximab (Erbix) used as initial treatment in combination with sotorasib or adagrasib for individuals with unresectable metachronous metastases (KRAS G12C mutation positive) (pMMR/MSS only) and previous FOLFOX or CapeOX within the past 12 months
- Cetuximab (Erbix) for subsequent therapy for progression of advanced or metastatic disease (KRAS/NRAS/BRAF wild-type and left-sided tumors only) (pMMR/MSS or ineligible for or progression on checkpoint inhibitor immunotherapy for dMMR/MSI-H) in **any** of the following:
 - In combination with irinotecan, FOLFIRI, or as a single agent for individuals who cannot tolerate irinotecan, if previously treated with oxaliplatin-based therapy without irinotecan
 - In combination with irinotecan, FOLFOX, CapeOX, or as a single agent for individuals who cannot tolerate irinotecan if previously treated with irinotecan-based therapy without oxaliplatin
 - In combination with irinotecan or as a single agent for individuals who cannot tolerate irinotecan if previously treated with oxaliplatin and irinotecan
 - In combination with irinotecan or as a single agent for individuals who cannot tolerate irinotecan if previously treated without irinotecan or oxaliplatin followed by FOLFOX or CapeOX with or without bevacizumab
- Cetuximab (Erbix) for subsequent therapy (including for appendiceal adenocarcinoma) in combination with encorafenib for progression of advanced or metastatic disease (BRAF V600E mutation positive) (pMMR/MSS or ineligible for or progression on checkpoint inhibitor immunotherapy for dMMR/MSI-H) in individuals previously treated **with any** of the following:
 - Oxaliplatin-based therapy without irinotecan
 - Irinotecan-based therapy without oxaliplatin
 - Oxaliplatin and irinotecan
- Cetuximab (Erbix) for subsequent therapy (including for appendiceal adenocarcinoma) in combination with encorafenib for progression of advanced or metastatic disease (BRAF V600E mutation positive) (pMMR/MSS or ineligible for or progression on checkpoint inhibitor immunotherapy for dMMR/MSI-H) in individuals previously treated **without any** of the following:
 - Irinotecan or oxaliplatin
 - Irinotecan or oxaliplatin followed by FOLFOX or CapeOX with or without bevacizumab
- Cetuximab (Erbix) for subsequent therapy in combination with sotorasib or adagrasib for progression of advanced or metastatic disease (KRAS G12C mutation positive)

(pMMR/MSS or ineligible for or progression on checkpoint inhibitor immunotherapy for dMMR/MSI-H) in individuals previously treated **with any** of the following:

- Oxaliplatin-based therapy without irinotecan
- Irinotecan-based therapy without oxaliplatin
- Oxaliplatin and irinotecan
- Cetuximab (Erbix) for subsequent therapy in combination with sotorasib or adagrasib for progression of advanced or metastatic disease (KRAS G12C mutation positive) (pMMR/MSS or ineligible for or progression on checkpoint inhibitor immunotherapy for dMMR/MSI-H) in individuals previously treated **without any** of the following:
 - Irinotecan or oxaliplatin
 - Irinotecan or oxaliplatin followed by FOLFOX or CapeOX with or without bevacizumab

Rectal Cancer

- Cetuximab (Erbix) used in combination with FOLFIRI, CapeOX, or FOLFOX for tumors that express the KRAS/NRAS/BRAF wild-type gene only (pMMR/MSS or ineligible for or progression on checkpoint inhibitor immunotherapy for dMMR/MSI-H) in individuals appropriate for intensive therapy, in **any** of the following:
 - As primary treatment for T3, N Any; T1-2, N1-2; T4, N Any; or locally unresectable or medically inoperable disease if resection is contraindicated following neoadjuvant or total neoadjuvant therapy (pMMR/MSS only or ineligible for or progression on checkpoint inhibitor immunotherapy for dMMR/MSI-H) or neoadjuvant/definitive immunotherapy (dMMR/MSI-H only)
 - As primary treatment for synchronous abdominal/peritoneal metastases that are nonobstructing, or following local therapy for individuals with existing or imminent obstruction
 - As primary treatment for synchronous unresectable metastases of other sites
 - As primary treatment for unresectable isolated pelvic/anastomotic recurrence
 - As initial treatment for unresectable metachronous metastases in individuals who have not received previous adjuvant FOLFOX or CapeOX within the past 12 months, who have received previous 5-FU/LV or capecitabine therapy, or who have not received any previous chemotherapy
 - For individuals who progressed on nonintensive therapy, except if received previous fluoropyrimidine, with improvement in functional status
- Cetuximab (Erbix) as primary treatment of synchronous liver only and/or lung only metastases (KRAS/NRAS/BRAF wild-type gene only) (pMMR/MSS only or dMMR/MSI-H only and not a candidate for immunotherapy) that are unresectable or medically inoperable, in combination with FOLFIRI or FOLFOX
- Cetuximab (Erbix), as initial treatment, used in combination with irinotecan or FOLFIRI in individuals with unresectable metachronous metastases (KRAS/NRAS/BRAF wild-type gene only) (pMMR/MSS only) and previous FOLFOX or CapeOX within the past 12 months
- Cetuximab (Erbix) as initial treatment, used in combination with sotorasib or adagrasib for individuals with unresectable metachronous metastases (KRAS G12C

mutation positive) (pMMR/MSS only) and previous FOLFOX or CapeOX within the past 12 months

- Cetuximab (Erbix), as initial treatment, used in combination with encorafenib for individuals with unresectable metachronous metastases (BRAF V600E mutation positive) (pMMR/MSS only) and previous adjuvant FOLFOX or CapeOX within the past 12 months
- Cetuximab (Erbix) as subsequent therapy for progression of advanced or metastatic disease (KRAS/NRAS/BRAF wild-type gene only) (pMMR/MSS or ineligible for or progression on checkpoint inhibitor immunotherapy for dMMR/MSI-H), in **any** of the following:
 - In combination with irinotecan, FOLFIRI, or as a single agent for individuals who cannot tolerate irinotecan, if previously treated with oxaliplatin-based therapy without irinotecan
 - In combination with irinotecan, FOLFOX, CapeOX, or as a single agent for individuals who cannot tolerate irinotecan, if previously treated with irinotecan-based therapy without oxaliplatin
 - In combination with irinotecan, or as a single agent for individuals who cannot tolerate irinotecan, if previously treated with oxaliplatin and irinotecan
 - In combination with irinotecan, or as a single agent for individuals who cannot tolerate irinotecan, if previously treated without irinotecan or oxaliplatin followed by FOLFOX or CapeOX with or without bevacizumab
- Cetuximab (Erbix) for subsequent therapy in combination with encorafenib for progression of advanced or metastatic disease (BRAF V600E mutation positive) (pMMR/MSS or ineligible for or progression on checkpoint inhibitor immunotherapy for dMMR/MSI-H) in individuals previously treated **with any** of the following:
 - Oxaliplatin-based therapy without irinotecan
 - Irinotecan-based therapy without oxaliplatin
 - Oxaliplatin and irinotecan
- Cetuximab (Erbix) for subsequent therapy in combination with encorafenib for progression of advanced or metastatic disease (BRAF V600E mutation positive) (pMMR/MSS or ineligible for or progression on checkpoint inhibitor immunotherapy for dMMR/MSI-H) in individuals previously treated **without any** of the following:
 - Irinotecan or oxaliplatin
 - Irinotecan or oxaliplatin followed by FOLFOX or CapeOX with or without bevacizumab
- Cetuximab (Erbix) for subsequent therapy in combination with sotorasib or adagrasib for progression of advanced or metastatic disease (KRAS G12C mutation positive) (pMMR/MSS or ineligible for or progression on checkpoint inhibitor immunotherapy for dMMR/MSI-H) in individuals previously treated **with any** of the following:
 - Oxaliplatin-based therapy without irinotecan
 - Irinotecan-based therapy without oxaliplatin
 - Oxaliplatin and irinotecan

- Cetuximab (Erbix) for subsequent therapy in combination with sotorasib or adagrasib for progression of advanced or metastatic disease (KRAS G12C mutation positive) (pMMR/MSS or ineligible for or progression on checkpoint inhibitor immunotherapy for dMMR/MSI-H) in individuals previously treated **without any** of the following:
 - Irinotecan or oxaliplatin
 - Irinotecan or oxaliplatin followed by FOLFOX or CapeOX with or without bevacizumab

HEAD AND NECK CANCER

Cetuximab (Erbix) for the treatment of head and neck cancer is considered medically necessary and, therefore, covered when the dosing and frequency requirements listed in Attachment A and **any** of the following indications are met:

- Cetuximab (Erbix) used in combination with radiation therapy (RT) is indicated for the initial treatment of locally or regionally advanced squamous cell cancer of the head and neck
- Cetuximab (Erbix) used in combination with platinum-based therapy with 5-FU is indicated for the first-line treatment of recurrent locoregional disease or metastatic squamous cell carcinoma of the head and neck
- Cetuximab (Erbix) administered as a single agent is indicated for the treatment of recurrent or metastatic squamous cell cancer of the head and neck in individuals who previously failed or are refractory to platinum-based chemotherapy

Non-nasopharyngeal Cancer

Cetuximab (Erbix) is indicated for the treatment of non-nasopharyngeal cancer, in **any** of the following:

- Administered as a single agent given weekly as sequential systemic therapy/RT following induction systemic therapy for individuals with performance status (PS) 0-1 who have **any** of the following:
 - Newly diagnosed T4b, N0-3, M0 disease
 - Newly diagnosed unresectable nodal disease with no metastases
 - Newly diagnosed nonmetastatic disease and who are unfit for surgery
 - Unresectable locoregional recurrence or persistent disease and who have not received prior RT
- Administered as a single agent given weekly as sequential systemic therapy/RT following combination systemic therapy in individuals with resectable locoregional recurrence or persistent disease and who have not received prior RT
- Systemic first-line treatment as a single agent for individuals with **any** of the following:
 - PS 3 for newly diagnosed T4b, N0-3, M0 disease, newly diagnosed unresectable nodal disease with no metastases, or for individuals with newly diagnosed non-metastatic disease who are unfit for surgery
 - PS 0-3 for metastatic (M1) disease at initial presentation
 - PS 3 and unresectable locoregional recurrence or unresectable persistent disease without prior RT

- PS 0-3 and unresectable locoregional recurrence with prior RT, unresectable second primary with prior RT, or unresectable persistent disease with prior RT, or recurrent/persistent disease with distant metastases
- Subsequent-line treatment as a single agent for individuals with **any** of the following:
 - Alternate option for PS 0-3 for metastatic (M1) disease at initial presentation
 - PS 3 and unresectable locoregional recurrence or unresectable persistent disease without prior RT
 - Alternate option for PS 0-3 and unresectable locoregional recurrence with prior RT, unresectable second primary with prior RT, or unresectable persistent disease with prior RT, or recurrent/persistent disease with distant metastases
- Administered as a single agent as postoperative systemic therapy/RT if cisplatin ineligible for positive margin and/or extranodal extension in **either** of the following:
 - Resectable locoregional recurrence or persistent disease without prior RT
 - Resectable locoregional recurrence, second primary, or persistent disease with prior RT
- As combination systemic first-line, or subsequent-line treatment, in individuals with PS 0-1, given:
 - As part of **any** of the following regimens:
 - 5-FU and cisplatin
 - 5-FU and carboplatin
 - Docetaxel and cisplatin
 - Docetaxel and carboplatin
 - Paclitaxel and cisplatin
 - Paclitaxel and carboplatin
 - Cisplatin
 - Nivolumab
 - Pembrolizumab
 - Paclitaxel
 - For **any** of the following:
 - Metastatic (M1) disease at initial presentation
 - Recurrent/persistent disease with distant metastases
 - Unresectable locoregional recurrence with prior RT
 - Unresectable second primary with prior RT
 - Unresectable persistent disease with prior RT
- As combination systemic therapy for resectable locoregional recurrence or persistent disease without prior RT given as part of **any** of the following regimens:
 - 5-FU and cisplatin
 - 5-FU and carboplatin
 - Docetaxel and cisplatin
 - Docetaxel and carboplatin
 - Paclitaxel and cisplatin
 - Paclitaxel and carboplatin
 - Cisplatin

- Nivolumab
- Pembrolizumab
- Paclitaxel

Ethmoid Sinus Cancer

Cetuximab (Erbix) administered as a single agent given weekly is indicated for the treatment of cancer of the ethmoid sinus as sequential systemic therapy/RT following a complete response to induction chemotherapy for newly diagnosed T3, T4a disease

Nasopharynx Cancer

- Cetuximab (Erbix) used in combination with carboplatin is indicated for the treatment of very advanced cancer of the nasopharynx as systemic first-line or subsequent-line (if not previously used) treatment in individuals with PS 0-1 for **any** of the following:
 - Recurrent/persistent disease with distant metastases
 - Unresectable locoregional recurrence with prior RT
 - Unresectable second primary with prior RT
 - Unresectable persistent disease with prior RT
- Cetuximab (Erbix) used in combination with carboplatin is indicated as first-line systemic therapy for the treatment of T1-4, N0-3, M1 disease for **either** of the following:
 - Oligometastatic disease and PS 0-2
 - Widely metastatic disease and good PS (0-2)
- Cetuximab (Erbix) used in combination with carboplatin, if not previously used, as subsequent-line systemic therapy for the treatment of T1-4, N0-3, M1 disease for **either** of the following:
 - Oligometastatic disease and PS 0-2
 - Widely metastatic disease and good PS (0-2)

Oral Cavity Cancer (including Mucosal Lip)

Cetuximab (Erbix) administered as a single agent is indicated for the treatment of cancer of the oral cavity (including mucosal lip) as postoperative systemic therapy/RT in individuals who are cisplatin ineligible with any of the following:

- Extranodal extension with or without positive margin for T1-3, N0-3; or T4a, N0-3 disease
- With positive margins for T3, N0; T1-3, N1-3; or T4a, N0-3 disease
- May be considered with positive margin in T1-2, N0 disease

Oropharynx Cancer

Cetuximab (Erbix) administered as a single agent is indicated for the treatment of cancer of the oropharynx for **any** of the following:

- As primary concurrent systemic therapy/RT for **either** p16-negative disease:
 - T3-4a, N0-1 disease

- T1-4a, N2-3 disease
- As primary concurrent systemic therapy/RT for **either** p16 (human papillomavirus [HPV]-positive disease):
 - T0-2, N1 (single node >3 cm, or 2 or more ipsilateral nodes 6 cm or less), T0-2, N2 or T3, N0-2 disease (treatment modality preferred if clinical evidence of fixed or matted nodes or obvious extranodal extension)
 - T0-3, N3 or T4, N0-3 disease (National Comprehensive Cancer Network [NCCN] preferred)
- As sequential systemic therapy/RT given weekly following induction chemotherapy for **either** p16-negative disease:
 - T3-4a, N0-1 disease
 - T1-4a, N2-3 disease
- As sequential systemic therapy/RT given weekly following induction chemotherapy for **either** p16 (human papillomavirus [HPV])-positive disease:
 - T0-2, N1 (single node >3 cm, or two or more ipsilateral nodes 6 cm or less), T0-2, N2 or T3, N0-2 disease
 - T0-3, N3 or T4, N0-3 disease

Supraglottic Larynx Cancer

Cetuximab (Erbix) administered as a single agent is indicated for the treatment of cancer of the supraglottic larynx, in **either** of the following:

- Following a partial response at the primary site to induction chemotherapy given weekly for **any** of the following:
 - T3, N0 and most T3, N1-3 disease requiring (amenable to) total laryngectomy
 - T1-2, N+ and selected T3, N1 disease amenable to larynx-preserving (conservation) surgery
 - T4a, N0-3 disease for individuals who decline surgery
- As postoperative systemic therapy/RT if cisplatin ineligible for **either** of the following:
 - Most individuals with T1-2, N0 and selected T3 disease amenable to larynx-preserving (conservation) surgery for **either** of the following:
 - Extranodal extension
 - May be considered for discovery of positive node for disease with a positive margin
 - For individuals with extranodal extension and/or positive margin for **any** of the following:
 - T3, N0 and most T3, N1-3 disease requiring (amenable to) total laryngectomy
 - T1-2, N+ and selected T3, N1 disease amenable to larynx-preserving (conservation) surgery
 - T4a, N0-3 disease
 - T1-2, N+ and T3-4a, N0-3 disease following surgery with less than partial response at the primary site to induction chemotherapy

Glottic Larynx Cancer

Cetuximab (Erbix) administered as a single agent is indicated for the treatment of cancer of the glottic larynx, in **either** of the following:

- Following partial response at the primary site to induction chemotherapy given weekly for **either** of the following:
 - T3, N0-3 disease requiring (amenable to) total laryngectomy
 - Selected individuals with T4a disease who decline surgery
- As postoperative systemic therapy/RT in individuals ineligible for cisplatin with extranodal extension in **any** of the following:
 - For T1-2, N0 or select T3, N0 disease amenable to larynx-preserving (conservation) surgery
 - And/or positive margin for T3, N0-3 disease requiring (amenable to) total laryngectomy
 - And/or positive margin for T3, N0-3 disease following laryngectomy and less than partial response at the primary site to induction chemotherapy
 - And/or positive margin for T4a, N0-3 disease

Hypopharynx Cancer

Cetuximab (Erbix) administered as a single agent is indicated for the treatment of cancer of the hypopharynx, in **any** of the following:

- As primary concurrent systemic therapy/RT or induction chemotherapy for **either** of the following:
 - T1, N+ disease
 - T2-3, N0-3 disease requiring (amenable to) pharyngectomy with partial or total laryngectomy
- As sequential systemic therapy/RT given weekly for T4a, N0-3 disease for **either** of the following:
 - A partial response at the primary site and stable or improved disease in the neck following induction chemotherapy
 - A complete response at the primary site and stable or improved disease in the neck following induction chemotherapy
- As postoperative systemic therapy/RT in individuals who are cisplatin ineligible with **any** of the following:
 - Extranodal extension with or without positive margin for most T1, N0 or selected T2, N0 tumors amenable to larynx-preserving (conservation) surgery
 - May be considered with positive margin for T2, N0 tumors amenable to larynx-preserving (conservation) surgery
 - Extranodal extension and/or positive margin and **any** of the following:
 - T1, N+ or T2-3, N0-3 disease requiring (amenable to) pharyngectomy with partial or total laryngectomy
 - T1, N+ or T2-3, N0-3 disease with partial response and stable or improved disease in the neck or less than partial response at the primary site following induction chemotherapy

- T4a, N0-3 disease
- T4a, N0-3 disease with less than partial response at the primary site following induction chemotherapy

Occult Primary Head and Neck Cancer

Cetuximab (Erbix) administered as a single agent for occult primary head and neck cancer, in **any** of the following:

- For initial definitive treatment as sequential systemic therapy/RT given weekly following induction chemotherapy for N2-3 disease with **any** of the following histology:
 - Poorly differentiated or nonkeratinizing squamous cell
 - Anaplastic (not thyroid)
 - Squamous cell carcinoma
 - Not otherwise specified (NOS)
- As primary concurrent systemic therapy/RT for p16 (HPV)-positive disease in **any** of the following:
 - N1 (single node >3 cm, or 2 or more ipsilateral nodes 6 cm or less) disease
 - N2 disease
 - N3 disease (NCCN preferred)
- As postoperative systemic therapy/RT if cisplatin ineligible for disease with extranodal extension after neck dissection of disease in levels IV or V with adenocarcinoma histology of neck node, thyroglobulin and calcitonin negative
- As sequential systemic therapy/RT given weekly following induction chemotherapy for p16 (HPV)-positive disease in **either** of the following:
 - N1 (single node >3 cm, or 2 or more ipsilateral nodes 6 cm or less) disease
 - N2-3 disease

NON-SMALL CELL LUNG CANCER (NSCLC)

Cetuximab (Erbix) for the treatment of NSCLC is considered medically necessary and, therefore, covered, when the dosing and frequency requirements listed in Attachment A are met, and is used in combination with afatinib as subsequent therapy for recurrent (excluding locoregional recurrence or symptomatic local disease with no evidence of disseminated disease; however, including mediastinal lymph node recurrence with prior RT), advanced or metastatic disease in individuals with EGFR exon 19 deletion or exon 21 L858R or EGFR S768I, L861Q, and/or G719X mutation positive disease, for **any** of the following:

- Who have progressed on EGFR tyrosine kinase inhibitor therapy for asymptomatic disease, symptomatic brain lesions, or symptomatic systemic limited progression
- Who are T790M negative, have progressed on EGFR tyrosine kinase inhibitor therapy, and have multiple symptomatic systemic lesions
- Who are T790M positive, who have progressed on osimertinib, and have multiple symptomatic systemic lesions

PENILE CANCER

Cetuximab (Erbix) for the treatment of penile cancer is considered medically necessary and, therefore, covered when the dosing and frequency requirements listed in Attachment A are met and is used as a single agent as subsequent-line systemic therapy for metastatic/recurrent disease, especially if not treated with a similar class of agent.

SQUAMOUS CELL SKIN CANCER

Cetuximab (Erbix) for the treatment of squamous cell skin cancer is considered medically necessary and, therefore, covered when the dosing and frequency requirements listed in Attachment A are met, and is used in **either** of the following:

- As a single agent with concurrent RT for **any** of the following:
 - For locally advanced or unresectable disease as **either** of the following:
 - Primary treatment for non-surgical candidates
 - Additional treatment if positive surgical margins and re-resection not feasible
 - Resected high-risk regional disease of the head and neck (pathologic extranodal extension [ENE] or incompletely excised nodal disease)
 - Regional disease that is unresectable, inoperable, or incompletely resected
 - Regional recurrence or distant metastatic disease
- As a single agent or in combination with carboplatin and paclitaxel if ineligible for, or progressed on, immune checkpoint inhibitors and clinical trials as treatment in **any** of the following:
 - For locally advanced or unresectable disease as **either** of the following:
 - Primary treatment if curative surgery and curative RT are not feasible
 - Additional treatment if positive surgical margins and curative surgery and curative RT are not feasible
 - Regional disease that is unresectable, inoperable, or incompletely resected if curative RT not feasible
 - Regional recurrence or distant metastatic disease

Duration of authorization: 12 months

Version Effective Date: 02/26/2024

Title: Cetuximab (Erbix[®])

MEDICALLY NECESSARY:

DOSING AND FREQUENCY REQUIREMENTS

The Company reserves the right to modify the Dosing and Frequency Requirements listed in this Policy to ensure consistency with the most recently published recommendations for the use of cetuximab (Erbix[®]). Changes to these guidelines are based on a consensus of information obtained from resources such as, but not limited to: the US Food and Drug Administration (FDA); Company-recognized authoritative pharmacology compendia; or published peer-reviewed clinical research. The professional provider must supply supporting documentation (i.e., published peer-reviewed literature) in order to request coverage for an amount of cetuximab (Erbix) outside of the Dosing and Frequency Requirements listed in this Policy. For a list of Company-recognized pharmacology compendia, view our policy on off-label coverage for prescription drugs and biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of this drug. If the member's dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider **must** submit those changes to the Company for a new approval based on those changes as part of the precertification process. The Company reserves the right to conduct post-payment review and audit procedures for any claims submitted for cetuximab (Erbix).

DOSING AND FREQUENCY REQUIREMENTS FOR CETUXIMAB (ERBITUX[®])

Indication	Dosing and Frequency
Colorectal Cancer (metastatic)⁴ 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 19, 21, 22, 28, 29 ,30, 31, 33, 34, 35	Metastatic Colorectal Cancer (mCRC) Cetuximab (Erbix) in combination with FOLFIRI (5-fluorouracil [5-FU], leucovorin [LV], irinotecan) as first-line treatment Use either regimen: • Standard dosage of 400 mg/m² as an initial dose. The subsequent weekly dose is 250 mg/m². Continue until disease progression or unacceptable toxicity¹ • 500 mg/m² every 2 weeks until disease progression or unacceptable toxicity¹ Cetuximab (Erbix) in combination with FOLFOX (5-FU, LV, oxaliplatin) as first-line treatment Use:

- Standard dosage of 400 mg/m² as an initial dose. The subsequent weekly dose is 250 mg/m². Continue until disease progression or unacceptable toxicity.^{3,15}

Cetuximab (Erbix) in combination with irinotecan in individuals who are refractory to irinotecan-based chemotherapy

Use either regimen:

- Standard dosage of 400 mg/m² as an initial dose. The subsequent weekly dose is 250 mg/m². Continue until disease progression or unacceptable toxicity.¹
- 500 mg/m² every 2 weeks until disease progression or unacceptable toxicity.¹

Cetuximab (Erbix) as a single agent in individuals who are intolerant to irinotecan or after failure of both irinotecan-based and oxaliplatin-based chemotherapy

Use either regimen:

- Standard dosage of 400 mg/m² as an initial dose. The subsequent weekly dose is 250 mg/m². Continue until disease progression or unacceptable toxicity.¹
- 500 mg/m² every 2 weeks until disease progression or unacceptable toxicity.¹

Colon Cancer

Cetuximab (Erbix) used in combination with FOLFIRI, CapeOX (capecitabine, oxaliplatin), or FOLFOX for therapy for KRAS/NRAS/BRAF wild-type gene and left-sided only tumors in individuals appropriate for intensive therapy:

- As primary therapy for locally unresectable or medically inoperable disease
- As primary treatment for synchronous abdominal/peritoneal metastases that are nonobstructing, or following local therapy for individuals with imminent or existing obstruction
- For unresectable synchronous metastases of other sites
- As initial treatment for unresectable metachronous metastases in individuals who have not received previous FOLFOX or CapeOX (capecitabine and

	oxaliplatin) within the past 12 months, who have received previous 5-FU/LV or capecitabine therapy, or who have not received any previous chemotherapy - For individuals who progressed on nonintensive therapy, except if received previous fluoropyrimidine, with improvement in functional status Use either regimen: - Standard dosage of 400 mg/m² as an initial dose. The subsequent weekly dose is 250 mg/m². Continue until disease progression or unacceptable toxicity.^{20,43} 500 mg/m² every 2 weeks until disease progression or unacceptable toxicity^{20, 43} Cetuximab (Erbix) used as primary treatment for unresectable synchronous liver and/or lung metastases (KRAS/NRAS/BRAF wild-type gene and left-sided tumors only) in combination with FOLFOX or FOLFIRI Use either regimen: - Standard dosage of 400 mg/m² as an initial dose. The subsequent weekly dose is 250 mg/m². Continue until disease progression or unacceptable toxicity^{20, 43} 500 mg/m² every 2 weeks until disease progression or unacceptable toxicity^{20, 43} Cetuximab (Erbix) used in combination with irinotecan or FOLFIRI as initial treatment in individuals with unresectable metachronous metastases (KRAS/NRAS/BRAF wild-type gene and left-sided tumors only) and previous adjuvant FOLFOX or CapeOX within the past 12 months Use either regimen: - Standard dosage of 400 mg/m² as an initial dose. The subsequent weekly dose is 250 mg/m². Continue until disease progression or unacceptable toxicity.^{20, 43} 500 mg/m² every 2 weeks until disease progression or unacceptable toxicity.^{20, 43} Cetuximab (Erbix) used as initial treatment in combination with encorafenib for individuals with unresectable metachronous metastases (BRAF V600E mutation positive) and previous FOLFOX or CapeOX within the past 12 months

	Use either regimen: • Standard dosage of 400 mg/m² as an initial dose. The subsequent weekly dose is 250 mg/m². Continue until disease progression or unacceptable toxicity.^{20, 43} • 500 mg/m² every 2 weeks until disease progression or unacceptable toxicity.^{20,43} Cetuximab (Erbix) used as initial treatment in combination with sotorasib or adagrasib for individuals with unresectable metachronous metastases (KRAS G12C mutation positive) and previous FOLFOX or CapeOX within the past 12 months Use: • 500 mg/m² every 2 weeks until disease progression or unacceptable toxicity^{20, 43} Cetuximab (Erbix) for subsequent therapy for progression of advanced or metastatic disease (KRAS/NRAS/BRAF wild-type and left-sided tumors only) • In combination with irinotecan, FOLFIRI, or as a single agent in individuals who cannot tolerate irinotecan, if previously received oxaliplatin-based regimens without irinotecan • In combination with irinotecan, FOLFOX, CapeOX, or as a single agent for individuals who cannot tolerate irinotecan if previously treated with irinotecan-based therapy without oxaliplatin • In combination with irinotecan or as a single agent for individuals who cannot tolerate irinotecan in individuals previously treated with oxaliplatin and irinotecan regimen • In combination with irinotecan or as a single agent for individuals who cannot tolerate irinotecan in individuals previously treated without irinotecan or oxaliplatin followed by FOLFOX or CapeOX with or without bevacizumab Use either regimen: • Standard dosage of 400 mg/m² as an initial dose. The subsequent weekly dose is 250 mg/m². Continue until disease progression or unacceptable toxicity.^{20,43}

	• 500 mg/m² every 2 weeks until disease progression or unacceptable toxicity.^{20,43} Cetuximab (Erbix) for subsequent therapy (including for appendiceal adenocarcinoma) in combination with encorafenib for progression of advanced or metastatic disease (BRAF V600E mutation positive) in individuals previously treated with any of the following: • Oxaliplatin-based therapy without irinotecan • Irinotecan-based therapy without oxaliplatin • Oxaliplatin and irinotecan Use either regimen: • Standard dosage of 400 mg/m² as an initial dose. The subsequent weekly dose is 250 mg/m². Continue until disease progression or unacceptable toxicity.^{20, 43} • 500 mg/m² every 2 weeks until disease progression or unacceptable toxicity.^{20,43} Cetuximab (Erbix) for subsequent therapy (including for appendiceal adenocarcinoma) in combination with encorafenib for progression of advanced or metastatic disease (BRAF V600E mutation positive) in individuals previously treated without either of the following: • Irinotecan or oxaliplatin • Irinotecan or oxaliplatin followed by FOLFOX or CapeOX with or without bevacizumab Use either regimen: • Standard dosage of 400 mg/m² as an initial dose. The subsequent weekly dose is 250 mg/m². Continue until disease progression or unacceptable toxicity.^{20,43} • 500 mg/m² every 2 weeks until disease progression or unacceptable toxicity.^{20,43} Cetuximab (Erbix) for subsequent therapy in combination with sotorasib or adagrasib for progression of advanced or metastatic disease (KRAS G12C mutation positive) in individuals previously treated with any of the following:

	• Oxaliplatin-based therapy without irinotecan • Irinotecan-based therapy without oxaliplatin • Oxaliplatin and irinotecan Use: • 500 mg/m² every 2 weeks until disease progression or unacceptable toxicity^{20, 43} Cetuximab (Erbix) for subsequent therapy in combination with sotorasib or adagrasib for progression of advanced or metastatic disease (KRAS G12C mutation positive) in individuals previously treated without any of the following: • Irinotecan or oxaliplatin • Irinotecan or oxaliplatin followed by FOLFOX or CapeOX with or without bevacizumab Use: • 500 mg/m² every 2 weeks until disease progression or unacceptable toxicity^{20, 43} Rectal Cancer Cetuximab (Erbix) used in combination with FOLFIRI, CapeOX, or FOLFOX for tumors that express the KRAS/NRAS/BRAF wild-type gene in individuals appropriate for intensive therapy, in any of the following: • As primary treatment for T3, N Any; T1-2, N1-2; T4, N Any; or locally unresectable or medically inoperable disease if resection is contraindicated following total neoadjuvant therapy • As primary treatment for synchronous abdominal/peritoneal metastases that are nonobstructing, or following local therapy for individuals with existing or imminent obstruction • As primary treatment for synchronous unresectable metastases of other sites • As primary treatment for unresectable isolated pelvic/anastomotic recurrence • As initial treatment for unresectable metachronous metastases in individuals who have not received previous adjuvant FOLFOX or CapeOX within the past

	12 months, who have received previous 5-FU/LV or capecitabine therapy, or who have not received any previous chemotherapy - For individuals who progressed on nonintensive therapy, except if received previous fluoropyrimidine, with improvement in functional status Use either regimen: - Standard dosage of 400 mg/m² as an initial dose. The subsequent weekly dose is 250 mg/m². Continue until disease progression or unacceptable toxicity.^{42,43} 500 mg/m² every 2 weeks until disease progression or unacceptable toxicity.^{42,43} Cetuximab (Erbix) as primary treatment of synchronous liver only and/or lung only metastases (KRAS/NRAS/BRAF wild-type gene only) that are unresectable or medically inoperable, in combination with FOLFIRI or FOLFOX Use either regimen: - Standard dosage of 400 mg/m² as an initial dose. The subsequent weekly dose is 250 mg/m². Continue until disease progression or unacceptable toxicity.^{42,43} 500 mg/m² every 2 weeks until disease progression or unacceptable toxicity.^{42,43} Cetuximab (Erbix), as initial treatment, used in combination with irinotecan or FOLFIRI in individuals with unresectable metachronous metastases (KRAS/NRAS/BRAF wild-type only) and previous FOLFOX or CapeOX within the past 12 months Use either regimen: - Standard dosage of 400 mg/m² as an initial dose. The subsequent weekly dose is 250 mg/m². Continue until disease progression or unacceptable toxicity.^{42,43} 500 mg/m² every 2 weeks until disease progression or unacceptable toxicity.^{42,43} Cetuximab (Erbix) used as initial treatment in combination with sotorasib or adagrasib for individuals with unresectable metachronous metastases (KRAS G12C mutation positive) and previous FOLFOX or CapeOX within the past 12 months Use:

	• 500 mg/m² every 2 weeks until disease progression or unacceptable toxicity^{42, 43} Cetuximab (Erbix), as initial treatment, used in combination with encorafenib for individuals with unresectable metachronous metastases (BRAF V600E mutation positive) and previous adjuvant FOLFOX or CapeOX within the past 12 months Use either regimen: • Standard dosage of 400 mg/m² as an initial dose. The subsequent weekly dose is 250 mg/m². Continue until disease progression or unacceptable toxicity.^{42,43} • 500 mg/m² every 2 weeks until disease progression or unacceptable toxicity.^{42,43} Cetuximab (Erbix) as subsequent therapy for progression of advanced or metastatic disease (KRAS/NRAS/BRAF wild-type gene only): • In combination with irinotecan, FOLFIRI, or as a single agent for individuals who cannot tolerate irinotecan, if previously treated with oxaliplatin-based therapy without irinotecan • In combination with irinotecan, FOLFOX, or as a single agent for individuals who cannot tolerate irinotecan, if previously treated with irinotecan-based therapy without oxaliplatin • In combination with irinotecan, or as a single agent for individuals who cannot tolerate irinotecan, if previously treated with oxaliplatin, and irinotecan • In combination with irinotecan, or as a single agent for individuals who cannot tolerate irinotecan, if previously treated without irinotecan or oxaliplatin followed by FOLFOX or CapeOX with or without bevacizumab Use either regimen: • Standard dosage of 400 mg/m² as an initial dose. The subsequent weekly dose is 250 mg/m². Continue until disease progression or unacceptable toxicity.^{42,43} • 500 mg/m² every 2 weeks until disease progression or unacceptable toxicity.^{42,43}

	Cetuximab (Erbix) for subsequent therapy in combination with encorafenib for progression of advanced or metastatic disease (BRAF V600E mutation positive) in individuals previously treated with any of the following: • Oxaliplatin-based therapy without irinotecan • Irinotecan-based therapy without oxaliplatin • Oxaliplatin and irinotecan Use either regimen: • Standard dosage of 400 mg/m² as an initial dose. The subsequent weekly dose is 250 mg/m². Continue until disease progression or unacceptable toxicity.^{42,43} • 500 mg/m² every 2 weeks until disease progression or unacceptable toxicity.^{42,43} Cetuximab (Erbix) for subsequent therapy in combination with encorafenib for progression of advanced or metastatic disease (BRAF V600E mutation positive) in individuals previously treated without either of the following: • Irinotecan or oxaliplatin • Irinotecan or oxaliplatin followed by FOLFOX or CapeOX with or without bevacizumab Use either regimen: • Standard dosage of 400 mg/m² as an initial dose. The subsequent weekly dose is 250 mg/m². Continue until disease progression or unacceptable toxicity.^{42,43} • 500 mg/m² every 2 weeks until disease progression or unacceptable toxicity.^{42,43} Cetuximab (Erbix) for subsequent therapy in combination with sotorasib or adagrasib for progression of advanced or metastatic disease (KRAS G12C mutation positive) in individuals previously treated with any of the following: • Oxaliplatin-based therapy without irinotecan • Irinotecan-based therapy without oxaliplatin • Oxaliplatin and irinotecan

	Use: • 500 mg/m² every 2 weeks until disease progression or unacceptable toxicity^{42, 43} Cetuximab (Erbix) for subsequent therapy in combination with sotorasib or adagrasib for progression of advanced or metastatic disease (KRAS G12C mutation positive) in individuals previously treated without any of the following: • Irinotecan or oxaliplatin • Irinotecan or oxaliplatin followed by FOLFOX or CapeOX with or without bevacizumab Use: • 500 mg/m² every 2 weeks until disease progression or unacceptable toxicity^{42, 43}
Head and Neck Cancers^{19, 23} , 25, 36, 37, 38, 39, 40, 44, 45, 46, 47, 50, 51, 52, 53	Cetuximab (Erbix) used in combination with radiation therapy (RT) for the initial treatment of locally or regionally advanced squamous cell cancer of the head and neck Use: • 400 mg/m² administered 1 week prior to initiation of a course of radiation therapy. The subsequent weekly dose (all other infusions) is 250 mg/m². Cetuximab (Erbix) administration continues for the duration of radiation therapy (6 to 7 weeks)^{1,25} Cetuximab (Erbix) used in combination with platinum-based therapy with 5-FU for the first-line treatment of recurrent locoregional disease or metastatic squamous cell carcinoma of the head and neck Use either regimen: • 400 mg/m² administered on the day of initiation of platinum-based therapy with 5-FU. The subsequent weekly dose (all other infusions) is 250 mg/m². Cetuximab (Erbix) administration continues until disease progression or unacceptable toxicity.^{1,25} • 500 mg/m² every 2 weeks until disease progression or unacceptable toxicity.¹ Cetuximab (Erbix) administered as a single agent for the treatment of recurrent or metastatic squamous cell cancer of

the head and neck in individuals who previously failed or are refractory to platinum-based chemotherapy

Use:

- 400 mg/m² as an initial dose. The subsequent weekly dose (all other infusions) is 250 mg/m² until disease progression or unacceptable toxicity^{1, 17, 18}

Non-nasopharyngeal Cancer

Cetuximab (Erbix) is indicated for the treatment of non-nasopharyngeal cancer:

Administered as a single agent given weekly as sequential systemic therapy/RT following induction systemic therapy for individuals with performance status (PS) 0-1 and who have one of the following:

- Newly diagnosed T4b, N0-3, M0 disease
- Newly diagnosed unresectable nodal disease with no metastases
- Newly diagnosed nonmetastatic disease and who are unfit for surgery
- Unresectable locoregional recurrence or persistent disease and who have not received prior RT

Use:

- 400 mg/m² administered 1 week prior to initiation of a course of radiation therapy. The subsequent weekly dose (all other infusions) is 250 mg/m². Cetuximab (Erbix) administration continues for the duration of radiation therapy (7 weeks).^{32,43}

Administered as a single agent given weekly as sequential systemic therapy/RT following combination systemic therapy in individuals with resectable locoregional recurrence or persistent disease and who have not received prior RT

Use

- 400 mg/m² administered 1 week prior to initiation of a course of radiation therapy. The subsequent weekly dose (all other infusions) is 250 mg/m². Cetuximab (Erbix) administration continues for the duration of radiation therapy (7 weeks).^{32,43}

	Administered as a single agent for the systemic first-line treatment for individuals with: • PS 3 and newly diagnosed T4b, N0-3, M0 disease, newly diagnosed unresectable nodal disease with no metastases or newly diagnosed nonmetastatic disease for individuals who are unfit for surgery • PS 0-3 and metastatic (M1) disease at initial presentation • PS 3 and unresectable locoregional recurrence or unresectable persistent disease without prior RT • PS 0-3 and unresectable locoregional recurrence with prior RT, unresectable second primary with prior RT, or unresectable persistent disease with prior RT, or recurrent/persistent disease with distant metastases Use: • 400 mg/m² as an initial dose. The subsequent weekly dose is 250 mg/m² until disease progression or unacceptable toxicity.^{32,43} Subsequent-line treatment as a single agent for individuals with: • Alternate option for PS 0-3 for metastatic (M1) disease at initial presentation • PS 3 and unresectable locoregional recurrence or unresectable persistent disease without prior RT • Alternate option for PS 0-3 and unresectable locoregional recurrence with prior RT, unresectable second primary with prior RT, or unresectable persistent disease with prior RT, or recurrent/persistent disease with distant metastases Use: • 400 mg/m² as an initial dose. The subsequent weekly dose is 250 mg/m² until disease progression or unacceptable toxicity.^{32,43} Administered as a single agent as postoperative systemic therapy/RT if cisplatin ineligible for positive margin and/or extranodal extension in • Resectable locoregional recurrence or persistent disease without prior RT or • Resectable locoregional recurrence, second primary, or persistent disease with prior RT

Use:

- 400 mg/m² administered 1 week prior to initiation of a course of radiation therapy. The subsequent weekly dose (all other infusions) is 250 mg/m². Cetuximab (Erbix) administration continues for the duration of radiation therapy (7 weeks).^{32,43}

As combination systemic first-line, or subsequent-line treatment, in individuals with PS 0-1, given:

- As part of any of the following regimens:
 - 5-FU and cisplatin
 - 5-FU and carboplatin
 - Docetaxel and cisplatin
 - Docetaxel and carboplatin
 - Paclitaxel and cisplatin
 - Paclitaxel and carboplatin
 - Cisplatin
 - Nivolumab
 - Pembrolizumab
 - Paclitaxel
- For any of the following:
 - Metastatic (M1) disease at initial presentation
 - Recurrent/persistent disease with distant metastases
 - Unresectable locoregional recurrence with prior RT
 - Unresectable second primary with prior RT
 - Unresectable persistent disease with prior RT

For 5-FU and cisplatin, 5-FU and carboplatin, cisplatin, pembrolizumab, or paclitaxel

Use:

- 400 mg/m² as an initial dose. The subsequent weekly dose is 250 mg/m² until disease progression or unacceptable toxicity^{32, 43}

For docetaxel and cisplatin or docetaxel and carboplatin

Use:

- 400 mg/m² as an initial dose. The subsequent weekly dose is 250 mg/m² for a maximum of **3** cycles followed by 500 mg/m² every 2 weeks until disease progression or unacceptable toxicity^{32, 43}

For paclitaxel and cisplatin or paclitaxel and carboplatin

Use:

- 400 mg/m² as an initial dose. The subsequent weekly dose is 250 mg/m² for a maximum of **5** cycles followed

by 500 mg/m² every 2 weeks until disease progression or unacceptable toxicity^{32,43}

For nivolumab

Use:

- 500 mg/m² administered every 2 weeks (starting 2 weeks prior to initiation of nivolumab) until disease progression or unacceptable toxicity^{32, 43}

As combination systemic therapy for resectable locoregional recurrence or persistent disease without prior RT given as part of any of the following regimens:

- 5-FU and cisplatin
- 5-FU and carboplatin
- Docetaxel and cisplatin
- Docetaxel and carboplatin
- Paclitaxel and cisplatin
- Paclitaxel and carboplatin
- Cisplatin
- Nivolumab
- Pembrolizumab
- Paclitaxel

For 5-FU and cisplatin, 5-FU and carboplatin, cisplatin, pembrolizumab, or paclitaxel

Use:

- 400 mg/m² as an initial dose. The subsequent weekly dose is 250 mg/m² until disease progression or unacceptable toxicity^{32,43}

For docetaxel and cisplatin or docetaxel and carboplatin

Use:

- 400 mg/m² as an initial dose. The subsequent weekly dose is 250 mg/m² for a maximum of **3** cycles followed by 500 mg/m² every 2 weeks until disease progression or unacceptable toxicity^{32,43}

For paclitaxel and cisplatin or paclitaxel and carboplatin

Use:

- 400 mg/m² as an initial dose. The subsequent weekly dose is 250 mg/m² for a maximum of **5** cycles followed by 500 mg/m² every 2 weeks until disease progression or unacceptable toxicity^{32,43}

For nivolumab

Use:

- 500 mg/m² administered every 2 weeks (starting 2 weeks prior to initiation of nivolumab) until disease progression or unacceptable toxicity^{32, 43}

Ethmoid Sinus Cancer

Cetuximab (Erbix) administered as a single agent given weekly is indicated for the treatment of cancer of the ethmoid sinus as sequential systemic therapy/RT following a complete response to induction chemotherapy for newly diagnosed T3, T4a disease

Use

- 400 mg/m² administered 1 week prior to initiation of a course of radiation therapy. The subsequent weekly dose (all other infusions) is 250 mg/m². Cetuximab (Erbix) administration continues for the duration of radiation therapy (7 weeks)^{32,43}

Nasopharynx Cancer

Cetuximab (Erbix) used in combination with carboplatin is indicated for the treatment of very advanced cancer of the nasopharynx as systemic first-line or subsequent-line (if not previously used) treatment in individuals with PS 0-1 for:

- Recurrent/persistent disease with distant metastases
- Unresectable locoregional recurrence with prior RT
- Unresectable second primary with prior RT
- Unresectable persistent disease with prior RT

Use:

- 400 mg/m² as an initial dose. The subsequent weekly dose is 250 mg/m² until disease progression or unacceptable toxicity^{32,43}

Cetuximab (Erbix) used in combination with carboplatin is indicated as first-line systemic therapy for the treatment of T1-4, N0-3, M1 disease for:

- Oligometastatic disease and PS 0-2

- Widely metastatic disease and good PS (0-2)

Cetuximab (Erbix) used in combination with carboplatin, if not previously used, as subsequent-line systemic therapy for the treatment of T1-2, N0-3, M1 disease for:

- Oligometastatic disease and PS 0-2
- Widely metastatic disease and good PS (0-2)

Use:

- 400 mg/m² as an initial dose. The subsequent weekly dose is 250 mg/m² until disease progression or unacceptable toxicity^{32,43}

Oral Cavity Cancer (including Mucosal Lip)

Cetuximab (Erbix) administered as a single agent is indicated for the treatment of cancer of the oral cavity (including mucosal lip) as postoperative systemic therapy/RT in individuals who are cisplatin ineligible with one of the following:

- Extranodal extension with or without positive margin for T1-3, N0-3; or T4a, N0-3 disease
- With positive margins for T3, N0; T1-3, N1-3; or T4a, N0-3 disease
- May be considered with positive margin in T1-2, N0 disease

Use:

- 400 mg/m² administered 1 week prior to initiation of a course of radiation therapy. The subsequent weekly dose (all other infusions) is 250 mg/m². Cetuximab (Erbix) administration continues for the duration of radiation therapy (6 weeks)^{32,43}

Oropharynx Cancer

Cetuximab (Erbix) administered as a single agent is indicated for the treatment of cancer of the oropharynx for the following:

	As primary concurrent systemic therapy/RT for either p16-negative disease: • T3-4a, N0-1 disease • T1-4a, N2-3 disease As primary concurrent systemic therapy/RT for either p16 (human papillomavirus [HPV])-positive disease: • N0-2, N1 (single node >3 cm, or 2 or more ipsilateral nodes 6 cm or less), T0-2, N2 or T3, N0-2 disease (treatment modality preferred if clinical evidence of fixed or matted nodes or obvious extranodal extension) • T0-3, N3 or T4, N0-3 disease As sequential systemic therapy/RT following induction chemotherapy for either p16-negative • T3-4a, N0-1 disease • T1-4a, N2-3 disease As sequential systemic therapy/RT following induction chemotherapy for either p16 (human papillomavirus [HPV])-positive disease: • T0-2, N1 (single node >3 cm, or 2 or more ipsilateral nodes less than or equal to 6 cm), T0-2, N2 or T3, N0-2 disease • T0-3, N3 or T4, N0-3 disease (National Comprehensive Cancer Network [NCCN]-preferred regimen for primary concurrent systemic therapy/RT) Use: • 400 mg/m² administered 1 week prior to initiation of a course of radiation therapy. The subsequent weekly dose (all other infusions) is 250 mg/m². Cetuximab (Erbix) administration continues for the duration of radiation therapy (7 weeks)^{32,43} Supraglottic Larynx Cancer

	Cetuximab (Erbix) administered as a single agent is indicated for the treatment of cancer of the supraglottic larynx Following a partial response at the primary site to induction chemotherapy given weekly for: • T3, N0 and most T3, N1-3 disease requiring (amenable to) total laryngectomy • T1-2, N+ and selected T3, N1 disease amenable to larynx-preserving (conservation) surgery • T4a, N0-3 disease for individuals who decline surgery Use: • 400 mg/m² as an initial dose. The subsequent weekly dose is 250 mg/m² until disease progression or unacceptable toxicity^{32,43} As postoperative systemic therapy/RT if cisplatin ineligible for most individuals with T1-2, N0 and selected T3 disease amenable to larynx-preserving (conservation) surgery for: • Extranodal extension • May be considered for discovery of positive node for disease with a positive margin Use: • 400 mg/m² administered 1 week prior to initiation of a course of radiation therapy. The subsequent weekly dose (all other infusions) is 250 mg/m². Cetuximab (Erbix) administration continues for the duration of radiation therapy (6 weeks)^{32,43} As postoperative systemic therapy/RT if cisplatin ineligible for individuals with extranodal extension and/or positive margin for: • T3, N0 and most T3, N1-3 disease requiring (amenable to) total laryngectomy • T1-2, N+ and selected T3, N1 disease amenable to larynx-preserving (conservation) surgery • T4a, N0-3 disease • T1-2, N+ and T3-4a, N0-3 disease following surgery with less than partial response at the primary site to induction chemotherapy Use:

- 400 mg/m² administered 1 week prior to initiation of a course of radiation therapy. The subsequent weekly dose (all other infusions) is 250 mg/m². Cetuximab (Erbix) administration continues for the duration of radiation therapy (6 weeks).^{32,43}

Glottic Larynx Cancer

Cetuximab (Erbix) administered as a single agent is indicated for the treatment of cancer of the glottic larynx Following partial response at the primary site to induction chemotherapy given weekly for:

- T3, N0-3 disease requiring (amenable to) total laryngectomy
- Selected individuals with T4a who decline surgery

Use:

- 400 mg/m² as an initial dose. The subsequent weekly dose is 250 mg/m² until disease progression or unacceptable toxicity^{32, 43}

As postoperative systemic therapy/RT in individuals ineligible for cisplatin with extranodal extension:

- For T1-2, N0 or select T3, N0 disease amenable to larynx-preserving (conservation) surgery
- And/or positive margin for T3, N0-3 disease requiring (amenable to) total laryngectomy
- And/or positive margin for T3, N0-3 disease following laryngectomy and less than partial response at the primary site to induction chemotherapy
- And/or positive margin for T4a, N0-3 disease

Use:

- 400 mg/m² administered 1 week prior to initiation of a course of radiation therapy. The subsequent weekly dose (all other infusions) is 250 mg/m². Cetuximab (Erbix) administration continues for the duration of radiation therapy (6 weeks)^{32,43}

Hypopharynx Cancer

Cetuximab (Erbix) administered as a single agent is

	indicated for the treatment of cancer of the hypopharynx: As primary concurrent systemic therapy/RT or induction chemotherapy for the following: • T1, N+ disease • T2-3, N0-3 disease requiring (amenable to) pharyngectomy with partial or total laryngectomy Use: • 400 mg/m² administered 1 week prior to initiation of a course of radiation therapy. The subsequent weekly dose (all other infusions) is 250 mg/m². Cetuximab (Erbix) administration continues for the duration of radiation therapy (7 weeks)^{32, 43} As sequential systemic therapy/RT given weekly for T4a, N0-3 disease for the following • A partial response at the primary site and stable or improved disease in the neck following induction chemotherapy • A complete response at the primary site and stable or improved disease in the neck following induction chemotherapy Use: • 400 mg/m² administered 1 week prior to initiation of a course of radiation therapy. The subsequent weekly dose (all other infusions) is 250 mg/m². Cetuximab (Erbix) administration continues for the duration of radiation therapy (7 weeks)^{32,43} As postoperative systemic therapy/RT in individuals who are cisplatin ineligible with one of the following: • Extranodal extension with or without positive margin for most T1, N0 or selected T2, N0 tumors amenable to larynx-preserving (conservation) surgery • May be considered with positive margin for T2, N0 tumors amenable to larynx-preserving (conservation) surgery • Extranodal extension and/or positive margin and any of the following: ○ T1, N+ or T2-3, N0-3 disease requiring (amenable to) pharyngectomy with partial or total laryngectomy ○ T1, N+ or T2-3, N0-3 disease with partial response and stable or improved disease in the

	neck or less than partial response at the primary site following induction chemotherapy ○ T4a, N0-3 disease ○ T4a, N0-3 disease with less than partial response at the primary site following induction chemotherapy Use: • 400 mg/m² administered 1 week prior to initiation of a course of radiation therapy. The subsequent weekly dose (all other infusions) is 250 mg/m². Cetuximab (Erbix) administration continues for the duration of radiation therapy (6 weeks)^{32,43} Occult Primary Head and Neck Cancer Cetuximab (Erbix) administered as a single agent for occult primary head and neck cancer: For initial definitive treatment as sequential systemic therapy/RT given weekly following induction chemotherapy for N2-3 disease with any of the following histology: • Poorly differentiated or nonkeratinizing squamous cell • Anaplastic (not thyroid) • Squamous cell carcinoma • Not otherwise specified (NOS) Use: • 400 mg/m² administered 1 week prior to initiation of a course of radiation therapy. The subsequent weekly dose (all other infusions) is 250 mg/m². Cetuximab (Erbix) administration continues for the duration of radiation therapy (7 weeks)^{32,43} As primary concurrent systemic therapy/RT for p16 (HPV)-positive disease in any of the following: • N1 (single node >3 cm, or 2 or more ipsilateral nodes 6 cm or less) disease • N2 disease • N3 disease Use:

	• 400 mg/m² administered as the initial dose. The subsequent weekly dose (all other infusions) is 250 mg/m². Cetuximab (Erbix) administration continues for the duration of radiation therapy (7 weeks)^{32,43} As postoperative systemic therapy/RT if cisplatin ineligible for disease with extranodal extension after neck dissection of disease in levels IV or V with adenocarcinoma histology of neck node, thyroglobulin and calcitonin negative Use: • 400 mg/m² administered 1 week prior to initiation of a course of radiation therapy. The subsequent weekly dose (all other infusions) is 250 mg/m². Cetuximab (Erbix) administration continues for the duration of radiation therapy (6 weeks)^{32,43} As sequential systemic therapy/RT given weekly following induction chemotherapy for p16 (HPV)-positive disease in either of the following: • N1 (single node >3 cm, or 2 or more ipsilateral nodes 6 cm or less) disease • N2-3 disease Use: • 400 mg/m² administered 1 week prior to initiation of a course of radiation therapy. The subsequent weekly dose (all other infusions) is 250 mg/m². Cetuximab (Erbix) administration continues for the duration of radiation therapy (6 weeks).^{32,43}
Non-Small Cell Lung Cancer^{26, 41}	Cetuximab (Erbix) in combination with afatinib as subsequent therapy for recurrent (excluding locoregional recurrence or symptomatic local disease with no evidence of disseminated disease; however, including mediastinal lymph node recurrence with prior RT), advanced or metastatic disease in individuals with EGFR exon 19 deletion or exon 21 L858R or EGFR S768I, L861Q, and/or G719X mutation positive disease: • Who have progressed on EGFR tyrosine kinase inhibitor therapy for asymptomatic disease, symptomatic brain lesions, or symptomatic systemic limited progression

	• Who are T790M negative, have progressed on EGFR tyrosine kinase inhibitor therapy, and have multiple symptomatic systemic lesions • Who are T790M positive, who have progressed on osimertinib, and have multiple symptomatic systemic lesions Use: 500 mg/m² on day 1 of a 14-day cycle until disease progression or unacceptable toxicity^{24,43}
Penile Cancer ⁴⁹	Cetuximab (Erbix) as single-agent therapy for subsequent-line systemic treatment for metastatic/recurrent disease, especially if not treated with a similar class of agent Use: • 400 mg/m² as an initial dose. The subsequent weekly dose is 250 mg/m² until disease progression or unacceptable toxicity.^{27,43}
Squamous Cell Skin Cancer ^{48, 54, 55}	Cetuximab (Erbix) administered for the treatment of squamous cell skin cancer: • As a single agent with concurrent RT for any of the following: ○ For locally advanced or unresectable disease as either of the following: ▪ Primary treatment for non-surgical candidates ▪ Additional treatment if positive surgical margins and re-resection not feasible ○ Resected high-risk regional disease of the head and neck (pathologic extranodal extension [ENE] or incompletely excised nodal disease) ○ Regional disease that is unresectable, inoperable, or incompletely resected ○ Regional recurrence or distant metastatic disease

	- As a single agent or in combination with carboplatin and paclitaxel if ineligible for, or progressed on, immune checkpoint inhibitors and clinical trials as treatment in any of the following: - For locally advanced or unresectable disease as either of the following: - Primary treatment if curative surgery and curative RT are not feasible - Additional treatment if positive surgical margins and curative surgery and curative RT are not feasible - Regional disease that is unresectable, inoperable, or incompletely resected if curative RT no feasible - Regional recurrence or distant metastatic disease Use: 400 mg/m² as an initial dose. The subsequent weekly dose is 250 mg/m² until disease progression or unacceptable toxicity^{2,43}

Duration of authorization: 12 months

Version Effective Date: 02/26/2024

Title: Cetuximab (Erbix[®])

MEDICALLY NECESSARY:

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

C00.0 Malignant neoplasm of external upper lip
C00.1 Malignant neoplasm of external lower lip
C00.2 Malignant neoplasm of external lip, unspecified
C00.3 Malignant neoplasm of upper lip, inner aspect
C00.4 Malignant neoplasm of lower lip, inner aspect
C00.5 Malignant neoplasm of lip, unspecified, inner aspect
C00.6 Malignant neoplasm of commissure of lip, unspecified
C00.8 Malignant neoplasm of overlapping sites of lip
C00.9 Malignant neoplasm of lip, unspecified
C01 Malignant neoplasm of base of tongue
C02.0 Malignant neoplasm of dorsal surface of tongue
C02.1 Malignant neoplasm of border of tongue
C02.2 Malignant neoplasm of ventral surface of tongue
C02.3 Malignant neoplasm of anterior two-thirds of tongue, part unspecified
C02.4 Malignant neoplasm of lingual tonsil
C02.8 Malignant neoplasm of overlapping sites of tongue
C02.9 Malignant neoplasm of tongue, unspecified
C03.0 Malignant neoplasm of upper gum
C03.1 Malignant neoplasm of lower gum
C03.9 Malignant neoplasm of gum, unspecified
C04.0 Malignant neoplasm of anterior floor of mouth
C04.1 Malignant neoplasm of lateral floor of mouth
C04.8 Malignant neoplasm of overlapping sites of floor of mouth
C04.9 Malignant neoplasm of floor of mouth, unspecified
C05.0 Malignant neoplasm of hard palate

- C05.1 Malignant neoplasm of soft palate
- C05.2 Malignant neoplasm of uvula
- C05.8 Malignant neoplasm of overlapping sites of palate
- C05.9 Malignant neoplasm of palate, unspecified
- C06.0 Malignant neoplasm of cheek mucosa
- C06.1 Malignant neoplasm of vestibule of mouth
- C06.2 Malignant neoplasm of retromolar area
- C06.80 Malignant neoplasm of overlapping sites of unspecified parts of mouth
- C06.89 Malignant neoplasm of overlapping sites of other parts of mouth
- C06.9 Malignant neoplasm of mouth, unspecified
- C09.0 Malignant neoplasm of tonsillar fossa
- C09.1 Malignant neoplasm of tonsillar pillar (anterior) (posterior)
- C09.8 Malignant neoplasm of overlapping sites of tonsil
- C09.9 Malignant neoplasm of tonsil, unspecified
- C10.0 Malignant neoplasm of vallecula
- C10.1 Malignant neoplasm of anterior surface of epiglottis
- C10.2 Malignant neoplasm of lateral wall of oropharynx
- C10.3 Malignant neoplasm of posterior wall of oropharynx
- C10.4 Malignant neoplasm of branchial cleft
- C10.8 Malignant neoplasm of overlapping sites of oropharynx
- C10.9 Malignant neoplasm of oropharynx, unspecified
- C11.0 Malignant neoplasm of superior wall of nasopharynx
- C11.1 Malignant neoplasm of posterior wall of nasopharynx
- C11.2 Malignant neoplasm of lateral wall of nasopharynx
- C11.3 Malignant neoplasm of anterior wall of nasopharynx
- C11.8 Malignant neoplasm of overlapping sites of nasopharynx
- C11.9 Malignant neoplasm of nasopharynx, unspecified
- C12 Malignant neoplasm of pyriform sinus
- C13.0 Malignant neoplasm of postcricoid region
- C13.1 Malignant neoplasm of aryepiglottic fold, hypopharyngeal aspect
- C13.2 Malignant neoplasm of posterior wall of hypopharynx
- C13.8 Malignant neoplasm of overlapping sites of hypopharynx
- C13.9 Malignant neoplasm of hypopharynx, unspecified
- C14.0 Malignant neoplasm of pharynx, unspecified
- C14.2 Malignant neoplasm of Waldeyer's ring
- C14.8 Malignant neoplasm of overlapping sites of lip, oral cavity and pharynx
- C18.0 Malignant neoplasm of cecum
- C18.1 Malignant neoplasm of appendix
- C18.2 Malignant neoplasm of ascending colon
- C18.3 Malignant neoplasm of hepatic flexure
- C18.4 Malignant neoplasm of transverse colon
- C18.5 Malignant neoplasm of splenic flexure
- C18.6 Malignant neoplasm of descending colon
- C18.7 Malignant neoplasm of sigmoid colon

C18.8 Malignant neoplasm of overlapping sites of colon
C18.9 Malignant neoplasm of colon, unspecified
C19 Malignant neoplasm of rectosigmoid junction
C20 Malignant neoplasm of rectum
C21.8 Malignant neoplasm of overlapping sites of rectum, anus and anal canal
C30.0 Malignant neoplasm of nasal cavity
C30.1 Malignant neoplasm of middle ear
C31.0 Malignant neoplasm of maxillary sinus
C31.1 Malignant neoplasm of ethmoidal sinus
C32.0 Malignant neoplasm of glottis
C32.1 Malignant neoplasm of supraglottis
C32.2 Malignant neoplasm of subglottis
C32.3 Malignant neoplasm of laryngeal cartilage
C32.8 Malignant neoplasm of overlapping sites of larynx
C32.9 Malignant neoplasm of larynx, unspecified
C33 Malignant neoplasm of trachea
C34.01 Malignant neoplasm of right main bronchus
C34.02 Malignant neoplasm of left main bronchus
C34.11 Malignant neoplasm of upper lobe, right bronchus or lung
C34.12 Malignant neoplasm of upper lobe, left bronchus or lung
C34.2 Malignant neoplasm of middle lobe, bronchus or lung
C34.31 Malignant neoplasm of lower lobe, right bronchus or lung
C34.32 Malignant neoplasm of lower lobe, left bronchus or lung
C34.81 Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82 Malignant neoplasm of overlapping sites of left bronchus and lung
C34.91 Malignant neoplasm of unspecified part of right bronchus or lung
C34.92 Malignant neoplasm of unspecified part of left bronchus or lung
C44.02 Squamous cell carcinoma of skin of lip
C44.1221 Squamous cell carcinoma of skin of right upper eyelid, including canthus
C44.1222 Squamous cell carcinoma of skin of right lower eyelid, including canthus
C44.1291 Squamous cell carcinoma of skin of left upper eyelid, including canthus
C44.1292 Squamous cell carcinoma of skin of left lower eyelid, including canthus
C44.222 Squamous cell carcinoma of skin of right ear and external auricular canal
C44.229 Squamous cell carcinoma of skin of left ear and external auricular canal
C44.320 Squamous cell carcinoma of skin of unspecified parts of face
C44.321 Squamous cell carcinoma of skin of nose
C44.329 Squamous cell carcinoma of skin of other parts of face
C44.42 Squamous cell carcinoma of skin of scalp and neck
C44.520 Squamous cell carcinoma of anal skin
C44.521 Squamous cell carcinoma of skin of breast
C44.529 Squamous cell carcinoma of skin of other part of trunk
C44.622 Squamous cell carcinoma of skin of right upper limb, including shoulder
C44.629 Squamous cell carcinoma of skin of left upper limb, including shoulder
C44.722 Squamous cell carcinoma of skin of right lower limb, including hip

C44.729 Squamous cell carcinoma of skin of left lower limb, including hip
C44.82 Squamous cell carcinoma of overlapping sites of skin
C44.92 Squamous cell carcinoma of skin, unspecified
C60.0 Malignant neoplasm of prepuce
C60.1 Malignant neoplasm of glans penis
C60.2 Malignant neoplasm of body of penis
C60.8 Malignant neoplasm of overlapping sites of penis
C60.9 Malignant neoplasm of penis, unspecified
C63.7 Malignant neoplasm of other specified male genital organs
C63.8 Malignant neoplasm of overlapping sites of male genital organs
C76.0 Malignant neoplasm of head, face and neck
C77.0 Secondary and unspecified malignant neoplasm of lymph nodes of head, face and neck
C78.01 Secondary malignant neoplasm of right lung
C78.02 Secondary malignant neoplasm of left lung
C78.6 Secondary malignant neoplasm of retroperitoneum and peritoneum
C78.7 Secondary malignant neoplasm of liver and intrahepatic bile duct
D37.01 Neoplasm of uncertain behavior of lip
D37.02 Neoplasm of uncertain behavior of tongue
D37.05 Neoplasm of uncertain behavior of pharynx
D37.09 Neoplasm of uncertain behavior of other specified sites of the oral cavity
D38.0 Neoplasm of uncertain behavior of larynx
D38.5 Neoplasm of uncertain behavior of other respiratory organs
D38.6 Neoplasm of uncertain behavior of respiratory organ, unspecified

Duration of authorization: 12 months

Version Effective Date: 02/26/2024

Title: Chimeric Antigen Receptor (CAR) Therapy

MEDICALLY NECESSARY:

AXICABTAGENE CILOLEUCEL (YESCARTA)

B-Cell Lymphomas

Diffuse large B-cell lymphoma, primary mediastinal large B-cell lymphoma, high-grade B-cell lymphoma, acquired immunodeficiency syndrome/human immunodeficiency virus-related diffuse large B-cell lymphoma, primary effusion lymphoma, human herpesvirus 8-positive diffuse large B-cell lymphoma

Axicabtagene ciloleucel (Yescarta) is considered medically necessary and, therefore, covered for the autologous treatment of relapsed or refractory (R/R) diffuse large B-cell lymphoma (DLBCL), R/R primary mediastinal large B-cell lymphoma (BCL), R/R high-grade BCL with or without MYC and BCL2 and/or BCL6 rearrangement, R/R acquired immunodeficiency syndrome (AIDS)/human immunodeficiency virus (HIV)-related DLBCL, R/R primary effusion lymphoma, or human herpesvirus 8 (HHV8)-positive DLBCL, not otherwise specified, who have received, at a minimum, an anti-cluster of differentiation (CD)20 monoclonal antibody (e.g., rituximab) (unless the tumor is CD20 negative) and an anthracycline (e.g., doxorubicin)-containing chemotherapy regimen, when administered at healthcare facilities enrolled in the US Food and Drug Administration (FDA) risk evaluation and mitigation strategies (REMS), and **all** of the following criteria are met:

- Diagnosis of one of the above types of R/R BCLs
- Used as **one** of the following:
 - Additional therapy for R/R disease greater than 12 months after completion of first-line therapy in individuals who have partial response following second-line therapy
 - Additional therapy for individuals with primary refractory disease (partial response, no response, or progression) or relapsed disease less than 12 months after completion of first-line therapy
 - Third-line and subsequent therapy (if anti-CD19 chimeric antigen receptor [CAR] T-cell therapy [e.g., axicabtagene ciloleucel {Yescarta}, brexucabtagene autoleucel {Tecartus}, lisocabtagene maraleucel {Breyanzi}, tisagenlecleucel {Kymriah}] was not previously given) of disease in second relapse or greater in individuals with partial response, relapse, or progressive disease following therapy for R/R disease (National Comprehensive Cancer Network [NCCN] preferred)
- The individual does not have clinically significant active systemic infection or inflammatory disorder including, but not limited to, hepatitis B; hepatitis C; HIV infection; presence of fungal, bacterial, viral, or other infection that is uncontrolled
- The individual does not have primary central nervous system (CNS) lymphoma or malignancy
- The individual does not have a history of prior CAR T-cell therapy or prior gene therapy
- The individual is 18 years or older at the time of infusion

Follicular lymphoma (grade 1 to 2), marginal zone lymphoma*

Axicabtagene ciloleucel (Yescarta) is considered medically necessary and, therefore, covered for the autologous treatment of R/R follicular lymphoma (FL; grade 1 to 2) or R/R marginal zone lymphoma* (MZL) when administered at healthcare facilities enrolled in the FDA REMS, and **all** of the following criteria are met:

- Diagnosis of one of the above types of R/R BCLs
- Used as third-line and subsequent therapy (if not previously given) for partial response, no response, relapsed, or progressive disease in individuals with indications for treatment after two or more prior chemoimmunotherapy regimens (NCCN preferred)
- The individual does not have clinically significant active systemic infection or inflammatory disorder including, but not limited to, hepatitis B; hepatitis C; HIV infection; presence of fungal, bacterial, viral, or other infection that is uncontrolled
- The individual does not have primary CNS lymphoma or malignancy
- The individual does not have a history of prior CAR T-cell therapy or prior gene therapy
- The individual is 18 years or older at the time of infusion

*Includes extranodal MZL of the stomach (formerly gastric mucosa-associated lymphoid tissue [MALT]), extranodal MZL of nongastric sites (noncutaneous) (formerly nongastric MALT), nodal MZL, and splenic MZL.

Histologic transformation of indolent lymphomas to diffuse large B-cell lymphoma (e.g., from follicular lymphoma, nodal marginal zone lymphoma)

Axicabtagene ciloleucel (Yescarta) is considered medically necessary and, therefore, covered for the autologous treatment of R/R histologic transformation of indolent lymphomas to DLBCL (e.g., from FL [individual must have chemorefractory disease after transformation to DLBCL] or nodal MZL) when administered at healthcare facilities enrolled in the FDA REMS, and **all** of the following criteria are met:

- Diagnosis of one of the above types of R/R BCLs
- Used as additional therapy (if anti-CD19 CAR T-cell therapy [e.g., axicabtagene ciloleucel {Yescarta}, brexucabtagene autoleucel {Tecartus}, lisocabtagene maraleucel {Breyanzi}, tisagenlecleucel {Kymriah}] was not previously given) in individuals who are candidates for additional therapy and have received multiple lines of prior therapies including two or more chemoimmunotherapy regimens for indolent or transformed disease (individuals should have received at least one anthracycline [e.g., doxorubicin]-based regimen, unless contraindicated)
- The individual does not have clinically significant active systemic infection or inflammatory disorder including, but not limited to, hepatitis B; hepatitis C; HIV infection; presence of fungal, bacterial, viral, or other infection that is uncontrolled
- The individual does not have primary CNS lymphoma or malignancy
- The individual does not have a history of prior CAR T-cell therapy or prior gene therapy
- The individual is 18 years or older at the time of infusion

Monomorphic post-transplant lymphoproliferative disorder (B-cell type)

Axicabtagene ciloleucel (Yescarta) is considered medically necessary and, therefore, covered

for the autologous treatment of R/R monomorphic post-transplant lymphoproliferative disorder (PTLD) (B-cell type) when administered at healthcare facilities enrolled in the FDA REMS, and **all** of the following criteria are met:

- Diagnosis of R/R monomorphic PTLD (B-cell type)
- Used as **one** of the following:
 - Additional therapy for R/R disease greater than 12 months after completion of initial treatment with chemoimmunotherapy in individuals who have partial response following second-line chemoimmunotherapy
 - Additional therapy for individuals with primary refractory disease (partial response, no response, or progression) or relapsed disease less than 12 months after completion of initial treatment with chemoimmunotherapy
 - Third-line and subsequent therapy (if anti-CD19 CAR T-cell therapy [e.g., axicabtagene ciloleucel {Yescarta}, brexucabtagene autoleucel {Tecartus}, lisocabtagene maraleucel {Breyanzi}, tisagenlecleucel {Kymriah}] not previously given) of disease in second relapse or greater in individuals with partial response, no response, or progressive disease following therapy for R/R disease (NCCN preferred)
- The individual does not have clinically significant active systemic infection or inflammatory disorder including, but not limited to, hepatitis B; hepatitis C; HIV infection; presence of fungal, bacterial, viral, or other infection that is uncontrolled
- The individual does not have primary CNS lymphoma or malignancy
- The individual does not have a history of prior CAR T-cell therapy or prior gene therapy
- The individual is 18 years or older at the time of infusion

Pediatric aggressive mature B-cell lymphoma (primary mediastinal large B-cell lymphoma)

Axicabtagene ciloleucel (Yescarta) is considered medically necessary and, therefore, covered for the autologous treatment of R/R pediatric aggressive mature BCL (primary mediastinal large BCL) when administered at healthcare facilities enrolled in the FDA REMS and **all** of the following are met:

- Diagnosis of R/R pediatric aggressive mature BCL (primary mediastinal large BCL)
- Used as consolidation/additional therapy if partial response achieved after therapy for R/R disease (after use of two or more chemoimmunotherapy regimens) (NCCN preferred)
- The individual does not have clinically significant active systemic infection or inflammatory disorder including, but not limited to, hepatitis B; hepatitis C; HIV infection; presence of fungal, bacterial, viral, or other infection that is uncontrolled
- The individual does not have primary CNS lymphoma or malignancy
- The individual does not have a history of prior CAR T-cell therapy or prior gene therapy

BREXUCABTAGENE AUTOLEUCEL (TECARTUS)

Mantle cell lymphoma

Brexucabtagene autoleucel (Tecartus) is considered medically necessary and, therefore,

covered for the autologous treatment for R/R mantle cell lymphoma (MCL) when administered at healthcare facilities enrolled in the FDA REMS, and **all** of the following criteria are met:

- Diagnosis of R/R MCL
- Used as second-line and subsequent-line therapy for individuals who have received prior covalent Bruton tyrosine kinase (BTK) inhibitor (e.g., ibrutinib, acalabrutinib) resulting in **one** of the following:
 - No response or progressive disease following second-line therapy with covalent BTK inhibitor or other non–time-limited regimens (e.g., lenalidomide and rituximab)
 - Partial response, no response, or progressive disease following second-line therapy with time-limited regimens
 - Relapsed or progressive disease (relapse #2 or greater) if not previously given
- The individual does not have clinically significant active systemic infection or inflammatory disorder including, but not limited to, hepatitis B; hepatitis C; HIV infection; presence of fungal, bacterial, viral, or other infection that is uncontrolled
- The individual does not have a history of prior CAR T-cell therapy or prior gene therapy
- The individual is 18 years or older at time of infusion

B-Cell Precursor Acute lymphoblastic leukemia

Brexucabtagene autoleucel (Tecartus) is considered medically necessary and, therefore, covered for the autologous treatment for R/R B-cell precursor acute lymphoblastic leukemia (B-ALL) when administered at healthcare facilities enrolled in the FDA REMS, and **all** of the following are met:

- Used as single-agent therapy when the individual meets **one** of the following:
 - R/R Philadelphia chromosome (Ph)-positive B-ALL following therapy that has included tyrosine kinase inhibitors (TKIs) (e.g., bosutinib, dasatinib, imatinib, nilotinib, ponatinib)
 - R/R Ph-negative B-ALL (NCCN preferred)
- The individual does not have clinically significant active systemic infection or inflammatory disorder including, but not limited to, hepatitis B; hepatitis C; HIV infection; presence of fungal, bacterial, viral, or other infection that is uncontrolled
- The individual does not have **any** of the following:
 - Burkitt lymphoma/leukemia
 - Concomitant genetic syndrome (e.g., Fanconi anemia, Kostmann syndrome, Shwachman-Diamond syndrome, other known bone marrow failure syndrome)
 - Grade 2 to 4 graft-versus-host disease (GVHD)
- The individual does not have a history of prior CAR T-cell therapy or prior gene therapy
- The individual is 18 years or older at time of infusion

CILTACABTAGENE AUTOLEUCEL (CARVYKTI)

Multiple myeloma

Ciltacabtagene autoleucel (Carvykti) is considered medically necessary and, therefore, covered

for the autologous treatment for R/R multiple myeloma (MM) when administered at healthcare facilities enrolled in the FDA REMS, and **all** of the following are met:

- Diagnosis of late relapse or progressive MM
- The individual has been treated with **one** of the following regimens:
 - One prior line of therapy including **all** of the following (NCCN preferred):
 - A proteasome inhibitor (e.g., carfilzomib, ixazomib, bortezomib)
 - An immunomodulatory agent (e.g., thalidomide, lenalidomide, pomalidomide, cyclophosphamide)
 - Are refractory to lenalidomide
 - Three prior lines of therapy (NCCN preferred)
- The individual does not have clinically significant active systemic infection or inflammatory disorder including, but not limited to, hepatitis B; hepatitis C; HIV infection; presence of fungal, bacterial, viral, or other infection that is uncontrolled
- The individual does not have known active or prior history of significant CNS disease
- The individual does not have a history of prior therapy that is targeted to B-cell maturation antigen (BCMA) (e.g., belantamab mafodotin, teclistamab, idecabtagene vicleucel [Abecma])
- The individual has not undergone allogeneic hematopoietic stem cell transplantation (HSCT) within the past 6 months or an autologous HSCT 12 weeks or less before apheresis
- The individual does not have a history of prior CAR T-cell therapy or prior gene therapy
- The individual is 18 years or older at time of infusion

IDECABTAGENE VICLEUCEL (ABECMA)

Multiple myeloma

Idecabtagene vicleucel (Abecma) is considered medically necessary and, therefore, covered for the autologous treatment for R/R MM when administered at healthcare facilities enrolled in the FDA REMS, and **all** of the following are met:

- Diagnosis of late relapse or progressive MM
- The individual has been treated with **one** of the following regimens:
 - Two prior lines of therapy including **all** of the following (NCCN preferred):
 - A proteasome inhibitor (e.g., carfilzomib, ixazomib, bortezomib)
 - An immunomodulatory agent (e.g., thalidomide, lenalidomide, pomalidomide, cyclophosphamide)
 - An anti-CD38 monoclonal antibody (e.g., isatuximab, daratumumab)
 - At least three prior lines of therapy (NCCN preferred)
- The individual does not have clinically significant active systemic infection or inflammatory disorder including, but not limited to, hepatitis B; hepatitis C; HIV infection; presence of fungal, bacterial, viral, or other infection that is uncontrolled
- The individual does not have known active or prior history of significant CNS disease
- The individual does not have a history of prior CAR T-cell therapy or prior gene therapy
- The individual is 18 years or older at time of infusion

LISOCABTAGENE MARALEUCEL (BREYANZI)

B-Cell Lymphomas

Diffuse large B-cell lymphoma, high-grade B-cell lymphoma, primary mediastinal large B-cell lymphoma, T-cell/histiocyte-rich large B-cell lymphoma, follicular lymphoma (grade 3B), acquired immunodeficiency syndrome/human immunodeficiency virus-related diffuse large B-cell lymphoma, primary effusion lymphoma, human herpesvirus 8-positive diffuse large B-cell lymphoma

Lisocabtagene maraleucel (Breyanzi) is considered medically necessary and, therefore, covered for the autologous treatment of R/R DLBCL, R/R high-grade BCL with MYC and BCL2 and/or BCL6 rearrangements with DLBCL histology (double/triple-hit lymphoma), R/R primary mediastinal large BCL, R/R THRBCL, R/R FL (grade 3B), R/R AIDS/HIV-related DLBCL, R/R primary effusion lymphoma, and R/R HHV8-positive DLBCL, not otherwise specified when administered at healthcare facilities enrolled in the FDA REMS, and **all** of the following are met:

- Diagnosis of one of the above types of R/R B-cell lymphomas
- Used as **one** of the following:
 - Second-line therapy for R/R disease greater than 12 months after completion of first-line therapy if no intention to proceed to transplant (NCCN preferred) or are not eligible for HSCT due to comorbidities or age
 - Additional therapy for R/R disease greater than 12 months after completion of first-line therapy (with no intention to proceed to transplant [or are not eligible for HSCT due to comorbidities or age] in individuals with DLBCL or primary mediastinal large BCL only) in individuals with intention to proceed to transplant who have partial response following second-line therapy
 - Additional therapy for individuals with primary refractory disease (partial response, no response, or progression) or relapsed disease less than 12 months after completion of first-line therapy
 - Third-line and subsequent therapy (if anti-CD19 CAR T-cell therapy [e.g., axicabtagene ciloleucel {Yescarta}, brexucabtagene autoleucel {Tecartus}, lisocabtagene maraleucel {Breyanzi}, tisagenlecleucel {Kymriah}] was not previously given) of disease in second relapse or greater in individuals with partial response, no response, or progressive disease following therapy for R/R disease (NCCN preferred)
- The individual does not have clinically significant active systemic infection or inflammatory disorder including, but not limited to, hepatitis B; hepatitis C; HIV infection; presence of fungal, bacterial, viral, or other infection that is uncontrolled
- The individual does not have active CNS-only involvement by malignancy, but can have secondary CNS involvement
- The individual does not have a history of prior CAR T-cell therapy or prior gene therapy
- The individual is 18 years or older at time of infusion

Follicular lymphoma (grade 1 to 2)

Lisocabtagene maraleucel (Breyanzi) is considered medically necessary and, therefore, covered for the autologous treatment of R/R FL (grade 1 to 2) when administered at healthcare facilities enrolled in the FDA REMS and **all** of the following are met:

- Diagnosis of R/R FL (grade 1 to 2)
- Used as third-line and subsequent therapy (if not previously given) for partial response, no response, relapsed, or progressive disease in individuals with indications for treatment
- The individual does not have clinically significant active systemic infection or inflammatory disorder including, but not limited to, hepatitis B; hepatitis C; HIV infection; presence of fungal, bacterial, viral, or other infection that is uncontrolled
- The individual does not have active CNS-only involvement by malignancy, but can have secondary CNS involvement
- The individual does not have a history of prior CAR T-cell therapy or prior gene therapy
- The individual is 18 years or older at time of infusion

Mantle cell lymphoma

Lisocabtagene maraleucel (Breyanzi) is considered medically necessary and, therefore, covered for the autologous treatment of R/R MCL when administered at healthcare facilities enrolled in the FDA REMS and **all** of the following are met:

- Diagnosis of R/R MCL
- Used in **one** of the following regimens:
 - As second-line therapy for individuals who are appropriate for aggressive induction therapy and have received prior covalent Bruton tyrosine kinase (BTK) inhibitor (e.g., ibrutinib, acalabrutinib)
 - As third and subsequent-line therapy for individuals who are appropriate for less aggressive induction therapy resulting in one of the following:
 - No response or progressive disease following second-line therapy with covalent BTK inhibitor or other continuous treatment regimens (e.g., lenalidomide and rituximab)
 - Partial response, no response, or progressive disease following second-line therapy with fixed-duration regimens
 - Relapsed or progressive disease (relapse #2 or greater) if not previously given
- The individual does not have clinically significant active systemic infection or inflammatory disorder including, but not limited to, hepatitis B; hepatitis C; HIV infection; presence of fungal, bacterial, viral, or other infection that is uncontrolled
- The individual does not have active CNS-only involvement by malignancy, but can have secondary CNS involvement
- The individual does not have a history of prior CAR T-cell therapy or prior gene therapy
- The individual is 18 years or older at time of infusion

Histologic transformation of indolent lymphoma to diffuse large B-cell lymphoma (e.g., follicular lymphoma, marginal zone lymphoma*)

Lisocabtagene maraleucel (Breyanzi) is considered medically necessary and, therefore, covered

for the autologous treatment of R/R histologic transformation of indolent lymphomas to DLBCL (e.g., FL, MZL*) when administered at healthcare facilities enrolled in the FDA REMS and **all** of the following are met:

- Diagnosis of one of the above types of R/R BCLs
- Used as third-line and subsequent therapy (if anti-CD19 CAR T-cell therapy [e.g., axicabtagene ciloleucel {Yescarta}, brexucabtagene autoleucel {Tecartus}, lisocabtagene maraleucel {Breyanzi}, tisagenlecleucel {Kymriah}] was not previously given) for individuals who are candidates for additional therapy and who have received multiple lines of prior therapies including two or more chemoimmunotherapy regimens for indolent or transformed disease (individuals should have received at least one anthracycline [e.g., doxorubicin] or anthracenedione [e.g., mitoxantrone]-based regimen, unless contraindicated) (NCCN preferred)
- The individual does not have clinically significant active systemic infection or inflammatory disorder including, but not limited to, hepatitis B; hepatitis C; HIV infection; presence of fungal, bacterial, viral, or other infection that is uncontrolled
- The individual does not have active CNS-only involvement by malignancy, but can have secondary CNS involvement
- The individual does not have a history of prior CAR T-cell therapy or prior gene therapy
- The individual is 18 years or older at time of infusion

*Includes extranodal MZL of the stomach (formerly gastric mucosa-associated lymphoid tissue [MALT]), extranodal MZL of nongastric sites (noncutaneous) (formerly nongastric MALT), nodal MZL, and splenic MZL.

Monomorphic post-transplant lymphoproliferative disorder (B-cell type)

Lisocabtagene maraleucel (Breyanzi) is considered medically necessary and, therefore, covered for the autologous treatment of R/R monomorphic PTLD (B-cell type) when administered at healthcare facilities enrolled in the FDA REMS and **all** of the following are met:

- Diagnosis of R/R monomorphic PTLD (B-cell type)
- Used as **one** of the following:
 - Second-line therapy for R/R disease greater than 12 months after completion of first-line therapy if no intention to proceed to transplant or are not eligible for HSCT due to comorbidities or age
 - Additional therapy for R/R disease greater than 12 months after completion of initial treatment with chemoimmunotherapy in individuals who have partial response following second-line chemoimmunotherapy
 - Additional therapy for individuals with primary refractory disease (partial response, no response, or progression) or relapsed disease less than 12 months after completion of first-line therapy
 - Treatment (if anti-CD19 CAR T-cell therapy [e.g., axicabtagene ciloleucel {Yescarta}, brexucabtagene autoleucel {Tecartus}, lisocabtagene maraleucel {Breyanzi}, tisagenlecleucel {Kymriah}] not previously given) of disease in second relapse or greater in individuals with partial response, no response, or progressive disease following therapy for R/R disease

- The individual does not have clinically significant active systemic infection or inflammatory disorder including, but not limited to, hepatitis B; hepatitis C; HIV infection; presence of fungal, bacterial, viral, or other infection that is uncontrolled
- The individual does not have active CNS-only involvement by malignancy, but can have secondary CNS involvement
- The individual does not have a history of prior CAR T-cell therapy or prior gene therapy
- The individual is 18 years or older at time of infusion

Pediatric aggressive mature B-cell lymphoma (primary mediastinal large B-cell lymphoma)

Lisocabtagene maraleucel (Breyanzi) is considered medically necessary and, therefore, covered for the autologous treatment of R/R pediatric aggressive mature BCL (primary mediastinal large BCL) when administered at healthcare facilities enrolled in the FDA REMS and **all** of the following are met:

- Diagnosis of pediatric aggressive mature BCL (primary mediastinal large BCL)
- Used as consolidation/additional therapy if partial response achieved after therapy for R/R disease (after use of two or more chemoimmunotherapy regimens) (NCCN preferred)
- The individual does not have clinically significant active systemic infection or inflammatory disorder including, but not limited to, hepatitis B; hepatitis C; HIV infection; presence of fungal, bacterial, viral, or other infection that is uncontrolled
- The individual does not have active CNS-only involvement by malignancy, but can have secondary CNS involvement
- The individual does not have a history of prior CAR T-cell therapy or prior gene therapy

Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

Lisocabtagene maraleucel (Breyanzi) is considered medically necessary and, therefore, covered for the autologous treatment of R/R chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) when administered at healthcare facilities enrolled in the FDA REMS and **all** of the following criteria are met:

- Diagnosis of R/R CLL/SLL
- Used as **either** of the following:
 - R/R disease after prior therapy with BTK inhibitor- and venetoclax-based regimens in individuals with CLL/SLL with or without del(17p)/TP53 mutation who have indications for treatment (NCCN preferred)
 - Additional therapy for treatment of histologic (Richter) transformation to DLBCL (clonally related or unknown clonal status) in individuals with del(17p)/TP53 mutation or who are chemotherapy refractory or unable to receive chemoimmunotherapy
- The individual does not have clinically significant active systemic infection or inflammatory disorder including, but not limited to, hepatitis B; hepatitis C; HIV infection; presence of fungal, bacterial, viral, or other infection that is uncontrolled
- The individual does not have active CNS-only involvement by malignancy, but can have secondary CNS involvement
- The individual does not have a history of prior CAR T-cell therapy or prior gene therapy

- The individual is 18 years or older at time of infusion

TISAGENLEUCCEL (KYMRIAH)

B-Cell Precursor Acute Lymphoblastic Leukemia

Tisagenlecleucel (Kymriah) as a single-agent therapy is considered medically necessary and, therefore, covered for the autologous treatment of R/R B-ALL when administered at healthcare facilities enrolled in the FDA REMS and **all** of the following criteria are met:

- Confirmed diagnosis of CD19-positive B-ALL with morphologic bone marrow tumor involvement (five percent or greater lymphoblasts) in individuals 25 years and younger at the time of infusion with relapsed or refractory (R/R) disease and **one** of the following subtypes:
 - Ph-negative disease with refractory disease or two or more relapses (NCCN preferred regimen)
 - Ph-positive disease with refractory disease or two or more relapses following therapy that has included two TKIs (e.g., bosutinib, dasatinib, imatinib, nilotinib, ponatinib)
- The individual does not have **any** of the following:
 - Concomitant genetic syndromes associated with bone marrow failure states (e.g., Fanconi anemia; Kostmann syndrome; Shwachman-Diamond syndrome; any other bone marrow syndrome)
 - Burkitt lymphoma/leukemia
 - Grade 2 to 4 GVHD
- The individual does not have clinically significant active systemic infection or inflammatory disorder including, but not limited to, hepatitis B; hepatitis C; HIV infection; presence of fungal, bacterial, viral, or other infection that is uncontrolled
- The individual does not have primary CNS lymphoma or malignancy
- The individual does not have a history of prior CAR T-cell therapy or prior gene therapy

Pediatric B-Cell Precursor Acute Lymphoblastic Leukemia

Tisagenlecleucel (Kymriah), as a single-agent therapy, is considered medically necessary and, therefore, covered for the autologous treatment of R/R pediatric B-ALL when administered at healthcare facilities enrolled in the FDA REMS and **all** of the following criteria are met:

- Confirmed diagnosis of CD19-positive B-ALL with morphologic bone marrow tumor involvement (five percent or greater lymphoblasts) in individuals 18 years and younger and **one** of the following subtypes:
 - BCR::ABL1-negative (formerly called Ph-negative) disease and refractory or two or more relapses
 - BCR::ABL1-positive (formerly called Ph-positive) disease and TKI (e.g., bosutinib, dasatinib, imatinib, nilotinib, ponatinib) intolerant or refractory
 - BCR::ABL1-positive (formerly called Ph-positive) disease and relapse after HSCT
- The individual does not have **any** of the following:

- Concomitant genetic syndromes associated with bone marrow failure states (e.g., Fanconi anemia; Kostmann syndrome; Shwachman-Diamond syndrome; any other bone marrow syndrome)
- Burkitt lymphoma/leukemia
- Grade 2 to 4 GVHD
- The individual does not have clinically significant active systemic infection or inflammatory disorder including, but not limited to, hepatitis B; hepatitis C; HIV infection; presence of fungal, bacterial, viral, or other infection that is uncontrolled
- The individual does not have primary CNS lymphoma or malignancy
- The individual does not have a history of prior CAR T-cell therapy or prior gene therapy

B-Cell Lymphomas

Diffuse large B-cell lymphoma, high-grade B-cell lymphoma, acquired immunodeficiency syndrome/human immunodeficiency virus-related diffuse large B-cell lymphoma, primary effusion lymphoma, human herpesvirus 8-positive diffuse large B-cell lymphoma

Tisagenlecleucel (Kymriah) is considered medically necessary and, therefore, covered for the autologous treatment of R/R DLBCL (tisagenlecleucel [Kymriah] is not FDA approved for R/R primary mediastinal large BCL); R/R high-grade BCL with MYC rearrangement plus rearrangement of BCL2, BCL6, or both genes (double- or triple-hit lymphoma); R/R AIDS/HIV-related DLBCL; R/R primary effusion lymphoma; or R/R HHV8-positive DLBCL, not otherwise specified when administered at healthcare facilities enrolled in the FDA REMS, and **all** of the following criteria are met:

- Diagnosis of one of the above types of R/R BCLs
- Used as **one** of the following:
 - Third-line and subsequent therapy as additional therapy for R/R disease greater than 12 months after completion of first-line therapy in individuals who have partial response following second-line therapy
 - Third-line and subsequent therapy as treatment (if anti-CD19 CAR T-cell therapy [e.g., axicabtagene ciloleucel {Yescarta}, brexucabtagene autoleucel {Tecartus}, lisocabtagene maraleucel {Breyanzi}, tisagenlecleucel {Kymriah}] was not previously given) of disease in second relapse or greater in individuals with partial response, no response, or progressive disease following therapy for R/R disease (NCCN preferred)
- The individual does not have clinically significant active systemic infection or inflammatory disorder including, but not limited to, hepatitis B; hepatitis C; HIV infection; presence of fungal, bacterial, viral, or other infection that is uncontrolled
- The individual does not have primary CNS lymphoma or malignancy
- The individual does not have a history of prior CAR T-cell therapy or prior gene therapy
- The individual is 18 years or older at the time of infusion

Histologic transformation of indolent lymphomas (e.g., follicular lymphoma, nodal marginal zone lymphoma) to diffuse large B-cell lymphoma

Tisagenlecleucel (Kymriah) is considered medically necessary and, therefore, covered for the autologous treatment of R/R histologic transformation of indolent lymphomas (e.g., FL, nodal

MZL) to DLBCL when administered at healthcare facilities enrolled in the FDA REMS, and **all** of the following criteria are met:

- Diagnosis of one of the above types of R/R BCLs
- Used as third-line and subsequent therapy (if anti-CD19 CAR T-cell therapy [e.g., axicabtagene ciloleucel {Yescarta}, brexucabtagene autoleucel {Tecartus}, lisocabtagene maraleucel {Breyanzi}, tisagenlecleucel {Kymriah}] was not previously given) in individuals who are candidates for additional therapy and have received multiple lines of prior therapies including two or more chemoimmunotherapy regimens for indolent or transformed disease (individuals should have received at least one anthracycline [i.e., doxorubicin] or anthracenedione [e.g., mitoxantrone]-based regimen, unless contraindicated) (NCCN preferred)
- The individual does not have clinically significant active systemic infection or inflammatory disorder including, but not limited to, hepatitis B; hepatitis C; HIV infection; presence of fungal, bacterial, viral, or other infection that is uncontrolled
- The individual does not have primary CNS lymphoma or malignancy
- The individual does not have a history of prior CAR T-cell therapy or prior gene therapy
- The individual is 18 years or older at the time of infusion

Monomorphic post-transplant lymphoproliferative disorders (B-cell type)

Tisagenlecleucel (Kymriah) is considered medically necessary and, therefore, covered for the autologous treatment of R/R monomorphic PTLD (B-cell type) when administered at healthcare facilities enrolled in the FDA REMS, and **all** of the following criteria are met:

- Diagnosis of R/R monomorphic PTLD (B-cell type)
- Used as **one** of the following:
 - Third-line and subsequent therapy as additional therapy for R/R disease greater than 12 months after completion of initial treatment with chemoimmunotherapy in individuals who have partial response following second-line chemoimmunotherapy
 - Third-line and subsequent therapy as treatment (if anti-CD19 CAR T-cell therapy [e.g., axicabtagene ciloleucel {Yescarta}, brexucabtagene autoleucel {Tecartus}, lisocabtagene maraleucel {Breyanzi}, tisagenlecleucel {Kymriah}] not previously given) of disease in second relapse or greater in individuals with partial response, no response, or progressive disease following therapy for R/R disease (NCCN preferred)
- The individual does not have clinically significant active systemic infection or inflammatory disorder including, but not limited to, hepatitis B; hepatitis C; HIV infection; presence of fungal, bacterial, viral, or other infection that is uncontrolled
- The individual does not have primary CNS lymphoma or malignancy
- The individual does not have a history of prior CAR T-cell therapy or prior gene therapy
- The individual is 18 years or older at the time of infusion

Follicular lymphoma (grade 1 to 2)

Tisagenlecleucel (Kymriah) is considered medically necessary and, therefore, covered for the

autologous treatment of R/R FL (grade 1 to 2) when administered at healthcare facilities enrolled in the FDA REMS, and **all** of the following criteria are met:

- Diagnosis of R/R FL (grade 1 to 2)
- Used as third-line and subsequent therapy (if not previously given) for partial response, no response, relapsed, or progressive disease in individuals with indications for treatment after two or more prior chemoimmunotherapy regimens (NCCN preferred)
- The individual does not have evidence of histologic transformation
- The individual does not have clinically significant active systemic infection or inflammatory disorder including, but not limited to, hepatitis B; hepatitis C; HIV infection; presence of fungal, bacterial, viral, or other infection that is uncontrolled
- The individual does not have primary CNS lymphoma or malignancy
- The individual does not have a history of prior CAR T-cell therapy or prior gene therapy
- The individual is 18 years or older at the time of infusion

Duration of authorization: 12 months

Version Effective Date: 02/24/2025

Title: Coagulation Factors

MEDICALLY NECESSARY:

HEMOPHILIA A (FACTOR VIII DEFICIENCY)

The following coagulation factors are considered medically necessary and, therefore, covered for the prevention and/or treatment of bleeding episodes in individuals with hemophilia A (factor VIII deficiency):

- Human preparations: Alphanate, Koate-DVI, Hemofil M, Humate-P, and Wilate
- Recombinant preparations: Advate, Adynovate, AfstylA, Altuviiio, Eloctate, Esperoct, Jivi, Kogenate FS, Kovaltry, Novoeight, Nuwiiq, Recombinate, and Xyntha/Xyntha Solofuse
- Human monoclonal antibody: Hemlibra, Hymoviz

HEMOPHILIA B (FACTOR IX DEFICIENCY)

The following coagulation factors are considered medically necessary and, therefore, covered for the prevention and/or treatment of bleeding episodes in individuals with hemophilia B (factor IX deficiency):

- Human preparations: Alphanine SD, Profilnine
- Recombinant preparations: Alprolix, BeneFIX, Idelvion, Ixinity, Rebinyn, and Rixubis
- Human monoclonal antibody: Hymoviz

HEMOPHILIA C (FACTOR XI DEFICIENCY)

Factor XI concentrates are not currently available in the United States.

HEMOPHILIA WITH INHIBITORS TO FACTORS VIII OR IX

The following coagulation factors are considered medically necessary and, therefore, covered for the prevention and/or treatment of bleeding episodes in individuals with hemophilia with inhibitors to factors VIII or IX:

- Human and recombinant factors VIII or IX (see hemophilia A and B above)
- FEIBA (human plasma–derived activated prothrombin complex concentrate [APCC])
- Recombinant activated coagulation factor VIIa (e.g., NovoSevenRT, Sevenfact)
- Human monoclonal antibody (e.g., emicizumab-kxwh [Hemlibra]) for hemophilia with inhibitors to factor VIII

FACTOR I DEFICIENCY, ACQUIRED

Fibryga (fibrinogen concentrate [Human]) is considered medically necessary and, therefore, covered for the treatment of bleeding episodes in individuals with acquired fibrinogen deficiency (AFD).

FACTOR I DEFICIENCY, CONGENITAL

Fibryga and RiaSTAP (fibrinogen concentrate [Human]) are considered medically necessary and, therefore, covered for the treatment of bleeding episodes in individuals with congenital fibrinogen deficiency, including afibrinogenemia and hypofibrinogenemia. **NOTE:** See EXPERIMENTAL/INVESTIGATIONAL section regarding dysfibrinogenemia.

FACTOR VII DEFICIENCY, CONGENITAL

NovoSeven RT (recombinant-activated coagulation factor VIIa) is considered medically necessary and, therefore, covered for the prevention and/or treatment of bleeding episodes in individuals with congenital factor VII deficiency.

FACTOR VIII DEFICIENCY, ACQUIRED

The following coagulation factors are considered medically necessary and, therefore, covered for the prevention and/or treatment of bleeding episodes in individuals with acquired factor VIII deficiency:

- Factor VIII concentrates, including Obizur
- Alphanate (antihemophilic factor VIII/von Willebrand factor complex [human])
- NovoSeven RT (recombinant-activated coagulation factor VIIa)
- FEIBA (human plasma–derived APCC)

FACTOR X DEFICIENCY, ACQUIRED OR CONGENITAL

Coagadex is considered medically necessary and, therefore, covered for the prevention and/or treatment of bleeding episodes in individuals with factor X deficiency

FACTOR XIII DEFICIENCY, ACQUIRED OR CONGENITAL

The following coagulation factors are considered medically necessary and, therefore, covered for the prevention and/or treatment of bleeding episodes in individuals with acquired or congenital factor XIII deficiency:

- Corifact (factor XIII concentrate [Human])
- Tretten (factor XIII A-subunit [Recombinant])

GLANZMANN'S THROMBASTHENIA (GLYCOPROTEIN COMPLEX IIb/IIIa DEFICIENCY)

NovoSeven RT (recombinant-activated coagulation factor VIIa) is considered medically necessary and, therefore, covered for the prevention and/or treatment of bleeding episodes in individuals with Glanzmann's thrombasthenia with refractoriness to platelet transfusions, with or without antibodies to platelets.

VON WILLEBRAND DISEASE

The following coagulation factors are considered medically necessary and, therefore, covered for the prevention and/or treatment of bleeding episodes in individuals with von Willebrand disease when the use of desmopressin (1-desamino-8-D-arginine vasopressin [DDAVP]) is known or suspected to be ineffective or contraindicated:

- Human preparations: Alphanate, Humate-P, Wilate
- Recombinant preparation: Vonvendi

Duration of authorization: 12 months

Version Effective Date: 04/01/2025

Title: Collagenase clostridium histolyticum (Xiaflex[®]), collagenase clostridium histolyticum-aaes (Qwo[®])

MEDICALLY NECESSARY:

COLLAGENASE CLOSTRIDIUM HISTOLYTICUM (XIAFLEX)

Dupuytren's Contracture with a Palpable Cord

Collagenase clostridium histolyticum (Xiaflex) injection is considered medically necessary and, therefore, covered for the treatment of adult individuals with a diagnosis of Dupuytren's contracture with a palpable cord when all of the following criteria are met:

- The individual has a finger flexion contracture with a palpable cord in a metacarpophalangeal joint or a proximal interphalangeal joint.
- The contracture is at least 20 degrees.
- The individual had a positive tabletop test, defined as the inability to simultaneously place the affected finger(s) and palm flat against a table.

Peyronie's Disease

Collagenase clostridium histolyticum (Xiaflex) injection is considered medically necessary and, therefore, covered for the treatment of adult individuals with a diagnosis of Peyronie's disease when all of the following criteria are met:

- The individual has a palpable plaque inside the penis.
- The individual has curvature deformity of at least 30 degrees.
- The individual is experiencing pain or sexual dysfunction.

Duration of authorization: 12 months

Version Effective Date: 05/28/2025

Title: Coverage of Anticancer Prescription Oral and Injectable Drugs and Biologics and Supportive Agents

ORAL ANTICANCER DRUGS AND BIOLOGICS

When services can be administered in various settings, the Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition. This decision is based on the member's current medical condition and any required monitoring or additional services that may coincide with the delivery of this service.

- **For members who have prescription drug coverage:** Members who have a pharmacy benefit and prescription drug coverage through the Company will receive coverage for prescription oral anticancer drugs and biologics in accordance with the applicable pharmacy policies administered through the member's pharmacy benefit.
- **For members who do not have prescription drug coverage:** If a member does not have prescription drug coverage through the Company, coverage of prescription oral anticancer drugs and biologics will be facilitated through the **Company's Direct Ship Injectables Program** under the member's medical benefits. Prescription oral anticancer drugs and biologics are covered under the member's medical benefits only when the member does not have prescription drug coverage through the Company.

A prescription oral anticancer drug or biologic is considered medically necessary and, therefore, covered as provided under the Company's medical benefit when the member has no pharmacy benefit through the Company and the prescription oral anticancer drug or biologic meets one of the following criteria:

- The drug or biologic is prescribed for an FDA-approved use that is based on reliable evidence demonstrating a positive effect on health outcomes.
- The drug or biologic is prescribed for an off-label use when either of the following criteria are met:
 - The drug or biologic and its indication, dosage, frequency, or route of administration, etc., are recommended in the section below, titled Compendia for Oncologic Uses.
 - The drug or biologic and its indication, dosage, frequency, or route of administration, etc., are recommended in the section below titled, Published Clinical Research.

Compendia for Oncologic Uses (Anticancer Chemotherapy)

For coverage of an anticancer chemotherapy regimen, the off-label use is considered medically necessary and, therefore, covered when one of the following criteria are met:

- The narrative text in American Hospital Formulary Service–Drug Information (AHFS-DI®) is supportive of the use.
- The use is classified as Category 1 or 2A by National Comprehensive Cancer Network (NCCN®) Drugs and Biologics Compendium™.
- The use is classified as Class I or Class IIa in Micromedex® DrugDex® Compendium.

An anticancer chemotherapy regimen is considered experimental/investigational even when above criteria have been met, and when one of the following exists:

- The use is classified as Category 3 by NCCN® or Class III in Micromedex® DrugDex®.
- The narrative text in AHFS-DI® is not supportive of the use.
- Any of the compendia listed above state that the prescription drug and/or biologic is not indicated, is unsupported, is not recommended, or equivalent terms are used regarding the prescription drug and/or biologic.

When a compendia is considered neither supportive nor nonsupportive (i.e., Category 2B in NCCN, Class IIb in Micromedex® DrugDex®, or an absence of narrative text or evidence classification from any Company-recognized compendia), please refer to the Published Clinical Research section.

PUBLISHED CLINICAL RESEARCH

For an off-label use to be supported by published clinical research, **all** of the following criteria must be met:

- The prescription oral anticancer drug or biologic must have been studied in at least two clinical trials conducted at different centers, and the results must have been published in national or international peer-reviewed journals with an editorial committee composed of physicians. Peer-reviewed medical literature includes scientific, medical, and pharmaceutical publications. It does not include in-house publications of pharmaceutical manufacturing companies or abstracts (including meeting abstracts).
 - A use is considered supported by clinical research when it appears in at least two Phase III clinical trials that have definitively demonstrated its safety and effectiveness as an appropriate medical treatment for the condition. If no Phase III trial evidence is available, at least two Phase II clinical trials with reasonably large patient samples showing consistent results of safety and efficacy may be considered in certain instances (e.g., in rare diseases in which a Phase III study might be difficult to complete in a reasonable period of time after completion of the Phase II studies, or when overwhelmingly good evidence of safety and effectiveness is noted in the Phase II studies).
- Reliable evidence must demonstrate that the proposed off-label use for the specified medical condition is safe and effective and that the beneficial effects of the treatment outweigh its risks.
- In determining whether there is supportive clinical evidence for a particular use of a prescription drug or biologic, the Company considers the quality of the evidence in published, peer-reviewed medical literature. Among other things, such consideration involves the assessment of the following:
 - The prevalence and life history of the disease when evaluating the adequacy of the number of subjects and the response rate.
 - The effect on the individual's well-being and other responses to therapy that indicate effectiveness (e.g., reduction in mortality, morbidity, and signs and symptoms).
 - Whether the clinical characteristics of the beneficiary and the use are adequately represented in the published evidence.
 - Whether the study is appropriate to address the clinical question, such as:

- If the study design is appropriate to address investigative questions (e.g., in some clinical studies, it may be unnecessary or not feasible to use randomization, double-blind trials, placebos, or crossover).
- If nonrandomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
- Generally, case reports are considered uncontrolled, are based on anecdotal information, and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
- The off-label use is supported by published clinical research, and the results have been published in major peer-reviewed medical journals such as, but not limited to:

<i>American Journal of Medicine</i>	<i>Gynecologic Oncology</i>
<i>Annals of Internal Medicine</i>	<i>International Journal of Radiation,</i>
<i>Annals of Oncology</i>	<i>Oncology, Biology, and Physics</i>
<i>Annals of Surgical Oncology</i>	<i>Journal of Clinical Oncology</i>
<i>Biology of Blood and Marrow</i>	<i>Journal of the National Cancer Institute</i>
<i>Transplantation</i>	<i>Journal of the National Comprehensive</i>
<i>Blood</i>	<i>Cancer Network (NCCN®)</i>
<i>Bone Marrow Transplantation</i>	<i>Journal of Urology</i>
<i>British Journal of Cancer</i>	<i>Lancet</i>
<i>British Journal of Hematology</i>	<i>Lancet Oncology</i>
<i>British Medical Journal</i>	<i>Leukemia</i>
<i>Cancer</i>	<i>Radiation Oncology</i>
<i>Clinical Cancer Research</i>	<i>Journal of the American Medical</i>
<i>Drugs</i>	<i>Association</i>
<i>European Journal of Cancer</i>	<i>New England Journal of Medicine</i>

Duration of authorization: 12 months

Version Effective Date: 04/30/2025

Title: crizanlizumab-tmca (Adakveo®)

MEDICALLY NECESSARY:

INITIAL THERAPY

Crizanlizumab-tmca (Adakveo®) is considered medically necessary and, therefore, covered to reduce the frequency of vaso-occlusive crises (VOCs) in individuals aged 16 years or older with sickle cell disease, when used as monotherapy or concomitantly with hydroxyurea, when all of the following criteria, including Dosing and Frequency, are met:

- Individual has a documented diagnosis of sickle cell disease confirmed by one of the following tests:
 - Molecular genetic testing that reveals pathogenic variation(s) in the *HBB* gene causing sickle cell disease
 - Hemoglobin electrophoresis
- There is documentation of two or more vaso-occlusive crises (VOCs) in the past 12 months that required a visit to a medical facility and/or healthcare professional and receipt of treatments for condition such as acute pain episodes, acute chest syndrome, hepatic or splenic sequestration, priapism
- Individual has documentation of failure, contraindication, or intolerance to hydroxyurea
- Individual is not concomitantly receiving voxelotor (Oxbryta®)
- There are no long-term transfusion therapies planned
- Dosing and Frequency: 5 mg/kg as an intravenous (IV) infusion at Week 0, 2, and every four weeks thereafter

CONTINUATION THERAPY

Continuation of crizanlizumab-tmca (Adakveo®) is considered medically necessary and, therefore, covered for individuals who have demonstrated a documented reduction in the annual rate of sickle cell--related VOCs.

Duration of authorization: 12 months

Version Effective Date: 05/29/2024

Title: Crovalimab-akkz (PiaSky)

MEDICALLY NECESSARY:

PAROXYSMAL NOCTURNAL HEMOGLOBINURIA (PNH)

Crovalimab-akkz (PiaSky) is considered medically necessary and, therefore, covered for the treatment of PNH in adult and pediatric (13 years and older) individuals, when all of the following criteria are met, including dosing and frequency:

Initial Criteria

- The individual has body weight 40 kilograms or more
- Flow cytometry demonstrates one of the following:
 - At least 10% PNH type III red cells
 - Greater than 50% of glycosylphosphatidylinositol-anchored proteins (GPI-AP)–deficient polymorphonuclear (PM) cells
- The individual exhibits clinical manifestations of disease (e.g., lactate dehydrogenase [LDH] > 1.5 upper limit of normal [ULN], thrombosis, renal dysfunction, pulmonary hypertension, dysphagia)
- The individual is transfusion dependent due to PNH.
- The individual does not have unresolved *Neisseria meningitidis* infection.
- The individual is vaccinated against *N. meningitidis*, unless risk of delaying crovalimab-akkz (PiaSky) outweighs the risks of developing meningococcal infection.
- Crovalimab-akkz (PiaSky) will not be used in combination with another complement inhibitor (e.g., Empaveli, Fabhalta, Soliris, Ultomiris) for the treatment of PNH.
- Dosing and frequency for crovalimab-akkz (PiaSky)
 - 40 kg to less than 100 kg: Loading dosage, 1000 mg IV on Day 1 followed by 340 mg subQ once weekly on Days 2, 8, 15, and 22
 - 40 kg to less than 100 kg: Maintenance dosage, 680 mg subQ starting on Day 29 and administered every 4 weeks thereafter
 - 100 kg or greater: Loading dosage, 1500 mg IV on Day 1 followed by 340 mg subQ once weekly on Days 2, 8, 15, and 22
 - 100 kg or greater: Maintenance dosage, 1020 mg subQ starting on Day 29 and administered every 4 weeks thereafter

Continuation Criteria

Crovalimab-akkz (PiaSky) is considered medically necessary and, therefore, covered for continuation therapy, when documentation is provided of positive clinical response (e.g., reduction in hemolysis manifested by stabilization of hemoglobin levels and reduction in transfusions from baseline at initiation).

Duration of authorization: 12 months

Version Effective Date: 05/28/2025

Title: Daratumumab (Darzalex®), Daratumumab and Hyaluronidase-fihj (Darzalex Faspro®)

MEDICALLY NECESSARY:

Multiple Myeloma

Newly Diagnosed

Daratumumab (Darzalex) and daratumumab and hyaluronidase-fihj (Darzalex Faspro) are considered medically necessary and, therefore, covered for individuals who have been newly diagnosed with multiple myeloma, when **any** of the following criteria have been met:

- The individual is ineligible for autologous stem cell transplant, and daratumumab is used with any of the following combinations:
 - Bortezomib (Velcade), melphalan hydrochloride (Alkeran), and prednisone
 - Carfilzomib (Kyprolis), lenalidomide, and dexamethasone
 - Cyclophosphamide, bortezomib, and dexamethasone
 - Lenalidomide (Revlimid) and dexamethasone (a National Comprehensive Cancer Network [NCCN-preferred] regimen)
- The individual is eligible for autologous stem cell transplant, and daratumumab is used with any of the following combinations:
 - Bortezomib (Velcade), dexamethasone, and either lenalidomide (Revlimid) or thalidomide (Thalomid)
 - Carfilzomib (Kyprolis), lenalidomide, and dexamethasone
 - Cyclophosphamide, bortezomib, and dexamethasone

Maintenance Therapy

Daratumumab (Darzalex) and daratumumab and hyaluronidase-fihj (Darzalex Faspro) are considered medically necessary and, therefore, covered for the treatment of symptomatic multiple myeloma as a single agent or in combination with lenalidomide (for high-risk) when **any** of the following criteria have been met:

- After response to primary myeloma therapy for transplant candidates
- For response or stable disease following an autologous hematopoietic stem cell transplant (HCT)
- For response or stable disease following a tandem autologous or allogeneic HCT for high-risk individuals

Monotherapy for Relapsed, Progressive, or Refractory Disease

Daratumumab (Darzalex) and daratumumab and hyaluronidase-fihj (Darzalex Faspro) are considered medically necessary and, therefore, covered as monotherapy for the treatment of relapsed, progressive, or refractory multiple myeloma when either of the following criteria have been met:

- The individual has previously received at least three prior lines of therapy, including a proteasome inhibitor (PI)¹ AND an immunomodulatory agent²
- The individual is double-refractory to a PI¹ AND an immunomodulatory agent²

Combination Therapy for Relapsed, Progressive, or Refractory Disease

Daratumumab (Darzalex) and daratumumab and hyaluronidase-fihj (Darzalex Faspro) are considered medically necessary and, therefore, covered for the treatment of relapsed, progressive, or refractory multiple myeloma when any of the following criteria are met:

- At least one prior therapy and daratumumab is used in combination with any of the following:
 - Bortezomib (Velcade) and dexamethasone (an NCCN-preferred regimen)
 - Lenalidomide (Revlimid) and dexamethasone (an NCCN-preferred regimen), if ineligible for autologous stem cell transplant
 - Carfilzomib (Kyprolis) and dexamethasone (an NCCN-preferred regimen), cyclophosphamide, bortezomib, and dexamethasone
 - Pomalidomide and dexamethasone (an NCCN-preferred regimen) when prior therapy included lenalidomide and a PI¹
 - Cyclophosphamide, bortezomib, and dexamethasone
 - Selinexor (Xpovio) and dexamethasone
 - Ventoclax and dexamethasone for individuals with t(11:14)
- For disease relapse after 6 months following primary induction therapy with the same regimen in combination with lenalidomide and dexamethasone for non-transplant candidates (NCCN preferred regimen) in combination with cyclophosphamide, bortezomib, and dexamethasone (useful in certain circumstances for transplant candidates when used as primary therapy).

¹Examples of proteasome inhibitors (PI) include bortezomib (Velcade), carfilzomib (Kyprolis) and ixazomib (Ninlaro)

²Examples of immunomodulatory agents include lenalidomide (Revlimid), pomalidomide (Pomalyst), and thalidomide (Thalomid)

Systemic Light Chain Amyloidosis

Daratumumab (Darzalex) and daratumumab and hyaluronidase-fihj (Darzalex Faspro) are considered medically necessary and, therefore, covered for the treatment of relapsed or refractory disease as a single agent.

Daratumumab (Darzalex) daratumumab and hyaluronidase-fihj (Darzalex Faspro) is considered medically necessary and, therefore, covered as the NCCN-preferred treatment for newly diagnosed disease, or relapsed/refractory disease as a repeat of initial therapy if relapse-free for several years

- As a single agent OR as part of dose modified daratumumab and hyaluronidase-fihj (Darzalex Faspro), cyclophosphamide, bortezomib and dexamethasone regimen for stage IIIb if no significant neuropathy.
- As a single agent for all stages if significant neuropathy
- In combination with bortezomib, cyclophosphamide, and dexamethasone (up to 30 months total from start of therapy) (Darzalex only)

- In combination with bortezomib, cyclophosphamide, and dexamethasone (up to 30 months total from start of therapy) for stage I-IIIa if no significant neuropathy (Darzalex Faspro only)

Pediatric Acute Lymphoblastic Leukemia

Daratumumab (Darzalex) is considered medically necessary and, therefore, covered for the treatment of relapsed/refractory T-ALL as a component of daratumumab-containing regimen (daratumumab, vincristine, pegaspargase or calaspargase, doxorubicin, and prednisone or dexamethasone).

CONTINUATION THERAPY

Daratumumab (Darzalex) and daratumumab and hyaluronidase-fihj (Darzalex Faspro) are considered medically necessary and, therefore, covered for continuation therapy when the individual meets both of the following criteria:

- Individual has met the medical necessity criteria for Initial Therapy
- There is documentation of no evidence of unacceptable toxicity or disease progression while on the current regimen.

Duration of authorization: 12 months

Version Effective Date: 08/12/2024

Title: Delandistrogene moxeparvovec (delandistrogene moxeparvovec-rokl; Elevidys®)

Policy

Coverage is subject to the terms, conditions, and limitations of the member's contract.

BENEFIT EXCLUSION

Delandistrogene moxeparvovec-rokl (Elevidys®) is a benefit contract exclusion for most plans, and, therefore, not eligible for reimbursement consideration. Individual benefits must be verified.

Duration of authorization: 12 months

Version Effective Date: 05/28/2025

Title: Denosumab (Prolia®, Xgeva®) and related biosimilars, and Romosozumab-aqqg (Evenity®)

MEDICALLY NECESSARY:

DENOSUMAB (PROLIA) AND RELATED BIOSIMILARS

Initial Therapy

Denosumab (Prolia) and related biosimilars, administered subcutaneously by a professional provider, are considered medically necessary and, therefore, covered for the following indications:

- Treatment of postmenopausal individuals with a documented diagnosis of osteoporosis (defined as T-score less than or equal to -2.5 for osteoporosis or documented history of an osteoporotic non-collision fracture [e.g., vertebral, hip, nonvertebral]) when **EITHER** of the criteria listed below is met:
 - The individual has multiple risk factors for fracture (e.g., endocrine disorders, gastrointestinal disorders, use of medications associated with low bone mass or bone loss [e.g., daily systemic glucocorticoids and expected to continue for at least three months])
 - The individual has or has had **ONE** of the following:
 - Documented intolerance to at least one other osteoporosis medicine (e.g., oral or injectable bisphosphonates, estrogens) due to side effects
 - Documented inadequate response from at least one other available osteoporosis medicine (e.g., oral or injectable bisphosphonates, estrogens) after a trial of 12 months
 - A severely deteriorated condition indicating that the osteoporosis is so significant that a trial of bisphosphonates is not medically warranted (e.g., very low T-score [less than -3.0], high risk for falls/history of injurious falls, very high fracture probability by fracture risk assessment tool [FRAX] [e.g., major osteoporosis fracture >30 percent, hip fracture >4.5 percent])
 - Documented moderate to severe renal insufficiency (glomerular filtration rate [GFR] 30 to 35 mL/min or less)
- Treatment of males (genotypic males) 50 years of age and older with a documented diagnosis of osteoporosis (defined as T-score less than or equal to -2.5 for osteoporosis or documented history of an osteoporotic non-collision fracture [e.g., vertebral, hip, nonvertebral]) when **EITHER** of the criteria listed below are met:
 - The individual has multiple risk factors for fracture (e.g., endocrine disorders, gastrointestinal disorders, use of medications associated with low bone mass or bone loss [e.g., daily systemic glucocorticoids and expected to continue for at least three months])
 - The individual has or has had **ONE** of the following:
 - Documented intolerance to at least one other osteoporosis medicine (e.g., oral or injectable bisphosphonates) due to side effects

- Documented inadequate response from at least one other available osteoporosis medicine (e.g., oral or injectable bisphosphonates) after a trial of 12 months
 - A severely deteriorated condition indicating that the osteoporosis is so significant that a trial of bisphosphonates is not medically warranted (e.g., very low T-score [less than -3.0], high risk for falls/history of injurious falls, very high fracture probability by FRAX [e.g., major osteoporosis fracture >30 percent, hip fracture >4.5 percent])
 - Documented moderate to severe renal insufficiency (glomerular filtration rate [GFR] 30 to 35 mL/min or less)
- Treatment of individuals less than 50 years of age with documented diagnosis of glucocorticoid-induced osteoporosis **AND** history of an osteoporotic non-collision fracture contributing to high risk for fracture when **ALL** of the following criteria are met:
 - The individual is initiating or continuing daily systemic glucocorticoids and expected to continue for at least three months
 - The individual is not pregnant and is using effective contraception during therapy
 - The individual has or has had **ONE** of the following:
 - Documented intolerance to at least one other osteoporosis medicine (e.g., oral or injectable bisphosphonates, estrogens) due to side effects
 - Documented inadequate response from at least one other available osteoporosis medicine (e.g., oral or injectable bisphosphonates, estrogens) after a trial of 12 months
 - A severely deteriorated condition indicating that the osteoporosis is so significant that a trial of bisphosphonates is not medically warranted (e.g., very low T-score [less than -3.0], high risk for falls/history of injurious falls, very high fracture probability by FRAX [e.g., major osteoporosis fracture >30 percent, hip fracture >4.5 percent])
 - Documented moderate to severe renal insufficiency (glomerular filtration rate [GFR] 30 to 35 mL/min or less)
- Treatment of osteopenia (defined as T-score less than -1.0, but greater than -2.5), when the individual meets **EITHER** of the following criteria:
 - Receiving adjuvant aromatase inhibitor therapy for breast cancer (either invasive [with lobular, mixed, metaplastic, ductal/NST, micropapillary, pure tubular, pure mucinous, pure cribriform, encapsulated or solid papillary carcinoma, other rare forms, adenoid cystic and other salivary carcinomas, secretory carcinoma, rare low-grade forms of metaplastic carcinoma histology, ductal carcinoma in situ] or inflammatory) (assure that the individual is not pregnant and is using effective contraception during therapy)
 - Receiving androgen deprivation therapy for nonmetastatic prostate cancer
- For males (genotypic males) 50 years of age and older or postmenopausal individuals with a diagnosis of osteopenia (defined as T-score less than -1.0 but greater than -2.5) when the individual meets **BOTH** of the following criteria:
 - The individual has or has had **ONE** of the following:

- Documented intolerance to at least one other osteoporosis medicine (e.g., oral or injectable bisphosphonates, estrogens) due to side effects
- Documented inadequate response from at least one other available osteoporosis medicine (e.g., oral or injectable bisphosphonates, estrogens) after a trial of 12 months
- Documented moderate to severe renal insufficiency (glomerular filtration rate [GFR] 30 to 35 mL/min or less) not receiving dialysis or diagnosed with stage 5 kidney disease
- The individual has **ONE** of the following:
 - US-adapted World Health Organization (WHO) 10-year probability of a hip fracture based on the Fracture Risk Assessment tool (FRAX) assessment is three percent or more
 - WHO 10-year fracture probability of any major osteoporosis-related fracture based on the FRAX assessment is 20 percent or more

Continuation Therapy

Denosumab (Prolia) and related biosimilars are considered medically necessary and, therefore, covered for continuation therapy unless the individual has a documented intolerance, contraindication, or nonresponse to the drug.

ROMOSUZUMAB-AQQG (EVENITY)

Romosozumab-aqqg (Evenity), administered subcutaneously by a professional provider, for a limited duration of 12 monthly doses is considered medically necessary and, therefore, covered for the following indications:

- Treatment of postmenopausal individuals with a documented diagnosis of osteoporosis (defined as T-score less than or equal to -2.50 for osteoporosis or documented history of an osteoporotic non-collision fracture [e.g., vertebral, hip, nonvertebral]) when **BOTH** of the criteria listed below are met:
 - The individual has multiple risk factors for fracture (e.g., endocrine disorders, gastrointestinal disorders, use of medications associated with low bone mass or bone loss [e.g., daily systemic glucocorticoids and expected to continue for at least three months])
 - The individual has or has had documented intolerance due to side effects, or inadequate response after a trial of 12 months to Receptor Activator of Nuclear factor Kappa-B (RANK) ligand inhibitor (e.g., denosumab [Prolia] and related biosimilars)
- For individuals with a severely deteriorated condition indicating that the osteoporosis is so significant (i.e., T-score less than -3.5 or a T-score less than -2.5 with a history of fragility fractures) that a trial of bisphosphonates and RANK ligand inhibitor (e.g., denosumab [Prolia] and related biosimilars) is not medically warranted.

Romosozumab-aqqg (Evenity) is not recommended for individuals with a history of a myocardial infarction or stroke within the preceding year; (consider benefit versus risk in individuals with other cardiovascular risk factors).

Note:

The anabolic effect of romosozumab wanes after 12 monthly doses of therapy. Therefore, the duration of romosozumab-aqqg (Evenity) use is limited to 12 monthly doses. If osteoporosis therapy remains warranted after medically necessary romosozumab-aqqg (Evenity), continued therapy with an anti-resorptive agent (e.g., denosumab [Prolia] and related biosimilars, alendronate [Fosamax, Binosto]) should be considered.

DENOSUMAB (XGEVA) AND RELATED BIOSIMILARS

Denosumab (Xgeva) and related biosimilars, administered subcutaneously by a professional provider, are considered medically necessary and, therefore, covered for the following indications (assure that the individual is not pregnant and is using effective contraception during therapy):

- Prevention of skeletal-related events (i.e., pathologic fracture, need for radiation therapy to bone, need for surgery to bone, or spinal cord compression) in individuals with bone metastases from solid tumors. These include, but are not limited to, the following malignancy-related conditions:
 - Invasive (with lobular, mixed, metaplastic, ductal/NST, micropapillary, pure tubular, pure mucinous, pure cribriform, encapsulated or solid papillary carcinoma, other rare forms, adenoid cystic and other salivary carcinomas, secretory carcinoma, rare low-grade forms of metaplastic carcinoma histology) or inflammatory breast cancer:
 - Used with calcium and vitamin D supplementation in addition to chemotherapy or endocrine therapy for bone metastases in individuals with expected survival of three months or greater and adequate renal function
 - Non-small cell lung cancer (with squamous cell carcinoma, adenocarcinoma [with mixed subtypes], or large cell carcinoma histology):
 - Supportive therapy in individuals with bony metastases
 - Prostate cancer:
 - Individuals with bone metastases from castration-resistant prostate cancer (metastatic prostate cancer that has stopped responding to androgen deprivation therapy and continues to grow) with creatinine clearance greater than 30 mL/min (National Comprehensive Cancer Network [NCCN] preferred)
 - Thyroid cancer:
 - Individuals with bone metastases from any of the following thyroid cancer types: follicular, Hurthle cell/oncocytic, medullary, papillary carcinoma
 - Palliative care for bone metastases in individuals with anaplastic carcinoma
 - Kidney cancer (with either clear cell or non-clear cell histology):
 - As a component of best supportive care for individuals with bony metastases

- Prevention of skeletal-related events (i.e., pathologic fracture, need for radiation therapy to bone, need for surgery to bone, or spinal cord compression) in individuals with multiple myeloma
 - Used in combination with primary myeloma therapy. NCCN preferred agent in individuals with renal insufficiency
- Treatment of adult and skeletally mature (i.e., at least one mature long bone [e.g., closed epiphyseal growth plate of the humerus]) adolescent individuals with a giant cell tumor of the bone (GCTB) in the following circumstances:
 - When the GCTB is unresectable or where surgical resection is likely to result in severe morbidity
 - Treatment as a single agent (NCCN preferred) or combined with serial embolization, (NCCN preferred) and/or radiation therapy for resectable disease with unacceptable morbidity and/or unresectable axial lesions for individuals with localized disease, metastases at presentation, or disease recurrence
 - Treatment as a single agent (NCCN preferred) for unresectable metastatic disease at presentation, unresectable metastatic recurrence, or considered prior to surgery for resectable local recurrence
- Treatment of individuals with hypercalcemia of malignancy (i.e., albumin-corrected serum calcium level greater than 12.5 mg/dL [3.1 mmol/L]) refractory to bisphosphonate therapy
- Treatment of individuals with systemic mastocytosis as a second-line therapy for osteopenia/osteoporosis in individuals with bone pain not responding to bisphosphonates or for individuals who are not candidates for bisphosphonates because of renal insufficiency.

Duration of authorization: 12 months

Version Effective Date: 02/24/2025

Title: Denosumab (Prolia®, Xgeva®) and related biosimilars, and Romosozumab-aqqg (Evenity®)

MEDICALLY NECESSARY:

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

DENOSUMAB (PROLIA) AND DENOSUMAB-BBDZ (JUBBONTI) ARE MEDICALLY NECESSARY WHEN REPORTED WITH ANY OF THE FOLLOWING DIAGNOSIS CODES:

M80.011A Age-related osteoporosis with current pathological fracture, right pelvis, initial encounter for fracture

M80.011D Age-related osteoporosis with current pathological fracture, right pelvis, subsequent encounter for fracture with routine healing

M80.011G Age-related osteoporosis with current pathological fracture, right pelvis, subsequent encounter for fracture with delayed healing

M80.011K Age-related osteoporosis with current pathological fracture, right pelvis, subsequent encounter for fracture with nonunion

M80.011P Age-related osteoporosis with current pathological fracture, right pelvis, subsequent encounter for fracture with malunion

M80.011S Age-related osteoporosis with current pathological fracture, right pelvis, sequela

M80.012A Age-related osteoporosis with current pathological fracture, left pelvis, initial encounter for fracture

M80.012D Age-related osteoporosis with current pathological fracture, left pelvis, subsequent encounter for fracture with routine healing

M80.012G Age-related osteoporosis with current pathological fracture, left pelvis, subsequent encounter for fracture with delayed healing

M80.012K Age-related osteoporosis with current pathological fracture, left pelvis, subsequent encounter for fracture with nonunion

M80.012P Age-related osteoporosis with current pathological fracture, left pelvis, subsequent encounter for fracture with malunion

M80.012S Age-related osteoporosis with current pathological fracture, left pelvis, sequela

M80.022A Other osteoporosis with current pathological fracture, right pelvis, initial encounter for fracture

M80.022D Other osteoporosis with current pathological fracture, right pelvis, subsequent encounter for fracture with routine healing

M80.022G Other osteoporosis with current pathological fracture, right pelvis, subsequent encounter for fracture with delayed healing

M80.022K Other osteoporosis with current pathological fracture, right pelvis, subsequent encounter for fracture with nonunion

M80.022P Other osteoporosis with current pathological fracture, right pelvis, subsequent encounter for fracture with malunion

M80.022S Other osteoporosis with current pathological fracture, right pelvis, sequela

M80.031A Other osteoporosis with current pathological fracture, left pelvis, initial encounter for fracture

M80.031D Other osteoporosis with current pathological fracture, left pelvis, subsequent encounter for fracture with routine healing

M80.031G Other osteoporosis with current pathological fracture, left pelvis, subsequent encounter for fracture with delayed healing

M80.031K Other osteoporosis with current pathological fracture, left pelvis, subsequent encounter for fracture with nonunion

M80.031P Other osteoporosis with current pathological fracture, left pelvis, subsequent encounter for fracture with malunion

M80.031S Other osteoporosis with current pathological fracture, left pelvis, sequela

M80.041A Age-related osteoporosis with current pathological fracture, other site, initial encounter for fracture

M80.041D Age-related osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with routine healing

M80.041G Age-related osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with delayed healing

M80.041K Age-related osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with nonunion

M80.041P Age-related osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with malunion

M80.041S Age-related osteoporosis with current pathological fracture, other site, sequela

M80.042A Age-related osteoporosis with current pathological fracture, right shoulder, initial encounter for fracture

M80.042D Age-related osteoporosis with current pathological fracture, right shoulder, subsequent encounter for fracture with routine healing

M80.042G Age-related osteoporosis with current pathological fracture, right shoulder, subsequent encounter for fracture with delayed healing

M80.042K Age-related osteoporosis with current pathological fracture, right shoulder, subsequent encounter for fracture with nonunion

M80.042P Age-related osteoporosis with current pathological fracture, right shoulder, subsequent encounter for fracture with malunion

M80.042S Age-related osteoporosis with current pathological fracture, right shoulder, sequela

M80.051D Age-related osteoporosis with current pathological fracture, left shoulder, initial encounter for fracture

M80.051G Age-related osteoporosis with current pathological fracture, left shoulder, subsequent encounter for fracture with routine healing

M80.051K Age-related osteoporosis with current pathological fracture, left shoulder, subsequent encounter for fracture with delayed healing

M80.051P Age-related osteoporosis with current pathological fracture, left shoulder, subsequent encounter for fracture with nonunion

M80.051S Age-related osteoporosis with current pathological fracture, left shoulder, subsequent encounter for fracture with malunion

M80.052A Age-related osteoporosis with current pathological fracture, left shoulder, sequela

M80.052D Age-related osteoporosis with current pathological fracture, right humerus, initial encounter for fracture

M80.052G Age-related osteoporosis with current pathological fracture, right humerus, subsequent encounter for fracture with routine healing

M80.052K Age-related osteoporosis with current pathological fracture, right humerus, subsequent encounter for fracture with delayed healing

M80.052P Age-related osteoporosis with current pathological fracture, right humerus, subsequent encounter for fracture with nonunion

M80.052S Age-related osteoporosis with current pathological fracture, right humerus, subsequent encounter for fracture with malunion

M80.061A Age-related osteoporosis with current pathological fracture, right humerus, sequela

M80.061D Age-related osteoporosis with current pathological fracture, left humerus, initial encounter for fracture

M80.061G Age-related osteoporosis with current pathological fracture, left humerus, subsequent encounter for fracture with routine healing

M80.061K Age-related osteoporosis with current pathological fracture, left humerus, subsequent encounter for fracture with delayed healing

M80.061P Age-related osteoporosis with current pathological fracture, left humerus, subsequent encounter for fracture with nonunion

M80.061S Age-related osteoporosis with current pathological fracture, left humerus, subsequent encounter for fracture with malunion

M80.062A Age-related osteoporosis with current pathological fracture, left humerus, sequela

M80.062D Age-related osteoporosis with current pathological fracture, right forearm, initial encounter for fracture

M80.062G Age-related osteoporosis with current pathological fracture, right forearm, subsequent encounter for fracture with routine healing

M80.062K Age-related osteoporosis with current pathological fracture, right forearm, subsequent encounter for fracture with delayed healing

M80.062P Age-related osteoporosis with current pathological fracture, right forearm, subsequent encounter for fracture with nonunion

M80.062S Age-related osteoporosis with current pathological fracture, right forearm, subsequent encounter for fracture with malunion

M80.071A Age-related osteoporosis with current pathological fracture, right forearm, sequela

M80.071D Age-related osteoporosis with current pathological fracture, left forearm, initial encounter for fracture

M80.071G Age-related osteoporosis with current pathological fracture, left forearm, subsequent encounter for fracture with routine healing

M80.071K Age-related osteoporosis with current pathological fracture, left forearm, subsequent encounter for fracture with delayed healing

M80.071P Age-related osteoporosis with current pathological fracture, left forearm, subsequent encounter for fracture with nonunion

M80.071S Age-related osteoporosis with current pathological fracture, left forearm, subsequent encounter for fracture with malunion

M80.072A Age-related osteoporosis with current pathological fracture, left forearm, sequela

M80.072D Age-related osteoporosis with current pathological fracture, right hand, initial encounter for fracture

M80.072G Age-related osteoporosis with current pathological fracture, right hand, subsequent encounter for fracture with routine healing

M80.072K Age-related osteoporosis with current pathological fracture, right hand, subsequent encounter for fracture with delayed healing

M80.072P Age-related osteoporosis with current pathological fracture, right hand, subsequent encounter for fracture with nonunion

M80.072S Age-related osteoporosis with current pathological fracture, right hand, subsequent encounter for fracture with malunion

M80.08XA Age-related osteoporosis with current pathological fracture, right hand, sequela

M80.08XD Age-related osteoporosis with current pathological fracture, left hand, initial encounter for fracture

M80.08XG Age-related osteoporosis with current pathological fracture, left hand, subsequent encounter for fracture with routine healing

M80.08XK Age-related osteoporosis with current pathological fracture, left hand, subsequent encounter for fracture with delayed healing

M80.08XP Age-related osteoporosis with current pathological fracture, left hand, subsequent encounter for fracture with nonunion

M80.08XS Age-related osteoporosis with current pathological fracture, left hand, subsequent encounter for fracture with malunion

M80.0AXA Age-related osteoporosis with current pathological fracture, left hand, sequela

M80.0AXD Age-related osteoporosis with current pathological fracture, right femur, initial encounter for fracture

M80.0AXG Age-related osteoporosis with current pathological fracture, right femur, subsequent encounter for fracture with routine healing

M80.0AXK Age-related osteoporosis with current pathological fracture, right femur, subsequent encounter for fracture with delayed healing

M80.0AXP Age-related osteoporosis with current pathological fracture, right femur, subsequent encounter for fracture with nonunion

M80.0AXS Age-related osteoporosis with current pathological fracture, right femur, subsequent encounter for fracture with malunion

M80.0B1A Age-related osteoporosis with current pathological fracture, right femur, sequela

M80.0B1D Age-related osteoporosis with current pathological fracture, left femur, initial encounter for fracture

M80.0B1G Age-related osteoporosis with current pathological fracture, left femur, subsequent encounter for fracture with routine healing

M80.0B1K Age-related osteoporosis with current pathological fracture, left femur, subsequent encounter for fracture with delayed healing

M80.0B1P Age-related osteoporosis with current pathological fracture, left femur, subsequent encounter for fracture with nonunion

M80.0B1S Age-related osteoporosis with current pathological fracture, left femur, subsequent encounter for fracture with malunion

M80.0B2A Age-related osteoporosis with current pathological fracture, left femur, sequela

M80.0B2D Age-related osteoporosis with current pathological fracture, right lower leg, initial encounter for fracture

M80.0B2G Age-related osteoporosis with current pathological fracture, right lower leg, subsequent encounter for fracture with routine healing

M80.0B2K Age-related osteoporosis with current pathological fracture, right lower leg, subsequent encounter for fracture with delayed healing

M80.0B2P Age-related osteoporosis with current pathological fracture, right lower leg, subsequent encounter for fracture with nonunion

M80.0B2S Age-related osteoporosis with current pathological fracture, right lower leg, subsequent encounter for fracture with malunion

M80.0B9A Age-related osteoporosis with current pathological fracture, right lower leg, sequela

M80.0B9D Age-related osteoporosis with current pathological fracture, left lower leg, initial encounter for fracture

M80.0B9G Age-related osteoporosis with current pathological fracture, left lower leg, subsequent encounter for fracture with routine healing

M80.0B9K Age-related osteoporosis with current pathological fracture, left lower leg, subsequent encounter for fracture with delayed healing

M80.0B9P Age-related osteoporosis with current pathological fracture, left lower leg, subsequent encounter for fracture with nonunion

M80.0B9S Age-related osteoporosis with current pathological fracture, left lower leg, subsequent encounter for fracture with malunion

M80.8AXA Age-related osteoporosis with current pathological fracture, left lower leg, sequela

M80.8AXD Age-related osteoporosis with current pathological fracture, right ankle and foot, initial encounter for fracture

M80.8AXG Age-related osteoporosis with current pathological fracture, right ankle and foot, subsequent encounter for fracture with routine healing

M80.8AXK Age-related osteoporosis with current pathological fracture, right ankle and foot, subsequent encounter for fracture with delayed healing

M80.8AXP Age-related osteoporosis with current pathological fracture, right ankle and foot, subsequent encounter for fracture with nonunion

M80.8AXS Age-related osteoporosis with current pathological fracture, right ankle and foot, subsequent encounter for fracture with malunion

M80.8B1A Age-related osteoporosis with current pathological fracture, right ankle and foot, sequela

M80.8B1D Age-related osteoporosis with current pathological fracture, left ankle and foot, initial encounter for fracture

M80.8B1G Age-related osteoporosis with current pathological fracture, left ankle and foot, subsequent encounter for fracture with routine healing

M80.8B1K Age-related osteoporosis with current pathological fracture, left ankle and foot, subsequent encounter for fracture with delayed healing

M80.8B1P Age-related osteoporosis with current pathological fracture, left ankle and foot, subsequent encounter for fracture with nonunion

M80.8B1S Age-related osteoporosis with current pathological fracture, left ankle and foot, subsequent encounter for fracture with malunion

M80.8B2A Age-related osteoporosis with current pathological fracture, left ankle and foot, sequela

M80.8B2D Age-related osteoporosis with current pathological fracture, vertebra(e), initial encounter for fracture

M80.8B2G Age-related osteoporosis with current pathological fracture, vertebra(e), subsequent encounter for fracture with routine healing

M80.8B2K Age-related osteoporosis with current pathological fracture, vertebra(e), subsequent encounter for fracture with delayed healing

M80.8B2P Age-related osteoporosis with current pathological fracture, vertebra(e), subsequent encounter for fracture with nonunion

M80.8B2S Age-related osteoporosis with current pathological fracture, vertebra(e), subsequent encounter for fracture with malunion

M80.8B9A Age-related osteoporosis with current pathological fracture, vertebra(e), sequela

M80.8B9D Other osteoporosis with current pathological fracture, other site, initial encounter for fracture

M80.8B9G Other osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with routine healing

M80.8B9K Other osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with delayed healing

M80.8B9P Other osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with nonunion

M80.8B9S Other osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with malunion

M81.0 Other osteoporosis with current pathological fracture, other site, sequela

M81.8 Age-related osteoporosis without current pathological fracture

M85.80 Other osteoporosis without current pathological fracture

M85.811 Other specified disorders of bone density and structure, unspecified site

M85.812 Other specified disorders of bone density and structure, right shoulder

M85.821 Other specified disorders of bone density and structure, left shoulder

M85.822 Other specified disorders of bone density and structure, right upper arm

M85.831 Other specified disorders of bone density and structure, left upper arm

M85.832 Other specified disorders of bone density and structure, right forearm

M85.841 Other specified disorders of bone density and structure, left forearm

M85.842 Other specified disorders of bone density and structure, right hand

M85.851 Other specified disorders of bone density and structure, left hand

M85.852 Other specified disorders of bone density and structure, right thigh

M85.861 Other specified disorders of bone density and structure, left thigh

M85.862 Other specified disorders of bone density and structure, right lower leg

M85.871 Other specified disorders of bone density and structure, left lower leg

M85.872 Other specified disorders of bone density and structure, right ankle and foot

M85.88 Other specified disorders of bone density and structure, left ankle and foot

M85.89 Other specified disorders of bone density and structure, other site

MA80.051A Other specified disorders of bone density and structure, multiple sites

Z87.310 Personal history of (healed) osteoporosis fracture

DENOSUMAB (XGEVA) AND DENOSUMAB-BBDZ (WYOST) ARE MEDICALLY NECESSARY WHEN REPORTED WITH ANY OF THE FOLLOWING DIAGNOSIS CODES:

C79.51

Secondary malignant neoplasm of bone

C90.00 Multiple myeloma not having achieved remission

C90.02 Multiple myeloma in relapse

D47.02 Systemic mastocytosis

D48.0 Neoplasm of uncertain behavior of bone and articular cartilage

E83.52 Hypercalcemia

ROMOSUZUMAB-AQQG (EVENITY) IS MEDICALLY NECESSARY WHEN REPORTED WITH ANY OF THE FOLLOWING DIAGNOSIS CODES:

M80.011A Age-related osteoporosis with current pathological fracture, right shoulder, initial encounter for fracture

M80.011D Age-related osteoporosis with current pathological fracture, right shoulder, subsequent encounter for fracture with routine healing

M80.011G Age-related osteoporosis with current pathological fracture, right shoulder, subsequent encounter for fracture with delayed healing

M80.011K Age-related osteoporosis with current pathological fracture, right shoulder, subsequent encounter for fracture with nonunion

M80.011P Age-related osteoporosis with current pathological fracture, right shoulder, subsequent encounter for fracture with malunion

M80.011S Age-related osteoporosis with current pathological fracture, right shoulder, sequela

M80.012A Age-related osteoporosis with current pathological fracture, left shoulder, initial encounter for fracture

M80.012D Age-related osteoporosis with current pathological fracture, left shoulder, subsequent encounter for fracture with routine healing

M80.012G Age-related osteoporosis with current pathological fracture, left shoulder, subsequent encounter for fracture with delayed healing

M80.012K Age-related osteoporosis with current pathological fracture, left shoulder, subsequent encounter for fracture with nonunion

M80.012P Age-related osteoporosis with current pathological fracture, left shoulder, subsequent encounter for fracture with malunion

M80.012S Age-related osteoporosis with current pathological fracture, left shoulder, sequela

M80.021A Age-related osteoporosis with current pathological fracture, right humerus, initial encounter for fracture

M80.021D Age-related osteoporosis with current pathological fracture, right humerus, subsequent encounter for fracture with routine healing

M80.021G Age-related osteoporosis with current pathological fracture, right humerus, subsequent encounter for fracture with delayed healing

M80.021K Age-related osteoporosis with current pathological fracture, right humerus, subsequent encounter for fracture with nonunion

M80.021P Age-related osteoporosis with current pathological fracture, right humerus, subsequent encounter for fracture with malunion

M80.021S Age-related osteoporosis with current pathological fracture, right humerus, sequela

M80.022A Age-related osteoporosis with current pathological fracture, left humerus, initial encounter for fracture

M80.022D Age-related osteoporosis with current pathological fracture, left humerus, subsequent encounter for fracture with routine healing

M80.022G Age-related osteoporosis with current pathological fracture, left humerus, subsequent encounter for fracture with delayed healing

M80.022K Age-related osteoporosis with current pathological fracture, left humerus, subsequent encounter for fracture with nonunion

M80.022P Age-related osteoporosis with current pathological fracture, left humerus, subsequent encounter for fracture with malunion

M80.022S Age-related osteoporosis with current pathological fracture, left humerus, sequela

M80.031A Age-related osteoporosis with current pathological fracture, right forearm, initial encounter for fracture

M80.031D Age-related osteoporosis with current pathological fracture, right forearm, subsequent encounter for fracture with routine healing

M80.031G Age-related osteoporosis with current pathological fracture, right forearm, subsequent encounter for fracture with delayed healing

M80.031K Age-related osteoporosis with current pathological fracture, right forearm, subsequent encounter for fracture with nonunion

M80.031P Age-related osteoporosis with current pathological fracture, right forearm, subsequent encounter for fracture with malunion

M80.031S Age-related osteoporosis with current pathological fracture, right forearm, sequela

M80.032A Age-related osteoporosis with current pathological fracture, left forearm, initial encounter for fracture

M80.032D Age-related osteoporosis with current pathological fracture, left forearm, subsequent encounter for fracture with routine healing

M80.032G Age-related osteoporosis with current pathological fracture, left forearm, subsequent encounter for fracture with delayed healing

M80.032K Age-related osteoporosis with current pathological fracture, left forearm, subsequent encounter for fracture with nonunion

M80.032P Age-related osteoporosis with current pathological fracture, left forearm, subsequent encounter for fracture with malunion

M80.032S Age-related osteoporosis with current pathological fracture, left forearm, sequela

M80.041A Age-related osteoporosis with current pathological fracture, right hand, initial encounter for fracture

M80.041D Age-related osteoporosis with current pathological fracture, right hand, subsequent encounter for fracture with routine healing

M80.041G Age-related osteoporosis with current pathological fracture, right hand, subsequent encounter for fracture with delayed healing

M80.041K Age-related osteoporosis with current pathological fracture, right hand, subsequent encounter for fracture with nonunion

M80.041P Age-related osteoporosis with current pathological fracture, right hand, subsequent encounter for fracture with malunion

M80.041S Age-related osteoporosis with current pathological fracture, right hand, sequel

M80.042A Age-related osteoporosis with current pathological fracture, left hand, initial encounter for fracture

M80.042D Age-related osteoporosis with current pathological fracture, left hand, subsequent encounter for fracture with routine healing

M80.042G Age-related osteoporosis with current pathological fracture, left hand, subsequent encounter for fracture with delayed healing

M80.042K Age-related osteoporosis with current pathological fracture, left hand, subsequent encounter for fracture with nonunion

M80.042P Age-related osteoporosis with current pathological fracture, left hand, subsequent encounter for fracture with malunion

M80.042S Age-related osteoporosis with current pathological fracture, left hand, sequela

M80.051A Age-related osteoporosis with current pathological fracture, right femur, initial encounter for fracture

M80.051D Age-related osteoporosis with current pathological fracture, right femur, subsequent encounter for fracture with routine healing

M80.051G Age-related osteoporosis with current pathological fracture, right femur, subsequent encounter for fracture with delayed healing

M80.051K Age-related osteoporosis with current pathological fracture, right femur, subsequent encounter for fracture with nonunion

M80.051P Age-related osteoporosis with current pathological fracture, right femur, subsequent encounter for fracture with malunion

M80.051S Age-related osteoporosis with current pathological fracture, right femur, sequela

M80.052A Age-related osteoporosis with current pathological fracture, left femur, initial encounter for fracture

M80.052D Age-related osteoporosis with current pathological fracture, left femur, subsequent encounter for fracture with routine healing

M80.052G Age-related osteoporosis with current pathological fracture, left femur, subsequent encounter for fracture with delayed healing

M80.052K Age-related osteoporosis with current pathological fracture, left femur, subsequent encounter for fracture with nonunion

M80.052P Age-related osteoporosis with current pathological fracture, left femur, subsequent encounter for fracture with malunion

M80.052S Age-related osteoporosis with current pathological fracture, left femur, sequela

M80.061A Age-related osteoporosis with current pathological fracture, right lower leg, initial encounter for fracture

M80.061D Age-related osteoporosis with current pathological fracture, right lower leg, subsequent encounter for fracture with routine healing

M80.061G Age-related osteoporosis with current pathological fracture, right lower leg, subsequent encounter for fracture with delayed healing

M80.061K Age-related osteoporosis with current pathological fracture, right lower leg, subsequent encounter for fracture with nonunion

M80.061P Age-related osteoporosis with current pathological fracture, right lower leg, subsequent encounter for fracture with malunion

M80.061S Age-related osteoporosis with current pathological fracture, right lower leg, sequela

M80.062A Age-related osteoporosis with current pathological fracture, left lower leg, initial encounter for fracture

M80.062D Age-related osteoporosis with current pathological fracture, left lower leg, subsequent encounter for fracture with routine healing

M80.062G Age-related osteoporosis with current pathological fracture, left lower leg, subsequent encounter for fracture with delayed healing

M80.062K Age-related osteoporosis with current pathological fracture, left lower leg, subsequent encounter for fracture with nonunion

M80.062P Age-related osteoporosis with current pathological fracture, left lower leg, subsequent encounter for fracture with malunion

M80.062S Age-related osteoporosis with current pathological fracture, left lower leg, sequela

M80.071A Age-related osteoporosis with current pathological fracture, right ankle and foot, initial encounter for fracture

M80.071D Age-related osteoporosis with current pathological fracture, right ankle and foot, subsequent encounter for fracture with routine healing

M80.071G Age-related osteoporosis with current pathological fracture, right ankle and foot, subsequent encounter for fracture with delayed healing

M80.071K Age-related osteoporosis with current pathological fracture, right ankle and foot, subsequent encounter for fracture with nonunion

M80.071P Age-related osteoporosis with current pathological fracture, right ankle and foot, subsequent encounter for fracture with malunion

M80.071S Age-related osteoporosis with current pathological fracture, right ankle and foot, sequela

M80.072A Age-related osteoporosis with current pathological fracture, left ankle and foot, initial encounter for fracture

M80.072D Age-related osteoporosis with current pathological fracture, left ankle and foot, subsequent encounter for fracture with routine healing

M80.072G Age-related osteoporosis with current pathological fracture, left ankle and foot, subsequent encounter for fracture with delayed healing

M80.072K Age-related osteoporosis with current pathological fracture, left ankle and foot, subsequent encounter for fracture with nonunion

M80.072P Age-related osteoporosis with current pathological fracture, left ankle and foot, subsequent encounter for fracture with malunion

M80.072S Age-related osteoporosis with current pathological fracture, left ankle and foot, sequela

M80.08XA Age-related osteoporosis with current pathological fracture, vertebra(e), initial encounter for fracture

M80.08XD Age-related osteoporosis with current pathological fracture, vertebra(e), subsequent encounter for fracture with routine healing

M80.08XG Age-related osteoporosis with current pathological fracture, vertebra(e), subsequent encounter for fracture with delayed healing

M80.08XK Age-related osteoporosis with current pathological fracture, vertebra(e), subsequent encounter for fracture with nonunion

M80.08XP Age-related osteoporosis with current pathological fracture, vertebra(e), subsequent encounter for fracture with malunion

M80.08XS Age-related osteoporosis with current pathological fracture, vertebra(e), sequela

M80.0AXA Age-related osteoporosis with current pathological fracture, other site, initial encounter for fracture

M80.0AXD Age-related osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with routine healing

M80.0AXG Age-related osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with delayed healing

M80.0AXK Age-related osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with nonunion

M80.0AXP Age-related osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with malunion

M80.0AXS Age-related osteoporosis with current pathological fracture, other site, sequela

M80.0B1A Age-related osteoporosis with current pathological fracture, right pelvis, initial encounter for fracture

M80.0B1D Age-related osteoporosis with current pathological fracture, right pelvis, subsequent encounter for fracture with routine healing

M80.0B1G Age-related osteoporosis with current pathological fracture, right pelvis, subsequent encounter for fracture with delayed healing

M80.0B1K Age-related osteoporosis with current pathological fracture, right pelvis, subsequent encounter for fracture with nonunion

M80.0B1P Age-related osteoporosis with current pathological fracture, right pelvis, subsequent encounter for fracture with malunion

M80.0B1S Age-related osteoporosis with current pathological fracture, right pelvis, sequela

M80.0B2A Age-related osteoporosis with current pathological fracture, left pelvis, initial encounter for fracture

M80.0B2D Age-related osteoporosis with current pathological fracture, left pelvis, subsequent encounter for fracture with routine healing

M80.0B2G Age-related osteoporosis with current pathological fracture, left pelvis, subsequent encounter for fracture with delayed healing

M80.0B2K Age-related osteoporosis with current pathological fracture, left pelvis, subsequent encounter for fracture with nonunion

M80.0B2P Age-related osteoporosis with current pathological fracture, left pelvis, subsequent encounter for fracture with malunion

M80.0B2S Age-related osteoporosis with current pathological fracture, left pelvis, sequela

M80.8AXA Other osteoporosis with current pathological fracture, other site, initial encounter for fracture

M80.8AXD Other osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with routine healing

M80.8AXG Other osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with delayed healing

M80.8AXK Other osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with nonunion

M80.8AXP Other osteoporosis with current pathological fracture, other site, subsequent encounter for fracture with malunion

M80.8AXS Other osteoporosis with current pathological fracture, other site, sequela

M80.8B1A Other osteoporosis with current pathological fracture, right pelvis, initial encounter for fracture

M80.8B1D Other osteoporosis with current pathological fracture, right pelvis, subsequent encounter for fracture with routine healing

M80.8B1G Other osteoporosis with current pathological fracture, right pelvis, subsequent encounter for fracture with delayed healing

M80.8B1K Other osteoporosis with current pathological fracture, right pelvis, subsequent encounter for fracture with nonunion

M80.8B1P Other osteoporosis with current pathological fracture, right pelvis, subsequent encounter for fracture with malunion

M80.8B1S Other osteoporosis with current pathological fracture, right pelvis, sequela

M80.8B2A Other osteoporosis with current pathological fracture, left pelvis, initial encounter for fracture

M80.8B2D Other osteoporosis with current pathological fracture, left pelvis, subsequent encounter for fracture with routine healing

M80.8B2G Other osteoporosis with current pathological fracture, left pelvis, subsequent encounter for fracture with delayed healing

M80.8B2K Other osteoporosis with current pathological fracture, left pelvis, subsequent encounter for fracture with nonunion

M80.8B2P Other osteoporosis with current pathological fracture, left pelvis, subsequent encounter for fracture with malunion

M80.8B2S Other osteoporosis with current pathological fracture, left pelvis, sequela

M81.0 Age-related osteoporosis without current pathological fracture

Duration of authorization: 12 months

Version Effective Date: 02/24/2025

Title: Dofetilide (Tikosyn®) Use in the Inpatient Setting

MEDICALLY NECESSARY:

An inpatient admission for the initiation, dose escalation or reinitiation of dofetilide (Tikosyn) is considered medically necessary and, therefore, covered for either of the following indications:

- For conversion of atrial fibrillation (AF) and atrial flutter (AFL) (AF/AFL) to normal sinus rhythm (NSR)
- For the maintenance of NSR (delay in time recurrence of AF/AFL) in individuals with AF/AFL of greater than 1 week's duration who have been converted to NSR

Dofetilide (Tikosyn) should be reserved for individuals in whom AF/AFL is highly symptomatic because the drug can cause life-threatening ventricular arrhythmias.

Therapy with dofetilide (Tikosyn) for initiation, dose escalation (and, if necessary, reinitiation) must be done according to the product labeling, for a minimum of 3 days in an inpatient setting that provides continuous electrocardiographic (ECG) monitoring in the presence of personnel trained in the management of serious ventricular arrhythmias. Additionally, individuals should not be discharged within 12 hours of electrical or pharmacologic conversion to NSR.

- For information on maintenance therapy with dofetilide (Tikosyn), refer to the Guidelines section of this policy.

Duration of authorization: 12 months

Version Effective Date: 03/05/2025

Title: Dostarlimab-gxly (Jemperli)

MEDICALLY NECESSARY:

AMPULLARY ADENOCARCINOMA

Dostarlimab-gxly (Jemperli), as a single agent, is considered medically necessary and, therefore, covered for the subsequent treatment of adult individuals with mismatch repair deficient (dMMR) or microsatellite instability-high (MSI-H) recurrent or advanced ampullary adenocarcinoma, as determined by a US Food and Drug Administration (FDA)-approved test, and meet **BOTH** of the following:

- Have progressed on, or following, prior treatment
- Have no satisfactory alternative treatment option

ANAL CARCINOMA

Dostarlimab-gxly (Jemperli), as a single agent, is considered medically necessary and, therefore, covered for the treatment of adult individuals with recurrent or advanced metastatic squamous cell anal carcinoma as second-line and subsequent therapy if no prior immunotherapy received (National Comprehensive Cancer Network [NCCN] preferred)

BREAST CANCER

Dostarlimab-gxly (Jemperli), as a single agent, is considered medically necessary and, therefore, covered for the treatment of adult individuals with dMMR or MSI-H recurrent or advanced breast cancer, as determined by an FDA-approved test, and meet **ALL** of the following:

- Have progressed on, or following, prior treatment
- Have no satisfactory alternative treatment option
- **ONE** of the following is met:
 - Invasive breast cancer with **ALL** of the following:
 - **ONE** of the following histology types:
 1. Lobular
 2. Mixed
 3. Metaplastic
 4. Ductal/NST
 5. Micropapillary
 6. Pure tubular
 7. Pure mucinous
 8. Pure cribriform
 9. Encapsulated or solid papillary carcinoma
 10. Other rare forms
 11. Adenoid cystic and other salivary carcinomas
 12. Secretory carcinoma
 13. Rare low-grade forms of metaplastic carcinoma
 - **ONE** of the following levels of disease:
 1. Recurrent unresectable (local or regional) disease
 2. Stage IV (M1) disease
 - Inflammatory breast cancer (special consideration) with **ONE** of the following levels of disease:
 - No response to preoperative systemic therapy
 - Recurrent unresectable (local or regional) disease

- Stage IV (M1) disease
- As **ONE** of the following:
 - As third-line therapy and beyond for hormone receptor positive and human epidermal growth factor receptor 2 (HER2)-negative with visceral crisis or endocrine therapy refractory or for triple-negative breast cancer (TNBC)
 - As fourth-line and beyond for HER2-positive disease

COLON CANCER (INCLUDING APPENDICEAL ADENOCARCINOMA)

Dostarlimab-gxly (Jemperli), as a single agent, is considered medically necessary and, therefore, covered for the treatment of adult individuals with dMMR/MSI-H or polymerase epsilon/delta (POLE/POLD1) mutation with ultrahypermutated phenotype (e.g., tumor mutational burden [TMB] >50 mutations per megabase [mut/Mb]) recurrent or advanced metastatic colon cancer (including appendiceal adenocarcinoma), as determined by an FDA-approved test, and meet **ONE** of the following:

- As neoadjuvant therapy for clinical T4b or bulky nodal disease (NCCN preferred)
- As neoadjuvant therapy for resectable synchronous liver and/or lung metastases (if no previous treatment with a checkpoint inhibitor) (NCCN preferred)
- As initial treatment for resectable metachronous metastases if no previous immunotherapy
- Individual is a candidate for immunotherapy and no prior immunotherapy received in **ONE** of the following:
 - For locally unresectable or medically inoperable disease (NCCN preferred)
 - As primary treatment for synchronous abdominal/peritoneal metastases that are nonobstructing, or following local therapy for individuals with existing or imminent obstruction
 - For synchronous unresectable metastases
 - As treatment for unresectable metachronous metastases
- As systemic therapy for an individual with advanced or metastatic disease appendiceal adenocarcinoma who is a candidate for immunotherapy and has not received prior immunotherapy

ENDOMETRIAL CANCER

Dostarlimab-gxly (Jemperli) is considered medically necessary and, therefore, covered for the treatment of adult individuals with recurrent or advanced endometrial cancer and meet **ONE** of the following:

- Primary treatment, in combination with carboplatin and paclitaxel (for individuals with primary advanced disease: stage IIIA, IIIB, or IIIC1 with measurable disease postsurgery, stage IIIC1 with carcinosarcoma, clear cell, serous, or mixed histology regardless of the presence of measurable disease; and stage IIIC2 or stage IV regardless of the presence of measurable disease), and dostarlimab-gxly (Jemperli) continued as a single-agent maintenance therapy (NCCN preferred) for individuals with stage III to IV endometrioid adenocarcinoma in **ONE** of the following scenarios:
 - May be considered preoperatively for individuals presenting with abdominal/pelvic-confined disease that is suitable for primary surgery
 - With or without external beam radiation therapy (EBRT), stereotactic body radiation therapy (SBRT), and/or total hysterectomy/bilateral salpingo-oophorectomy (TH/BSO) for distant metastases that are suitable for primary surgery
 - With sequential EBRT and with or without brachytherapy for locoregional extrauterine disease that is not suitable for primary surgery
 - For locoregional extrauterine disease or distant metastases that are not suitable for primary surgery
- Adjuvant treatment, in combination with carboplatin and paclitaxel (for individuals with primary advanced disease: stage IIIA, IIIB, or IIIC1 with measurable disease postsurgery; stage IIIC1 with carcinosarcoma, clear cell, serous, or mixed histology regardless of the presence of measurable disease; and stage IIIC2 or stage IV regardless of the presence of measurable disease), and dostarlimab-gxly (Jemperli) continued as a single-agent maintenance

therapy (NCCN preferred), with or without EBRT and with or without vaginal brachytherapy for surgically staged individuals with stage III to IV endometrioid adenocarcinoma

- First-line therapy (or second-line or subsequent therapy as clinically appropriate), in combination with carboplatin and paclitaxel (for individuals with recurrent endometrial carcinoma with or without measurable disease), and dostarlimab-gxly (Jemperli) continued as a single-agent maintenance therapy (NCCN preferred), for recurrent disease in **ONE** of the following scenarios:
 - May be considered for isolated metastases (except as first-line therapy)
 - For disseminated metastases with or without sequential palliative EBRT
 - With sequential EBRT and with or without brachytherapy for locoregional recurrence in individuals with no prior RT to site of recurrence, or previous vaginal brachytherapy only
 - After surgical exploration, with sequential EBRT for locoregional recurrence in individuals with disease confined to the vagina or paravaginal soft tissue, or in pelvic or para-aortic lymph nodes
 - After surgical exploration, with or without sequential EBRT for locoregional recurrence in individuals with upper abdominal or peritoneal disease
 - With or without sequential palliative EBRT or brachytherapy for locoregional recurrence in individuals who have received prior EBRT to site of recurrence
- Used in combination with carboplatin and paclitaxel (for individuals with primary advanced endometrial carcinoma: stage IIIA, IIIB, or IIIC1 with measurable disease post-surgery; stage IIIC1 with carcinosarcoma, clear cell, serous, or mixed histology regardless of the presence of measurable disease; and stage IIIC2 or stage IV regardless of the presence of measurable disease), and dostarlimab-gxly (Jemperli) continued as a single-agent maintenance therapy (NCCN preferred), for stage III to IV tumors, including serous carcinoma, clear cell carcinoma, undifferentiated/dedifferentiated carcinoma, or carcinosarcoma in **ONE** of the following scenarios:
 - Is suitable for primary surgery as additional treatment with or without sequential EBRT and with or without vaginal brachytherapy after TH/BSO
 - Is not suitable for primary surgery as primary treatment with or without sequential EBRT and with or without brachytherapy
- First-line therapy (useful in certain circumstances after prior platinum-based therapy including neoadjuvant and adjuvant), or second-line or subsequent therapy, as clinically appropriate, as a single agent for recurrent MSI-H or dMMR disease, as determined by an FDA-approved test, that has progressed on or following prior treatment with a platinum-containing regimen in **ANY** of the following scenarios:
 - May be considered for isolated metastases (except as first-line therapy)
 - For disseminated metastases with or without sequential palliative EBRT
 - With sequential EBRT and with or without brachytherapy for locoregional recurrence in individuals with no prior RT to site of recurrence, or previous vaginal brachytherapy only
 - After surgical exploration, with sequential EBRT for locoregional recurrence in individuals with disease confined to the vagina or paravaginal soft tissue, or in pelvic or para-aortic lymph nodes
 - After surgical exploration, with or without sequential EBRT for locoregional recurrence in individuals with upper abdominal or peritoneal disease
 - With or without sequential palliative EBRT or brachytherapy for locoregional recurrence in individuals who have received prior EBRT to site of recurrence

ESOPHAGEAL AND ESOPHAGOGASTRIC JUNCTION CANCERS

Dostarlimab-gxly (Jemperli), as a single agent, is considered medically necessary and, therefore, covered for the treatment of adult individuals with recurrent or advanced esophageal or esophagogastric junction cancer and meet **ONE** of the following:

- As induction systemic therapy for relieving dysphagia in select individuals with MSI-H or dMMR squamous cell tumors, as determined by an FDA-approved test, (independent of PD-L1 status) who are medically fit and planned

for esophagectomy with cT2, N0 (high-risk lesions: lymphovascular invasion, 3 cm or greater, poorly differentiated), cT1b-cT2, N+, or cT3-cT4a, any N disease (NCCN preferred)

- As palliative therapy in individuals who meet **ALL** of the following:
 - Meet **ONE** of the following:
 - Are not surgical candidates
 - Have unresectable locally advanced, recurrent, or metastatic disease
 - Karnofsky performance status (PS) 60 percent or greater or Eastern Cooperative Oncology Group (ECOG) PS 2 or less
 - Meet **ONE** of the following:
 - First-line (NCCN preferred) for individuals with MSI-H or dMMR squamous cell or adenocarcinoma tumors, as determined by an FDA-approved test (independent of PD-L1 status) if no prior tumor progression while on therapy with a checkpoint inhibitor
 - As second-line or subsequent therapy (prior use of immuno-oncology therapy will make these individuals ineligible for dostarlimab-gxly [Jemperli]) for individuals with MSI-H or dMMR squamous cell or adenocarcinoma tumors, as determined by an FDA-approved test, whose cancer is progressing on or following prior treatment and who have no satisfactory alternative treatment options if no prior tumor progression while on therapy with a checkpoint inhibitor

GASTRIC CANCER

Dostarlimab-gxly (Jemperli), as a single agent, is considered medically necessary and, therefore, covered for the treatment of adult individuals with dMMR or MSI-H recurrent or advanced gastric tumors, as determined by an FDA-approved test, as **ONE** of the following:

- Primary treatment, independent of PD-L1 status, in individuals who are medically fit for surgery but with surgically unresectable locoregional disease (NCCN preferred)
- Palliative therapy, independent of PD-L1 status, in individuals who meet **ALL** of the following:
 - Are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease
 - Karnofsky PS 60 percent or greater or ECOG PS 2 or less
 - As first-line therapy (if no prior tumor progression while on therapy with a checkpoint inhibitor) (NCCN preferred)
- Palliative therapy for locoregional disease in individuals who meet **ALL** of the following:
 - Are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease (including peritoneal only metastatic disease, including positive cytology)
 - Karnofsky PS 60 percent or greater or ECOG PS 2 or less
 - Have progressed on or following prior treatment
 - Have no satisfactory alternative treatment options (if no prior tumor progression while on therapy with a checkpoint inhibitor)
 - As second-line or subsequent therapy (prior use of immuno-oncology therapy will make these individuals ineligible for dostarlimab-gxly [Jemperli])

OCCULT PRIMARY CANCER

Dostarlimab-gxly (Jemperli), as a single agent, is considered medically necessary and, therefore, covered for the treatment of adult individuals with dMMR/MSI-H recurrent or advanced occult primary tumors (with adenocarcinoma or carcinoma not otherwise specified histology), as determined by an FDA-approved test, in symptomatic individuals with ECOG PS 1 to 2 or asymptomatic individuals with PS 0 and aggressive recurrent or advanced disease that have progressed on or following prior treatment and who have no satisfactory alternative treatment option for **ANY** of the following:

- Axillary involvement in individuals with a prostate or postprostatectomy if clinically indicated
- Lung nodules or breast marker–negative pleural effusion
- Resectable liver disease

- Peritoneal mass or ascites with nonovarian histology
- Retroperitoneal mass of non-germ cell histology in selected individuals
- Unresectable liver disease or disseminated metastases

OVARIAN/FALLOPIAN TUBE/PRIMARY PERITONEAL CANCER

Dostarlimab-gxly (Jemperli), as a single agent, is considered medically necessary and, therefore, covered for the treatment of adult individuals with recurrent or advanced dMMR or MSI-H ovarian, fallopian tube, or primary peritoneal disease, as determined by an FDA-approved test, with persistent or recurrent tumors, and meet **BOTH** of the following:

- **ONE** of the following tumor histology types is present:
 - Endometrioid, serous
 - Carcinosarcoma (malignant mixed müllerian tumors)
 - Clear cell carcinoma
 - Mucinous carcinoma
 - Endometrioid, grade 1
- **ONE** of the following is present:
 - For progression on primary, maintenance, or recurrence therapy (platinum-resistant disease)
 - For stable or persistent disease (if not on maintenance therapy) (platinum-resistant disease)
 - For complete remission and relapse less than 6 months after completing chemotherapy (platinum-resistant disease)
 - For radiographic and/or clinical relapse in individuals with previous complete remission and relapse 6 months or more after completing prior chemotherapy (platinum-sensitive disease)

Dostarlimab-gxly (Jemperli) is considered medically necessary and, therefore, covered for the treatment of adult individuals with dMMR or MSI-H ovarian, fallopian tube, or primary peritoneal disease (with low-grade serous, borderline epithelial histology), as determined by an FDA-approved test, in recurrent or advanced tumors as therapy for platinum-sensitive or platinum-resistance recurrence.

PANCREATIC ADENOCARCINOMA

Dostarlimab-gxly (Jemperli), as a single agent, is considered medically necessary and, therefore, covered for the treatment of adult individuals with dMMR or MSI-H recurrent or advanced pancreatic adenocarcinoma (including adenosquamous and squamous histology), as determined by an FDA-approved test, with **BOTH** of the following:

- **ONE** of the following scenarios:
 - Local recurrence in the pancreatic operative bed after resection and no prior immunotherapy
 - Recurrent metastatic disease with or without local recurrence after resection and no prior immunotherapy
 - As subsequent therapy if no prior immunotherapy for locally advanced or metastatic disease and disease progression
- **ONE** of the following statuses:
 - Good ECOG PS (PS 0-1)
 - Intermediate ECOG PS (PS 2)

RECTAL CANCER

Dostarlimab-gxly (Jemperli), as a single agent, is considered medically necessary and, therefore, covered for the treatment of adult individuals with dMMR/MSI-H or POLE/POLD1 mutation with ultra-hypermutated phenotype (e.g., TMB >50 mut/Mb) recurrent or advanced rectal cancer, as determined by an FDA-approved test, and meet **ONE** of the following:

- Individual is a candidate for immunotherapy and has not received prior immunotherapy as **ONE** of the following:
 - As primary treatment for synchronous abdominal/peritoneal metastases that are nonobstructing, or following local therapy for individuals with existing or imminent obstruction
 - As primary treatment for synchronous unresectable metastases

- As primary treatment for potentially resectable or unresectable isolated pelvic/anastomotic recurrence
- As primary treatment for unresectable metachronous metastases
- As neoadjuvant/definitive immunotherapy (NCCN preferred) for T3, N any; T1-2, N1-2; T4, N any; or locally unresectable or medically inoperable disease (no previous treatment with a checkpoint inhibitor)
- As neoadjuvant treatment for resectable synchronous liver only and/or lung only metastases (no previous treatment with a checkpoint inhibitor) (NCCN preferred)
- As initial treatment for resectable metachronous metastases and no previous immunotherapy

SMALL BOWEL ADENOCARCINOMA

Dostarlimab-gxly (Jemperli), as a single agent, is considered medically necessary and, therefore, covered for the treatment of adult individuals with dMMR/MSI-H or POLE/POLD1 mutation with ultrahypermutated phenotype (e.g., TMB >50 mut/Mb) recurrent or advanced small bowel adenocarcinoma, as determined by an FDA-approved test, in **ONE** of the following scenarios:

- As primary treatment for locally unresectable or medically inoperable disease
- For any line of therapy for advanced or metastatic disease if no previous treatment with a checkpoint inhibitor

Duration of authorization: 12 months

Version Effective Date: 05/19/2025

Title: Durvalumab (Imfinzi®) and Tremelimumab-actl (Imjudo®)

MEDICALLY NECESSARY:

AMPULLARY ADENOCARCINOMA

Durvalumab (Imfinzi), in combination with gemcitabine and cisplatin, is considered medically necessary and, therefore, covered as a first-line therapy for ampullary adenocarcinoma when the individual meets **all** of the following:

- Good Eastern Cooperative Oncology Group (ECOG) performance status (PS) (PS 0-1)
- Good biliary drainage
- Adequate nutritional intake
- Pancreatobiliary and mixed type disease with **one** of the following:
 - Unresectable localized disease
 - Stage IV resected ampullary cancer
 - Metastatic disease at initial presentation

BILIARY TRACT CANCERS

Gallbladder Cancer

Durvalumab (Imfinzi), in combination with gemcitabine and cisplatin, is considered medically necessary and, therefore, covered for the treatment of gallbladder cancer for **any** of the following:

- As primary treatment for unresectable or resected gross residual (R2) disease, or metastatic disease (National Comprehensive Cancer Network [NCCN] preferred)
- For individuals who developed recurrent disease more than 6 months after surgery with curative intent and more than 6 months after completion of adjuvant therapy (NCCN preferred)
- Subsequent treatment for progression on or after systemic treatment for unresectable or resected gross residual (R2) disease, or metastatic disease in those who have not been previously treated with a checkpoint inhibitor
- As neoadjuvant chemotherapy for resectable locally advanced disease that presents as **one** of the following:
 - Incidental finding of suspicious mass during surgery where hepatobiliary surgery expertise unavailable
 - Incidental finding on pathologic review
 - Mass on imaging

Intrahepatic and Extrahepatic Cholangiocarcinoma

Durvalumab (Imfinzi), in combination with gemcitabine and cisplatin, is considered medically necessary and, therefore, covered for the treatment of intrahepatic and extrahepatic cholangiocarcinoma for **any** of the following:

- As primary treatment for unresectable or resected gross residual (R2) disease, or metastatic disease (NCCN preferred)

- For individuals who developed recurrent disease more than 6 months after surgery with curative intent and more than 6 months after completion of adjuvant therapy (NCCN preferred)
- Subsequent treatment for progression on or after systemic treatment for unresectable or resected gross residual (R2) disease, or metastatic disease in those who have not been previously treated with a checkpoint inhibitor

CERVICAL CANCER

Durvalumab (Imfinzi) is considered medically necessary and, therefore, covered for persistent, recurrent, or metastatic small cell neuroendocrine carcinoma of the cervix (NECC) when the individual meets **both** of the following:

- **One** of the following lines of therapy:
 - First-line
 - Second-line
 - Subsequent therapy (if not used previously as first line)
- In combination with **one** of the following regimens, and continued as single agent for maintenance:
 - Cisplatin and etoposide
 - Carboplatin and etoposide

ESOPHAGEAL AND ESOPHAGOGASTRIC JUNCTION CANCERS

Durvalumab (Imfinzi), in combination with tremelimumab-actl (Imjudo), is considered medically necessary and, therefore, covered as primary neoadjuvant immunotherapy for esophageal or esophagogastric junction adenocarcinoma if the tumor is microsatellite instability-high (MSI-H) or deficient mismatch repair (dMMR) and the individual is medically fit for surgery with cT2, N0 (high-risk lesions: lymphovascular invasion, 3 cm or greater, poorly differentiated), cT1b-cT2, N+ or cT3-cT4a, any N disease

GASTRIC CANCER

Durvalumab (Imfinzi), in combination with tremelimumab-actl (Imjudo), is considered medically necessary and, therefore, covered as primary neoadjuvant immunotherapy for gastric adenocarcinoma if the tumor is MSI-H or dMMR for potentially resectable locoregional disease (cT2 or higher, any N) if medically fit for surgery

HEPATOCELLULAR CARCINOMA (HCC)

Durvalumab (Imfinzi), as a single agent or in combination with tremelimumab-actl (Imjudo; NCCN preferred), is considered medically necessary and, therefore, covered for the treatment of HCC as first-line treatment for individuals with **any** of the following:

- Metastatic disease or extensive liver tumor burden
- Unresectable disease and are not a transplant candidate
- Liver-confined disease, inoperable by PS, comorbidity, or with minimal or uncertain extrahepatic disease

MALIGNANT MESOTHELIOMA OF PLEURA

Durvalumab (Imfinzi), in combination with pemetrexed and a platinum agent, is considered medically necessary and, therefore, covered as first-line treatment of individuals with unresectable malignant mesothelioma of the pleura

NON-SMALL CELL LUNG CARCINOMA (NSCLC)

Durvalumab (Imfinzi), as a single agent, is considered medically necessary and, therefore, covered for the treatment of individuals with unresectable stage II-III NSCLC as consolidation immunotherapy when **all** of the following are met:

- PS 0-1
- No disease progression after definitive concurrent chemoradiation (for individuals who have received sequential chemoradiation, durvalumab [Imfinzi] can be considered as consolidation immunotherapy)
- Histology demonstrates squamous cell carcinoma, adenocarcinoma (with mixed subtypes), or large cell carcinoma

Durvalumab (Imfinzi), in combination with tremelimumab-actl (Imjudo), is considered medically necessary and, therefore, covered for the treatment of individuals with NSCLC with adenocarcinoma (with mixed subtypes), large cell carcinoma, or squamous cell carcinoma histology in **one** of the following scenarios:

- As treatment for recurrent (excluding locoregional recurrence or symptomatic local disease but including mediastinal lymph node recurrence with prior radiation therapy), advanced, or metastatic disease as first-line therapy for programmed death ligand 1 (PD-L1) expression-positive (1-49 percent) tumors that are negative for actionable molecular biomarkers* (may be KRAS G12C mutation positive) and no contraindications** to programmed death 1 (PD-1) or PD-L1 inhibitors and PS 0-2 in **one** of the following regimens:
 - With albumin-bound paclitaxel and carboplatin
 - With pemetrexed and either carboplatin or cisplatin for nonsquamous cell histology
 - With gemcitabine and either carboplatin or cisplatin for squamous cell histology
- As treatment for recurrent (excluding locoregional recurrence or symptomatic local disease but including mediastinal lymph node recurrence with prior radiation therapy), advanced, or metastatic disease for individuals with PS 0-1 and no contraindications** to PD-1 or PD-L1 inhibitors when **both** of the following are met:
 - In **one** of the following regimens:
 - With albumin-bound paclitaxel and carboplatin
 - With pemetrexed and either carboplatin or cisplatin for nonsquamous cell histology
 - With gemcitabine and either carboplatin or cisplatin for squamous cell histology
 - In **one** of the following lines of therapy:
 - Initial systemic therapy for PD-L1 less than 1 percent and negative for actionable molecular biomarkers* (may be KRAS G12C mutation positive)
 - First-line therapy for EGFR exon 20 insertion mutation positive tumors

- First-line or subsequent therapy for BRAF V600E mutation positive tumors
- First-line or subsequent therapy for NTRK1/2/3 gene fusion positive tumors
- First-line or subsequent therapy for MET exon 14 skipping mutation positive tumors
- First-line or subsequent therapy for RET rearrangement positive tumors
- First-line therapy for ERBB2 (HER2) mutation positive tumors
- Subsequent therapy for EGFR exon 19 deletion or exon 21 L858R tumors and prior erlotinib with or without (ramucirumab or bevacizumab), afatinib, gefitinib, osimertinib, or dacomitinib therapy
- Subsequent therapy for EGFR S768I, L861Q, and/or G719X mutation positive tumors and prior afatinib, osimertinib, erlotinib, gefitinib, or dacomitinib therapy
- Subsequent therapy for ALK rearrangement positive tumors and prior crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib therapy
- Subsequent therapy for ROS1 rearrangement positive tumors and prior crizotinib, entrectinib, repotrectinib, ceritinib, or lorlatinib therapy

Durvalumab (Imfinzi), as a single agent, as continuation maintenance therapy for recurrent (excluding locoregional recurrence or symptomatic local disease but including mediastinal lymph node recurrence with prior radiation therapy), advanced, or metastatic disease, is considered medically necessary and, therefore, covered for the treatment of individuals with NSCLC with adenocarcinoma (with mixed subtypes), large cell carcinoma, or squamous cell carcinoma histology in **one** of the following scenarios:

- As treatment for individuals with **all** of the following:
 - PD-L1 expression 1-49 percent tumors that are negative for actionable molecular biomarkers* (may be KRAS G12C mutation positive)
 - No contraindications** to PD-1 or PD-L1 inhibitors
 - PS 0-2
 - Have achieved a response or stable disease following first-line therapy with durvalumab (Imfinzi) and tremelimumab-actl (Imjudo) plus chemotherapy
- As treatment for individuals with **all** of the following:
 - PD-L1 expression less than 1 percent tumors that are negative for actionable molecular biomarkers* (may be KRAS G12C mutation positive)
 - No contraindications** to PD-1 or PD-L1 inhibitors
 - PS 0-2
 - Have achieved a tumor response or stable disease following initial systemic therapy with durvalumab (Imfinzi) and tremelimumab-actl (Imjudo) plus chemotherapy

Durvalumab (Imfinzi), in combination with pemetrexed, as continuation maintenance therapy for recurrent (excluding locoregional recurrence or symptomatic local disease but including mediastinal lymph node recurrence with prior radiation therapy), advanced, or metastatic

disease, is considered medically necessary and, therefore, covered for the treatment of individuals with NSCLC with adenocarcinoma (with mixed subtypes) or large cell carcinoma histology in **one** of the following scenarios:

- As treatment for individuals with **all** of the following:
 - PD-L1 expression 1-49 percent tumors that are negative for actionable molecular biomarkers* (may be KRAS G12C mutation positive)
 - No contraindications** to PD-1 or PD-L1 inhibitors
 - PS 0-2
 - Have achieved a response or stable disease following first-line therapy with durvalumab (Imfinzi), tremelimumab-actl (Imjudo), and pemetrexed plus either carboplatin or cisplatin for nonsquamous cell histology
- As treatment for individuals with **all** of the following:
 - PD-L1 expression less than 1 percent tumors that are negative for actionable molecular biomarkers* (may be KRAS G12C mutation positive)
 - No contraindications** to PD-1 or PD-L1 inhibitors
 - PS 0-2
 - Have achieved a tumor response or stable disease following initial systemic therapy with durvalumab (Imfinzi), tremelimumab-actl (Imjudo), and pemetrexed plus either carboplatin or cisplatin for nonsquamous cell histology

*Complete genotyping for EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET, RET, and ERBB2 (HER2) via biopsy and/or plasma testing. If a clinically actionable marker is found, it is reasonable to start therapy based on the identified marker. Treatment is guided by available results and, if unknown, these individuals are treated as though they do not have driver oncogenes

**Contraindications for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or current use of immunosuppressive agents, and some oncogenic drivers (i.e., EGFR exon 19 deletion or exon 21 L858R, ALK rearrangements), have been shown to be associated with less benefit from PD-1/PD-L1 inhibitors

SMALL CELL LUNG CARCINOMA (SCLC)

Durvalumab (Imfinzi), in combination with etoposide and either carboplatin or cisplatin followed by single-agent maintenance, is considered medically necessary and, therefore, covered for primary treatment (NCCN preferred) of extensive-stage small cell lung cancer (ES-SCLC) in individuals with **any** of the following:

- Without localized symptomatic sites or brain metastases and good PS (PS 0-2)
- Without localized symptomatic sites or brain metastases and poor PS (PS 3-4) due to SCLC
- With localized symptomatic sites (used with radiation therapy [typically sequential] if spinal cord compression)
- With brain metastases

Duration of authorization: 12 months

Version Effective Date: 05/06/2024

Title: Durvalumab (Imfinzi®) and Tremelimumab-actl (Imjudo®)

MEDICALLY NECESSARY:

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

DURVALUMAB (IMFINZI®) IS MEDICALLY NECESSARY WHEN REPORTED WITH THE FOLLOWING DIAGNOSIS CODES:

C22.0 Liver cell carcinoma

C22.1 Intrahepatic bile duct carcinoma

C22.7 Other specified carcinomas of liver

C22.8 Malignant neoplasm of liver, primary, unspecified as to type

C22.9 Malignant neoplasm of liver, not specified as primary or secondary

C23 Malignant neoplasm of gallbladder

C24.0 Malignant neoplasm of extrahepatic bile duct

C24.1 Malignant neoplasm of ampulla of Vater

C24.8 Malignant neoplasm of overlapping sites of biliary tract

C24.9 Malignant neoplasm of biliary tract, unspecified

C33 Malignant neoplasm of trachea

C34.01 Malignant neoplasm of right main bronchus

C34.02 Malignant neoplasm of left main bronchus

C34.11 Malignant neoplasm of upper lobe, right bronchus or lung
C34.12 Malignant neoplasm of upper lobe, left bronchus or lung
C34.2 Malignant neoplasm of middle lobe, bronchus or lung
C34.31 Malignant neoplasm of lower lobe, right bronchus or lung
C34.32 Malignant neoplasm of lower lobe, left bronchus or lung
C34.81 Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82 Malignant neoplasm of overlapping sites of left bronchus and lung
C34.91 Malignant neoplasm of unspecified part of right bronchus or lung
C34.92 Malignant neoplasm of unspecified part of left bronchus or lung
C45.0 Mesothelioma of pleura
C53.0 Malignant neoplasm of endocervix
C53.1 Malignant neoplasm of exocervix
C53.8 Malignant neoplasm of overlapping sites of cervix uteri
C53.9 Malignant neoplasm of cervix uteri, unspecified
C7A.1 Malignant poorly differentiated neuroendocrine tumors
D06.0 Carcinoma in situ of endocervix
D06.1 Carcinoma in situ of exocervix
D06.7 Carcinoma in situ of other parts of cervix
D06.9 Carcinoma in situ of cervix, unspecified

TREMELIMUMAB-ACT (IMJUDO®) IN CONJUNCTION WITH DURVALUMAB (IMFINZI®) IS
MEDICALLY NECESSARY WHEN REPORTED WITH THE FOLLOWING DIAGNOSIS CODES:

C15.3 Malignant neoplasm of upper third of esophagus
C15.4 Malignant neoplasm of middle third of esophagus
C15.5 Malignant neoplasm of lower third of esophagus
C15.8 Malignant neoplasm of overlapping sites of esophagus

C15.9 Malignant neoplasm of esophagus, unspecified

C16.0 Malignant neoplasm of cardia

C16.1 Malignant neoplasm of fundus of stomach

C16.2 Malignant neoplasm of body of stomach

C16.3 Malignant neoplasm of pyloric antrum

C16.4 Malignant neoplasm of pylorus

C16.5 Malignant neoplasm of lesser curvature of stomach, unspecified

C16.6 Malignant neoplasm of greater curvature of stomach, unspecified

C16.8 Malignant neoplasm of overlapping sites of stomach

C16.9 Malignant neoplasm of stomach, unspecified

C22.0 Liver cell carcinoma

C22.7 Other specified carcinomas of liver

C22.8 Malignant neoplasm of liver, primary, unspecified as to type

C22.9 Malignant neoplasm of liver, not specified as primary or secondary

C33 Malignant neoplasm of trachea

C34.01 Malignant neoplasm of right main bronchus

C34.02 Malignant neoplasm of left main bronchus

C34.11 Malignant neoplasm of upper lobe, right bronchus or lung

C34.12 Malignant neoplasm of upper lobe, left bronchus or lung

C34.2 Malignant neoplasm of middle lobe, bronchus or lung

C34.31 Malignant neoplasm of lower lobe, right bronchus or lung

C34.32 Malignant neoplasm of lower lobe, left bronchus or lung

C34.81 Malignant neoplasm of overlapping sites of right bronchus and lung

C34.82 Malignant neoplasm of overlapping sites of left bronchus and lung

C34.91 Malignant neoplasm of unspecified part of right bronchus or lung

C34.92 Malignant neoplasm of unspecified part of left bronchus or lung

Duration of authorization: 12 months

Version Effective Date: 05/06/2024

Title: Eculizumab (Soliris®) and Related Biosimilars, Ravulizumab-cwvz (Ultomiris®) for intravenous administration

MEDICALLY NECESSARY:

AROXYSMAL NOCTURNAL HEMOGLOBINURIA (PNH)

ECULIZUMAB (SOLIRIS) AND RELATED BIOSIMILARS

Eculizumab (Soliris) and related biosimilars, the Company's non-preferred products for PNH, are considered medically necessary and, therefore, covered for the treatment of PNH in adult individuals, when all of the following criteria are met, including dosing and frequency:

Initial Criteria

- The coverage will be provided for eculizumab (Soliris) and related biosimilars when one of the following is present:
 - There is a documented contraindication or documented nonresponse to ravulizumab-cwvz (Ultomiris).
 - The individual is currently receiving or has previously received a non-preferred product (e.g., eculizumab [Soliris]). (See COMPANY-DESIGNATED PREFERRED PRODUCTS and NON-PREFERRED PRODUCTS sections below).
- Flow cytometry demonstrates one of the following:
 - At least 10% PNH type III red cells
 - Greater than 50% of glycosylphosphatidylinositol-anchored proteins (GPI-AP)–deficient polymorphonuclear (PM) cells
- The individual is transfusion dependent due to PNH.
- The individual has platelet counts of at least 100,000 per cubic millimeter.
- The individual does not have unresolved *Neisseria meningitidis* infection.
- The individual is vaccinated against *N. meningitidis*, unless risk of delaying eculizumab (Soliris) outweighs the risks of developing meningococcal infection.
- Dosing and frequency for eculizumab (Soliris) and related biosimilars: initial dose, 600 mg by intravenous (IV) infusion weekly for 4 weeks; maintenance, 900 mg for the fifth dose 1 week later, and then 900 mg every 2 weeks thereafter.

Continuation Criteria

Eculizumab (Soliris) and related biosimilars are considered medically necessary and, therefore, covered for continuation therapy, when documentation is provided of positive clinical response (e.g., reduction in hemolysis manifested by stabilization of hemoglobin levels and reduction in transfusions from baseline at initiation).

RAVULIZUMAB-CWVZ (ULTOMIRIS™)

Ravulizumab-cwvz (Ultomiris) is considered medically necessary and, therefore, covered for adult and pediatric individuals 1 month of age or older with PNH when all of the following criteria are met, including dosing and frequency:

Initial Criteria

- The individual has a diagnosis of PNH confirmed by high-sensitivity flow cytometry of red and white blood cells with granulocyte or monocyte clone size of at least 5%.
- The individual has lactate dehydrogenase (LDH) level $\geq 1.5 \times$ upper normal limit (UNL) (adult: 100 to 190 units/L at 37°C) at initiation of the therapy.
- The individual does not have history of bone marrow transplantation.
- The individual does not have unresolved *N. meningitidis* infection.
- The individual is vaccinated against *N. meningitidis*, unless risk of delaying ravulizumab-cwvz (Ultomiris) outweighs the risks of developing meningococcal infection.
- Dosing and frequency for intravenous ravulizumab-cwvz (Ultomiris):
 - 5 kg to < 10 kg: loading dose, 600 mg; maintenance dose, 300 mg every 4 weeks.
 - 10 kg to < 20 kg: loading dose, 600 mg; maintenance dose, 600 mg every 4 weeks.
 - 20 kg to < 30 kg: loading dose, 900 mg; maintenance dose, 2100 mg every 8 weeks.
 - 30 kg to < 40 kg: loading dose, 1200 mg; maintenance dose, 2700 mg every 8 weeks.
 - 40 kg to < 60 kg: loading dose, 2400 mg; maintenance dose, 3000 mg every 8 weeks.
 - 60 kg to < 100 kg: loading dose, 2700 mg; maintenance dose, 3300 mg every 8 weeks.
 - ≥ 100 kg: loading dose, 3000 mg; maintenance dose, 3600 mg every 8 weeks.

Continuation Criteria (After 26 Weeks of Therapy)

Ravulizumab-cwvz (Ultomiris) is considered medically necessary and, therefore, covered for continuation therapy following at least 26 weeks of therapy for the treatment of PNH, when documentation is provided of positive clinical response (e.g., reduction in hemolysis manifested by a stabilization of hemoglobin levels and reduction in transfusions from baseline at initiation).

ATYPICAL HEMOLYTIC–UREMIC SYNDROME (aHUS)

ECULIZUMAB (SOLIRIS) AND RELATED BIOSIMILARS

Eculizumab (Soliris) and related biosimilars, the Company's non-preferred products for aHUS, are considered medically necessary and, therefore, covered for the treatment of pediatric and adult individuals with aHUS, when all of the following criteria are met, including dosing and frequency:

Initial Criteria

- The coverage will be provided for eculizumab (Soliris) and related biosimilars, when one of the following is present:
 - There is a documented contraindication or documented nonresponse to ravulizumab-cwvz (Ultomiris)

- The individual is currently receiving or has previously received a non-preferred product (e.g., eculizumab [Soliris]). (See COMPANY-DESIGNATED PREFERRED PRODUCTS and NON-PREFERRED PRODUCTS sections below).
- Diagnosis of thrombocytopenic purpura (TTP) has been excluded (e.g., normal ADAMTS-13 activity, or ADAMTS-13 activity <5%) OR a trial of plasma exchange did not result in clinical improvement.
- The individual does not have unresolved *N. meningitidis* infection.
- The individual is vaccinated against *N. meningitidis*, unless risk of delaying eculizumab (Soliris) outweighs risks of developing meningococcal infection.
- The individual has an absence of Shiga toxin–producing *Escherichia coli* infection.
- Dosing and frequency for eculizumab (Soliris) and related biosimilars for adult individual: initial, 900 mg by IV infusion weekly for 4 weeks; maintenance, 1200 mg for the fifth dose 1 week later, and then 1200 mg every 2 weeks thereafter.
- Dosing and frequency for eculizumab (Soliris) and related biosimilars for infants ≥2 months, children, and adolescents:
 - 5 kg to <10 kg: Induction: 300 mg weekly for one dose; maintenance: 300 mg at week 2, then 300 mg every 3 weeks
 - 10 kg to <20 kg: Induction: 600 mg weekly for one dose; maintenance: 300 mg at week 2, then 300 mg every 2 weeks
 - 20 kg to <30 kg: Induction: 600 mg weekly for two doses; maintenance: 600 mg at week 3, then 600 mg every 2 weeks
 - 30 kg to <40 kg: Induction: 600 mg weekly for two doses; maintenance: 900 mg at week 3, then 900 mg every 2 weeks
 - ≥40 kg: Induction: 900 mg weekly for four doses; maintenance: 1200 mg at week 5, then 1200 mg every 2 weeks
- Supplemental dosing for individuals receiving plasmapheresis or plasma exchange for adults and pediatric patients:
 - If the most recent dose was 300 mg, the dose is 300 mg within 60 minutes after each plasmapheresis or plasma exchange. If the most recent dose was ≥600 mg, dose is 600 mg, within 60 minutes after each plasmapheresis or plasma exchange.
- Supplemental dosing for adult and pediatric individuals receiving fresh frozen plasma infusion: if most recent dose was ≥300 mg, dose is 300 mg within 60 minutes prior to each infusion of fresh frozen plasma.

Continuation Criteria (After 26 Weeks of Therapy)

Eculizumab (Soliris) and related biosimilars are considered medically necessary and, therefore, covered for continuation therapy following at least 26 weeks of therapy for the treatment of aHUS when documentation is provided of reduction in signs of complement-mediated thrombotic microangiopathy (TMA), including at least two of the following:

- Platelet count increase from baseline at initiation
- Hematologic normalization (maintenance of normal platelet counts and LDH levels for at least 4 weeks)

- Complete complement-mediated TMA response (hematologic normalization plus at least 25% reduction in serum creatinine from baseline for at least 4 weeks)
- TMA-event free status (absence for at least 12 weeks of a decrease in platelet count of greater than 25% from baseline, treatment with plasma exchange or plasma infusion, or new dialysis treatment)
- Reduction in the daily TMA intervention rate (defined as the number of plasma exchange or plasma infusion interventions and the number of new dialysis required per individual per day)

RAVULIZUMAB-CWVZ (ULTOMIRIS)

Ravulizumab-cwvz (Ultomiris) is considered medically necessary and, therefore, covered for adult and pediatric individuals 1 month of age and older with aHUS to inhibit complement-mediated TMA when all of the following criteria are met, including dosing and frequency:

Initial Criteria

- The individual has evidence of TMA, including low platelet count, hemolysis (breaking of red blood cells inside of blood vessels), and decreased kidney function.
- The individual does not have ADAMTS-13 activity <5%.
- The individual does not have unresolved *N. meningitidis* infection.
- The individual is vaccinated against *N. meningitidis* unless risk of delaying ravulizumab-cwvz (Ultomiris) outweighs risks of developing meningococcal infection.
- The individual has an absence of Shiga toxin-producing *E. coli* infection.
- The individual does not have positive direct Coombs test.
- Dosing and frequency for intravenous ravulizumab-cwvz (Ultomiris) for adults and pediatric individuals 1 month of age and older, starting 2 weeks after the loading dose, begin maintenance doses:
 - 5 kg to < 10 kg: loading dose, 600 mg; maintenance dose, 300 mg every 4 weeks
 - 10 kg to < 20 kg: loading dose, 600 mg; maintenance dose, 600 mg every 4 weeks
 - 20 kg to < 30 kg: loading dose, 900 mg; maintenance dose, 2100 mg every 8 weeks
 - 30 kg to < 40 kg: loading dose, 1200 mg; maintenance dose, 2700 mg every 8 weeks
 - 40 kg to < 60 kg: loading dose, 2400 mg; maintenance dose, 3000 mg every 8 weeks
 - 60 kg to < 100 kg: loading dose, 2700 mg; maintenance dose, 3300 mg every 8 weeks
 - ≥ 100 kg: loading dose, 3000 mg; maintenance dose, 3600 mg every 8 weeks
 - For individuals switching from eculizumab (Soliris) or related biosimilars to intravenous ravulizumab-cwvz (Ultomiris), the loading dose of intravenous ravulizumab-cwvz (Ultomiris) administered 2 weeks after the last eculizumab (Soliris) infusion or related biosimilars, and then maintenance doses once every 8 weeks or every 4 weeks (depending on body weight), starting 2 weeks after loading dose administration.

Continuation Criteria (After 26 Weeks of Therapy)

Ravulizumab-cwvz (Ultomiris) is considered medically necessary and, therefore, covered for continuation therapy, following treatment of aHUS for at least 26 weeks when there is documentation demonstrating a positive clinical response from baseline (e.g., reduction of plasma exchanges, reduction of dialysis, increased platelet count, reduction of hemolysis).

GENERALIZED MYASTHENIA GRAVIS (gMG)

ECULIZUMAB (SOLIRIS) AND RELATED BIOSIMILARS

Eculizumab (Soliris) and related biosimilars, the Company's non-preferred products for generalized myasthenia gravis (gMG), are considered medically necessary and, therefore, covered for the treatment of adult individuals with gMG, when all of the following criteria are met, including dosing and frequency:

Initial Criteria

- The coverage will be provided for eculizumab (Soliris) and related biosimilars when one of the following is present:
 - There is a documented contraindication or documented nonresponse to ravulizumab-cwvz (Ultomiris).
 - The individual is currently receiving or has previously received a non-preferred product (e.g., eculizumab [Soliris]). (See COMPANY-DESIGNATED PREFERRED PRODUCTS and NON-PREFERRED PRODUCTS sections below).
- The individual is positive for antiacetylcholine receptor (AChR) antibodies and one of the following:
 - - History of abnormal neuromuscular transmission test demonstrated by single-fiber electromyography (SFEMG) or repetitive nerve stimulation, or
 - History of positive anticholinesterase test, e.g., edrophonium chloride test, or
 - The individual has demonstrated improvement in myasthenia gravis (MG) signs on oral cholinesterase inhibitors, as assessed by the treating professional provider.
- The individual meets Myasthenia Gravis Foundation of America (MGFA) Clinical Classification* Class II to IV.
- The individual has a Myasthenia Gravis–Specific Activities of Daily Living scale (MG-ADL)** total score of six or greater.
- Documentation of prior treatments with one of the following regimens:
 - Two or more immunosuppressive agents (azathioprine [AZA], cyclophosphamide [CY], cyclosporine [CYC], mycophenolate mofetil [MFF], methotrexate [MTX], or tacrolimus [TAC]) without symptom control, or
 - One immunosuppressive therapy and chronic intravenous immunoglobulin or plasma exchange for 12 months without symptom control
- The individual does not have unresolved *N. meningitidis* infection.
- The individual is vaccinated against *N. meningitidis*, unless risk of delaying eculizumab (Soliris) outweighs risks of developing meningococcal infection.

- Dosing and frequency for eculizumab (Soliris) and related biosimilars for adults (18 and older): Initial 900 mg weekly for four doses; maintenance: 1200 mg at week 5, then 1200 mg every 2 weeks thereafter.
- Supplemental dosing for adult individuals receiving plasmapheresis or plasma exchange:
 - If the most recent dose was 300 mg, dose is 300 mg within 60 minutes after each plasmapheresis or plasma exchange. If most recent dose was ≥ 600 mg, dose is 600 mg within 60 minutes after each plasmapheresis or plasma exchange.
- Supplemental dosing for adult individuals receiving fresh frozen plasma infusion: if the most recent dose was ≥ 300 mg, dose is 300 mg within 60 minutes prior to each infusion of fresh frozen plasma.

Continuation Criteria (After 26 Weeks of Therapy)

Eculizumab (Soliris) and related biosimilars are considered medically necessary and, therefore, covered for continuation therapy following at least 26 weeks of therapy for the treatment of gMG when documentation is provided of positive clinical response (e.g., demonstration of a clinically meaningful response regarding daily activities [≥ 3 point improvement in the MG-ADL from baseline]).

RAVULIZUMAB-CWVZ (ULTOMIRIS)

Ravulizumab-cwvz (Ultomiris) is considered medically necessary and, therefore, covered for the treatment of adult individuals with gMG when all of the following criteria are met, including dosing and frequency:

Initial Criteria

- The individual is positive for AchR antibodies and one of the following:
 - History of abnormal neuromuscular transmission test demonstrated by SFEMG or repetitive nerve stimulation, or
 - History of positive anticholinesterase test, e.g., edrophonium chloride test, or
 - The individual has demonstrated improvement in MG signs on oral cholinesterase inhibitors, as assessed by the treating professional provider.
- The individual meets MGFA Clinical Classification* Class II to IV.
- The individual has a MG-ADL** total score of six or greater.
- Documentation of prior treatments with one of the following regimens:
 - Azathioprine: must have been on AZA for ≥ 6 months (180 days) and have been on a stable dose for ≥ 2 months (60 days)
 - Immunosuppressive therapies (i.e., MMF, MTX, CYC, TAC, or CY), must have been on the immunosuppressive therapy for ≥ 3 months (90 days) and have been on a stable dose for ≥ 1 month (30 days)
 - Oral corticosteroids, must have been on a stable dose for ≥ 4 weeks (28 days)
 - A cholinesterase inhibitor, at the time of the screening visit, must have been on a stable dose for ≥ 2 weeks (14 days)
- The individual does not have unresolved *N. meningitidis* infection.
- The individual is vaccinated against *N. meningitidis*, within 3 years, or individuals who initiate ravulizumab-cwvz (Ultomiris) treatment less than 2 weeks after receiving a

meningococcal vaccine must receive treatment with appropriate prophylactic antibiotics until 2 weeks after vaccination

- Body weight ≥ 40 kg
- Dosing and frequency for intravenous ravulizumab-cwvz (Ultomiris) for adults (18 and older):
 - 40 kg to <60 kg: loading dose 2400 mg; maintenance dose, 3000 mg every 8 weeks.
 - 60 kg to <100 kg: loading dose, 2700 mg; maintenance dose, 3300 mg every 8 weeks.
 - ≥ 100 kg: loading dose, 3000 mg; maintenance dose, 3600 mg 8 weeks.

Continuation Criteria (After 26 Weeks of Therapy)

Ravulizumab-cwvz (Ultomiris) is considered medically necessary and, therefore, covered for continuation therapy following at least 26 weeks of therapy for the treatment of gMG when documentation is provided of positive clinical response (e.g., demonstration of a clinically meaningful response regarding daily activities [≥ 3 point improvement in the MG-ADL from baseline]).

NEUROMYELITIS OPTICA SPECTRUM DISORDER (NMOSD)

ECULIZUMAB (SOLIRIS) AND RELATED BIOSIMILARS

Eculizumab (Soliris) and related biosimilars, the Company's non-preferred products for NMOSD, are considered medically necessary and, therefore, covered for the treatment of pediatric and adult individuals with NMOSD, when all of the following criteria are met, including dosing and frequency:

Initial Criteria

- The coverage will be provided for eculizumab (Soliris) and related biosimilars when one of the following is present:
 - There is a documented contraindication or documented nonresponse to ravulizumab-cwvz (Ultomiris).
 - The individual is currently receiving or has previously received a non-preferred product (e.g., eculizumab [Soliris]). (See COMPANY-DESIGNATED PREFERRED PRODUCTS and NON-PREFERRED PRODUCTS sections below).
- The individual has diagnosis of neuromyelitis optica NMOSD.
- The individual is anti-aquaporin-4 (AQP4) antibody seropositive.
- The individual had historical relapse of at least two relapses in the last 12 months or three relapses in the last 24 months, with at least one relapse in the 12 months prior to the initiation of the therapy.
- The individual does not have unresolved *N. meningitidis* infection.
- The individual is vaccinated against *N. meningitidis*, unless risk of delaying eclizumab (Soliris) outweighs the risks of developing meningococcal infection.
- Dosing and frequency for eculizumab (Soliris) and related biosimilars for adults (18 and older):

- 900 mg weekly for the first 4 weeks, followed by
- 1200 mg for the fifth dose 1 week later, then
- 1200 mg every 2 weeks thereafter.

Continuation Criteria

Eculizumab or related biosimilars are considered medically necessary for continued use in adult individuals with diagnosis of NMOSD when the initial criteria are met AND there is documentation of a positive clinical response (e.g., reductions in relapse or reduction in new onset of symptoms).

RAVULIZUMAB-CWVZ (ULTOMIRIS)

Ravulizumab-cwvz (Ultomiris) is considered medically necessary and, therefore, covered for the treatment of adult individuals with NMOSD when all of the following criteria are met, including dosing and frequency:

Initial Criteria

- The individual has diagnosis of neuromyelitis optica spectrum disorder (NMOSD)
- The individual is anti-aquaporin-4 (AQP4) antibody seropositive.
- The individual had at least one attack or relapse in the last 12 months prior to initiation of the therapy.
- The individual has Expanded Disability Status Scale score ≤ 7 .
- The individual has body weight ≥ 40 kilograms.
- The individual does not have unresolved N. meningitidis infection.
- The individual is vaccinated against N. meningitidis, unless risk of delaying eclizumab (Soliris) outweighs the risks of developing meningococcal infection.
- Dosing and frequency for intravenous ravulizumab-cwvz (Ultomiris):
 - 40 kg to < 60 kg: loading dose, 2400 mg; maintenance dose, 3000 mg every 8 weeks.
 - 60 kg to < 100 kg: loading dose, 2700 mg; maintenance dose, 3300 mg every 8 weeks.
 - ≥ 100 kg: loading dose, 3000 mg; maintenance dose, 3600 mg every 8 weeks.

Continuation Criteria

Ravulizumab-cwvz (Ultomiris) is considered medically necessary for continued use in adult individuals with diagnosis of NMOSD when the initial criteria are met AND there is documentation of a positive clinical response (e.g., reductions in relapse or reduction in new onset of symptoms).

COMPANY-DESIGNATED PREFERRED PRODUCTS FOR PAROXYSMAL NOCTURNAL HEMOGLOBINURIA, ATYPICAL HEMOLYTIC–UREMIC SYNDROME, GENERALIZED MYASTHENIA GRAVIS AND NEUROMYELITIS OPTICA SPECTRUM DISORDER

Although there are additional brand(s) of terminal complement inhibitor therapy on the market

for the treatment of PNH, aHUS, gMG, and NMOSD there is no reliable evidence of the superiority of any one brand compared with other brand(s). The Company has designated ravulizumab-cwvz (Ultomiris) as its preferred product.

This product is less costly and at least as likely to produce equivalent therapeutic results as the non-preferred products, which include, but are not limited to, eculizumab (Soliris) or related biosimilars.

For individuals who meet the above medical necessity criteria, use of the Company-designated preferred product, ravulizumab-cwvz (Ultomiris), is considered medically necessary and, therefore, covered.

NON-PREFERRED PRODUCTS FOR PAROXYSMAL NOCTURNAL HEMOGLOBINURIA, ATYPICAL HEMOLYTIC-UREMIC SYNDROME, GENERALIZED MYASTHENIA GRAVIS AND NEUROMYELITIS OPTICA SPECTRUM DISORDER

For individuals who meet the above medical necessity criteria, use of non-preferred products (which include, but are not limited to, eculizumab [Soliris]) or related biosimilars is considered medically necessary and, therefore, covered in at least one of the following instances*:

- Individual has a documented contraindication or documented non-response to the preferred product ravulizumab-cwvz (Ultomiris).
- Individual is currently receiving or has previously received a non-preferred product.

*Requests for the use of non-preferred products that do not meet either of these conditions are considered not medically necessary and, therefore, not covered.

Duration of authorization: 12 months

Version Effective Date: 04/01/2025

Title: Efbemalenograstim alfa-vuxw (Ryzneuta®), Eflapegrastim-xnst (Rolvedon™), Pegfilgrastim (Neulasta®) and Related Biosimilars

MEDICALLY NECESSARY:

COMPANY-DESIGNATED PREFERRED PRODUCTS

Although there are many pegfilgrastim products on the market, there is no reliable evidence of the superiority of any of these products. The preferred products, pegfilgrastim (Neulasta) and pegfilgrastim-apgf (Nyvepria), are less costly and at least as likely to produce equivalent therapeutic results as the nonpreferred products.*

PREFERRED PEGFILGRASTIM PRODUCTS	NONPREFERRED PRODUCTS*
Pegfilgrastim (Neulasta)	pegfilgrastim-bmez [Ziextenzo]
Pegfilgrastim-apgf (Nyvepria)	pegfilgrastim-cbqv [Udenyca]
	pegfilgrastim-jmdb [Fulphila]
	pegfilgrastim-pbbk [Fylnetra]
	pegfilgrastim-fpgk [Stimufend]
	eflapegrastim-xnst [Rolvedon]
	efbemalenograstim alfa-vuxw [Ryzneuta]

According to the US Food and Drug Administration (FDA), “a biosimilar is a biological product that has no clinically meaningful differences from the existing FDA-approved reference product. All biosimilar products meet the FDA’s rigorous standards for approval for the indications described in the product labeling. Once a biosimilar has been approved by the FDA, the safety and effectiveness of these products have been established, just as they have been for the reference product.” Coverage of a biosimilar product as an alternate to a reference product is not considered a form of step therapy by the Company.

NONPREFERRED PRODUCTS*

Use of the nonpreferred pegfilgrastim/eflapegrastim/efbemalenograstim products is considered medically necessary and, therefore, covered only for individuals who are currently receiving or have previously received a nonpreferred product for the specified pegfilgrastim indication.

If the individual has not previously received a nonpreferred pegfilgrastim biosimilar, efbemalenograstim or eflapegrastim product to treat the specified indication, these nonpreferred products are only eligible for coverage when the individual has contraindication(s) or intolerance(s) to the Company-designated preferred products.

EFBEMALENOGRASTIM ALFA-VUXW (RYZNEUTA), EFLAPEGRASTIM-XNST (ROLVEDON), PEGFILGRASTIM (NEULASTA), AND RELATED BIOSIMILARS

Efbemalenograstim alfa-vuxw (Ryzneuta), eflapegrastim-xnst (Rolvedon), pegfilgrastim (Neulasta), and related biosimilars are considered medically necessary and, therefore, covered when used as recommended by the then-current National Comprehensive Cancer Network (NCCN) and American Society of Clinical Oncology (ASCO) guidelines for any of the following indications:

- Prophylaxis of myelosuppressive chemotherapy-induced febrile neutropenia or other dose-limiting neutropenic events in high-risk[†] (>20% overall risk of febrile neutropenia) individuals with solid tumors and nonmyeloid malignancies receiving treatment in the curative/adjuvant or palliative settings
- Prophylaxis of myelosuppressive chemotherapy-induced febrile neutropenia or other dose-limiting neutropenic events in intermediate-risk* (10%–20% overall risk of febrile neutropenia with one of more risk factors below) or low-risk[†] (<10% overall risk of febrile neutropenia with two or more risk factors below) in individuals with solid tumors and nonmyeloid malignancies receiving treatment in the curative/adjuvant or palliative settings who have one or more of the following risk factors:
 - Prior chemotherapy or radiation therapy
 - Persistent neutropenia
 - Bone marrow involvement by tumor
 - Recent surgery and/or open wounds
 - Liver dysfunction (bilirubin >2 mg/dL)
 - Renal dysfunction (creatinine clearance <50 mL/min)
 - Age greater than 65 years receiving full chemotherapy dose intensity
 - Poor performance status (Eastern Cooperative Oncology Group [ECOG] Performance Status 3–4)
 - Human immunodeficiency virus (HIV) infection with low CD4 counts (450 cells/mm³ or less)
 - Chronic immunosuppression in the posttransplant setting, including organ transplant

^{*†}*See Attachment A for examples of disease settings and chemotherapy regimens with a high (>20%) or intermediate (10%–20%) risk for febrile neutropenia (Note: These are not all-inclusive lists.)*

- Prophylaxis of chemotherapy-induced febrile neutropenia in individuals with one of the following indications, regardless of risk status:
 - Acute lymphoblastic leukemia (ALL) or acute myeloid leukemia (AML) in pediatric individuals who have relapsed disease and have serious/life-threatening neutropenic infection
 - Diffuse aggressive lymphoma in individuals age 65 years and older treated with the curative chemotherapy regimen cyclophosphamide, doxorubicin, vincristine, prednisone, and rituximab (R-CHOP)
 - In pediatric individuals in whom dose-intense chemotherapy is administered for an indication that is known to have a survival benefit (e.g., Ewing sarcoma)
 - Dose-dense therapy (standard doses given more frequently) for the adjuvant treatment of high-risk breast cancer or for use of high-dose intensity methotrexate, vinblastine, doxorubicin, and cisplatin (HD-MVAC) in urothelial cancer
- Prophylaxis of chemotherapy-induced febrile neutropenia in individuals with Wilms tumor (nephroblastoma), when administered with Regimen M and Regimen I for courses of either:
 - Cyclophosphamide and etoposide
 - Cyclophosphamide, doxorubicin, and vincristine
- Secondary prophylaxis in individuals who have experienced a neutropenic event from a prior cycle of chemotherapy (for which primary prophylaxis was not received), in which a reduced dose or treatment delay may compromise disease-free or overall survival or treatment outcome
- Therapeutic use in individuals with cancer who have fever and neutropenia and are at high risk for infection-associated complications or who have prognostic factors that are predictive of poor clinical outcomes. High-risk features include the following factors:
 - Expected prolonged (>10 days) and profound (<0.1 × 10⁹/L) neutropenia
 - Age greater than 65 years
 - Pneumonia

- Hypotension and multiorgan dysfunction (sepsis syndrome)
 - Invasive fungal infection
 - Hospitalization at the time of fever development
 - Other clinically documented infections
 - Prior episode of febrile neutropenia
- Hematopoietic subsyndrome of acute radiation syndrome (H-ARS): Therapeutic use after accidental or intentional total body radiation of myelosuppressive doses (>2 Gy), if prolonged delays secondary to neutropenia are expected.
 - Use of the on-body injector for Neulasta (Neulasta Onpro kit) has not been studied and is not recommended for this indication.
- Mobilization of peripheral blood progenitor cells prior to autologous transplantation in individuals with hematological malignancies, when used alone, after chemotherapy, or in combination with plerixafor.
- After autologous or allogeneic hematopoietic stem cell transplant to reduce the duration of severe neutropenia.

Duration of authorization: 12 months Version

Effective Date: 06/16/2025

Title: Efgartigimod alfa - fcab (Vyvgart) and efgartigimod alfa and hyaluronidase-qvfc (Vyvgart Hytrulo)

MEDICALLY NECESSARY:

EFGARTIGIMOD ALFA-FCAB (VYVGART) AND EFGARTIGIMOD ALFA AND HYALURONIDASE-QVFC (VYVGART HYTRULO)

Generalized myasthenia gravis (gMG)

Efgartigimod alfa-fcab (Vyvgart) and efgartigimod alfa and hyaluronidase-qvfc (Vyvgart Hytrulo) are considered medically necessary and, therefore, covered for the treatment of adult individuals with generalized gMG when all of the following criteria are met:

- The individual is anti-acetylcholine receptor (AChR) antibody-positive.
- The individual meets Myasthenia Gravis Foundation of America (MGFA) Clinical Classification Class II to IV.
- The individual has a Myasthenia Gravis–Specific Activities of Daily Living scale (MG-ADL) total score of five or greater.
- The individual is on a stable dose of MG therapy either in combination or alone of any of the following medication:
 - Acetylcholinesterase (AChE) inhibitors
 - Steroids
 - Nonsteroidal immunosuppressive therapies (NSISTs)

EFGARTIGIMOD ALFA AND HYALURONIDASE-QVFC (VYVGART HYTRULO)

Chronic inflammatory demyelinating polyneuropathy (CIDP)

Efgartigimod alfa and hyaluronidase-qvfc (Vyvgart Hytrulo) is considered medically necessary and, therefore, covered for the treatment of adult individuals with CIDP when all of the following criteria are met:

- The individual is 18 years of age or older
- The individual has a diagnosis of CIDP when all of the following criteria are met:
 - The individual has progressive or relapsing motor or sensory impairment caused by neuropathy in more than one limb for at least 2 months
 - The individual has at least one of the following electrodiagnostic findings of demyelination:
 - Motor distal latency prolongation in two nerves
 - Reduction of motor conduction velocity in two nerves
 - Prolongation of F-wave latency in two nerves
 - Absence of F-waves in at least one nerve
 - Motor conduction block in at least one nerve
 - Abnormal temporal dispersion in at least two nerves
 - Distal compound muscle action potential (CMAP) duration increase in at least one nerve
- The individual is being treated by or under the supervision of a neurologist

- The individual has had previous treatment with, or has contraindication or intolerance to, an intravenous immune globulin (IVIG) or subcutaneous immune globulin (SCIG) product

Duration of authorization: 12 months

Version Effective Date: 10/07/2024

Title: Eladocagene exuparvovec-tneq (Kebilidi™)

MEDICALLY NECESSARY:

Eladocagene exuparvovec-tneq (Kebilidi™) is considered medically necessary, and, therefore, covered when ALL of the following criteria are met in individuals with aromatic L-amino acid decarboxylase (AADC) deficiency:

- Adults and pediatric individuals who have achieved skull maturity assessed by neuroimaging
- Prescribed by or in consultation with a pediatric neurologist or a neurologist for adults
- Individual's diagnosis is confirmed based on ALL of the following:
 - Genetic testing showing biallelic pathogenic variation(s) in the DOPA decarboxylase (DDC) gene
 - Reduced levels of 5-hydroxyindoleacetic acid (5-HIAA), homovanillic acid (HVA) and 3-methoxy-4-hydroxyphenylglycol (MHPG) and high concentrations of 3-O-methyldopa (3-OMD), L-Dopa, and 5-OH tryptophan (5-HTP) in the cerebral spinal fluid (CSF)
 - Reduced aromatic L-amino acid decarboxylase (AADC) activity in the plasma
- Individual presents with classic clinical characteristics of AADC deficiency, such as oculogyric crises, hypotonia, and developmental delay
- Individual does not have any significant structural brain abnormality
- Individual experiences persistent neurological defects despite standard medical therapy (e.g., dopamine agonists, monoamine oxidase inhibitor, pyridoxine or other forms of vitamin B6)
- Individual does not have an anti-AAV2 neutralizing antibody titer over 1200 folds
- Individual does not have pyridoxine 5'-phosphate oxidase or tetrahydrobiopterin (BH4) deficiency
- Individual has not received prior gene therapy treatment

Duration of authorization: 12 months

Version Effective Date: 05/05/2025

Title: Elivaldogene Autotemcel [eli-cel (Skysona®)]

MEDICALLY NECESSARY:

Elivaldogene autotemcel (Skysona®) is considered medically necessary and, therefore, covered for the treatment of cerebral adrenoleukodystrophy (CALD) when the individual meets ALL of the following criteria:

- Male, age 4 years to 17 years
- Documentation of adrenoleukodystrophy as demonstrated by meeting BOTH of the following:
 - Genetic confirmation of a pathogenic variant, or likely pathogenic variant, in the adenosine triphosphate binding cassette, sub family D member 1 (ABCD1) gene
 - Elevated very-long-chain fatty acid levels according to the standard reference values of the performing laboratory
- Documentation of early, active CALD as demonstrated by meeting ALL of the following:
 - Neurologic function score (NFS) less than or equal to 1
 - Gadolinium enhancement (GdE+) on brain magnetic resonance imaging (MRI)
 - Loes score between 0.5 and 9
- Has not received a prior allogeneic hematopoietic stem cell transplant (allo-HSCT)
- Documentation of ALL of the following:
 - Adequate hepatic function by meeting ALL of the following:
 - Aspartate aminotransferase values are no greater than 2.5 times the upper limit of normal
 - Alanine aminotransferase values are no greater than 2.5 times the upper limit of normal
 - Total bilirubin values are no greater than 3.0 mg/dL
 - Adequate hematological function as evidenced by ALL of the following:
 - Peripheral blood absolute neutrophil count of at least 1,500 cells/mm³
 - Platelet count of at least 100,000 cells/mm³
 - Hemoglobin of at least 10 g/dL
 - No uncorrected bleeding disorder
 - Adequate renal function by meeting ONE of the following:
 - Estimated creatinine clearance is at least 50 mL/min
 - Estimated glomerular filtration rate is at least 70 mL/minute/1.73 m²
 - Adequate cardiac function as evidenced by a left ventricular ejection fraction greater than 40%
 - Prior to collection of cells for manufacturing, screening for ALL of the following is negative:
 - Hepatitis B virus
 - Hepatitis C virus
 - Human T-lymphotropic virus 1 and 2
 - Human immunodeficiency virus 1 and 2
- Gene replacement therapy is prescribed by a hematologist, a neurologist, and/or a stem cell transplant specialist, who attest(s) to the following:

- No active bacterial, viral, fungal or parasitic infection
- No prior or current malignancy or myeloproliferative disorder
- No familial cancer syndrome or a history of such in their immediate family
- The individual would otherwise have been eligible to receive HSCT, but is unable to receive due to not having a matched sibling donor (10/10 HLA match [excluding female heterozygotes])

Duration of authorization: 12 months

Version Effective Date: 06/26/2024

Title: Elranatamab-bcmm (Elrexio™)

MEDICALLY NECESSARY:

Elranatamab-bcmm (Elrexio) injection is considered medically necessary and, therefore, covered as a single agent in adult individuals with refractory or relapsed multiple myeloma (RRMM) who have received at least four prior therapies, including a proteasome inhibitor (e.g., bortezomib, carfilzomib, ixazomib), an immunomodulatory agent (e.g., thalidomide, lenalidomide, pomalidomide), and an anti-CD38 monoclonal antibody (isatuximab-irfc, daratumumab) as National Comprehensive Cancer Network (NCCN)-preferred therapy.

HOSPITAL ADMISSION FOR ADMINISTRATION

When the medical necessity criteria has been met, the hospital admission for first cycle administration of elranatamab-bcmm (Elrexio), as recommended by the US Food and Drug Administration (FDA), is covered in accordance with the following timeframes*:

- First cycle: Individuals should be hospitalized for 48 hours after administration of the first step-up dose, and for 24 hours after administration of the second step-up dose due to the risk of cytokine release syndrome (CRS) and immune effector cell–associated neurotoxicity syndrome (ICANS)

*Hospital stays that are longer than the preceding timeframes must be re-evaluated for medical necessity.

Duration of authorization: 12 months

Version Effective Date: 04/02/2025

Title: Emapalumab-lzsg (Gamifant®)

MEDICALLY NECESSARY:

Emapalumab-lzsg (Gamifant®) is considered medically necessary and, therefore, covered for the treatment of pediatric (newborn and older) and adult individuals with the diagnosis of primary hemophagocytic lymphohistiocytosis (HLH)* when all of the following criteria are met, including dosing and frequency:

- Diagnosis of primary HLH confirmed by criteria described below*
- Individual has refractory, recurrent, or progressive disease
- Individual has a documented failure, contraindication, or intolerance to conventional HLH therapy (i.e., dexamethasone and etoposide [VP-16]. Intrathecal methotrexate and hydrocortisone for those with central nervous system disease)
- Individual has body weight of 3 kilograms or more
- Emapalumab-lzsg (Gamifant) is not administered concurrently with any biologic
- Dosing and frequency:
 - Initial dosing: 1 mg/kg intravenous (IV) infusion twice per week (every 3 to 4 days); titration, may increase to 3 mg/kg on Day 3 or to 6 mg/kg on Day 6 onwards for unsatisfactory improvement in clinical condition and at least one of the following:
 - Fever persistence/recurrence, splenomegaly worsening, coagulopathy (D-dimer abnormal at baseline and not improved plus fibrinogen at <100 mg/dL); ferritin less than 20 percent decrease from baseline of 3000 ng/mL or greater or any increase above 3000 ng/mL from baseline below 3000 ng/mL; neutrophil count not improved to above 500/mm³ from baseline of less than 500/mm³ or decreased to less than 500/mm³ from baseline of 500 to 1000/mm³ or decreased to less than 1000/mm³ from baseline of 1000 to 1500/mm³; platelet count not improved to more than 50,000/mm³ from baseline of less than 50,000/mm³ or less than 30 percent improvement from baseline of greater than 50,000/mm³ or any decrease to under 100,000/mm³ from baseline greater than 100,000/mm³
 - From Day 9 onwards, may increase to 10 mg/kg dose if clinically indicated; decrease dose to previous level once stabilized
 - Continuation: administer until hematopoietic stem cell transplantation is performed or until unacceptable toxicity; discontinue when individual no longer requires therapy for treatment of the condition
 - Emapalumab-lzsg (Gamifant) must be administered with dexamethasone

*The diagnosis of HLH is made based on the presence of clinical criteria and is confirmed by molecular genetic testing for this autosomal recessive disease. Five disease subtypes (FHL1, FHL2, FHL3, FHL4, and FHL5) are described in the literature and can be inherited in a homozygous or compound heterozygous pattern. Four genes in which pathogenic variants are causative have been identified: PRF1 (FHL2), UNC13D (FHL3), STX11 (FHL4), and STXBP2 (FHL5).

Examples of pathogenic variants for PRF1 include but not limited to: p. 54R > C/91A > V and p.47G > V

Examples of pathogenic variants for UNC13D include but not limited to: c.118-308C>T and (253-kb inversion)

Examples of pathogenic variants for STX 11 include but not limited to: 73 G > T (E25X) and 106G > C (E36Q)

Examples of pathogenic variants for STXBP2 include but not limited to: c.1430C>T and c.1214G>A

In adults, diagnosis confirmed by heterozygosity of one of the above genes together with clinical findings associated with HLH OR five of the following eight findings:

- Prolonged fever (more than 7 days) of 101.3°F or higher
- Splenomegaly
- Peripheral blood cytopenia, with at least two of the following: hemoglobin less than 9 g/dL (for infants <4 weeks, hemoglobin <10 g/dL); platelets less than 100,000/ μ L; absolute neutrophil count less than 1000/ μ L
- Hypertriglyceridemia (fasting triglycerides >265 mg/dL) and/or hypofibrinogenemia (fibrinogen <150 mg/dL)
- Hemophagocytosis in bone marrow, spleen, lymph node, or liver
- Low or absent Natural Killer cell activity
- Ferritin greater than 500 ng/mL
- Elevated soluble CD25 (soluble IL-2 receptor alpha [sIL-2R]) two standard deviations above age-adjusted laboratory-specific norms

Duration of authorization: 12 months

Version Effective Date: 10/21/2024

Title: Enfortumab vedotin-ejfv (Padcev®)

MEDICALLY NECESSARY:

INITIAL THERAPY

Locally Advanced or Metastatic Urothelial Cancer

Enfortumab vedotin-ejfv (Padcev) is considered medically necessary and, therefore, covered for adult individuals with locally advanced or metastatic urothelial cancer (la/mUC) when **all** of the following criteria listed below, including dosing and frequency, are met:

- In **one** of the following regimens:
 - In combination with pembrolizumab (Keytruda) as first-line systemic therapy
 - In combination with pembrolizumab (Keytruda) as first-line systemic therapy for individuals who are ineligible for cisplatin-containing chemotherapy (National Comprehensive Cancer Network [NCCN] preferred)
 - As a single agent
 - When **one** of the following is met:
 - Previously received a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor and platinum-containing chemotherapy
 - Are ineligible for cisplatin-containing chemotherapy and have previously received one or more prior lines of therapy
- Absent of active central nervous system metastases
- Eastern Cooperative Oncology Group (ECOG) performance status score of 0-2
- Dosing and frequency in **one** of the following regimens:
 - As a single agent: 1.25 mg/kg (up to a maximum dose of 125 mg) on Days 1, 8, and 15 of a 28-day cycle until disease progression or unacceptable toxicity
 - In combination with pembrolizumab (Keytruda): 1.25 mg/kg (up to a maximum dose of 125 mg) on Days 1 and 8 of a 21-day cycle until disease progression or unacceptable toxicity

Bladder Cancer

Enfortumab vedotin-ejfv (Padcev) is considered medically necessary and, therefore, covered for adult individuals with bladder cancer when **one** of the following criteria are met, including dosing and frequency:

- First-line therapy in combination with pembrolizumab (Keytruda) as NCCN-preferred for metastatic disease
- First-line therapy in combination with pembrolizumab (Keytruda) as NCCN-preferred in one of the following scenarios:
 - Stage II (cT2, N0) disease or stage IIIA (cT3, N0; cT4a, N0; cT1-T4a, N1) disease if tumor is present following reassessment of tumor status 2 to 3 months after primary treatment with either:
 - Bladder-preserving concurrent chemoradiotherapy and maximal transurethral resection of bladder tumor (TURBT)

- Radiotherapy alone or TURBT
 - Stage IIIB (cT1-T4a, N2,3) disease as either:
 - Downstaging systemic therapy
 - Partial response or progression after primary treatment with concurrent chemoradiotherapy
 - Stage IVA (cT4b, any N, M0; any T, any N, M1a) disease
 - Stage IVA (cT4b, any N, M0) disease as consolidation systemic therapy if no tumor present following reassessment of tumor status 2 to 3 months after primary treatment with concurrent chemoradiotherapy
 - Stage IVA (cT4b, any N, M0) disease if tumor present following reassessment of tumor status 2 to 3 months after primary treatment with concurrent chemoradiotherapy
 - Metastatic stage IVB (any T, any N, M1b) disease
 - Muscle invasive local recurrence or persistent disease in a preserved bladder treated with curative intent
 - Metastatic or local recurrence post cystectomy treated with curative intent
- Second or subsequent-line systemic therapy when all criteria are met:
 - As a single agent in **one** of the following regimens:
 - Second-line systemic therapy postplatinum or other chemotherapy for cisplatin-ineligible individuals who received one or more prior lines of therapy (NCCN alternative preferred) or post-checkpoint inhibitor (NCCN preferred for cisplatin ineligible, chemotherapy naive)
 - Second-line systemic therapy if a first-line therapy containing both platinum chemotherapy and an immune checkpoint inhibitor was used, including maintenance checkpoint inhibitor
 - Subsequent-line systemic therapy (individuals should have already received platinum and a checkpoint inhibitor, if eligible), NCCN-preferred
 - For any of the following scenarios:
 - Stage II (cT2, N0) disease or IIIA (cT3, N0; cT4a, N0; cT1-T4a, N1) disease if tumor is present following reassessment of tumor status 2 to 3 months after primary treatment with concurrent bladder-preserving chemoradiotherapy and maximal transurethral resection of bladder tumor (TURBT)
 - Stage IIIB (cT1-T4a, N2,3) disease following partial response or progression after primary treatment with downstaging systemic therapy or concurrent chemoradiotherapy
 - Stage IVA (cT4b, and N, M0) disease if tumor is present following reassessment of tumor status after primary treatment with first-line systemic therapy or concurrent chemoradiotherapy
 - Stage IVA (any T, any N, M1a) disease if stable disease or progression following reassessment of tumor status after primary treatment with first-line systemic therapy
 - Metastatic stage IVB (any T, any N, M1b) disease

- Muscle invasive local recurrence or persistent disease in a preserved bladder treated with curative intent
- Metastatic or local recurrence post-cystectomy treated with curative intent
- Dosing and frequency in **one** of the following regimens:
 - As a single agent: 1.25 mg/kg (up to a maximum dose of 125 mg) days 1, 8, and 15 every 28-day cycle until disease progression or unacceptable toxicity
 - In combination with pembrolizumab (Keytruda): 1.25 mg/kg (up to a maximum dose of 125 mg) days 1 and 8 every 21-day cycle until disease progression or unacceptable toxicity

Upper Genitourinary (GU) Tract Tumors/Urothelial Carcinoma of the Prostate

Enfortumab vedotin-ejfv (Padcev) is considered medically necessary and, therefore, covered for adult individuals with upper genitourinary tract tumors, or urothelial carcinoma of the prostate as therapy for metastatic disease, when **both** of the following criteria are met, including dosing and frequency:

- In **one** of the following regimens:
 - In combination with pembrolizumab (Keytruda) as first-line systemic therapy (NCCN preferred)
 - As a single agent for **one** of the following:
 - Second-line systemic therapy for cisplatin-ineligible individuals who received one or more prior lines of therapy postplatinum or other chemotherapy (NCCN alternative preferred)
 - Second-line systemic therapy post-checkpoint inhibitor (NCCN preferred for cisplatin ineligible, chemotherapy naïve)
 - Second-line systemic therapy if a first-line therapy containing both platinum chemotherapy and an immune checkpoint inhibitor was used, including maintenance checkpoint inhibitor (NCCN preferred)
 - Subsequent-line systemic therapy (NCCN preferred) for individuals who received a first-line platinum-containing chemotherapy including maintenance checkpoint inhibitor, if eligible
- Dosing and frequency in **one** of the following regimens:
 - As a single agent: 1.25 mg/kg (up to a maximum dose of 125 mg) on Days 1, 8, and 15 of a 28-day cycle until disease progression or unacceptable toxicity
 - In combination with pembrolizumab (Keytruda): 1.25 mg/kg (up to a maximum dose of 125 mg) on Days 1 and 8 of a 21-day cycle until disease progression or unacceptable toxicity

Primary Carcinoma of the Urethra

Enfortumab vedotin-ejfv (Padcev) is considered medically necessary and, therefore, covered for adult individuals with primary carcinoma of the urethra as therapy for recurrent or metastatic disease, when **both** of the following criteria are met, including dosing and frequency:

- In **one** of the following regimens:

- In combination with pembrolizumab (Keytruda) as first-line systemic therapy for metastatic disease in cisplatin-ineligible individuals (NCCN preferred)
- As a single agent for recurrent (except stage T3-4 disease or palpable inguinal lymph nodes) or metastatic disease as **one** of the following:
 - Second-line systemic therapy for cisplatin-ineligible individuals who received one or more prior lines of therapy postplatinum or other chemotherapy (NCCN alternative preferred)
 - Second-line systemic therapy post–checkpoint inhibitor (NCCN preferred for cisplatin ineligible, chemotherapy naïve)
 - Second-line systemic therapy if a first-line therapy containing both platinum chemotherapy and an immune checkpoint inhibitor was used, including maintenance checkpoint inhibitor (NCCN preferred)
 - Subsequent-line systemic therapy (NCCN preferred) for individuals who received platinum-containing chemotherapy and a checkpoint inhibitor
- Dosing and frequency in **one** of the following regimens:
 - As a single agent: 1.25 mg/kg (up to a maximum dose of 125 mg) on Days 1, 8, and 15 of a 28-day cycle until disease progression or unacceptable toxicity
 - In combination with pembrolizumab (Keytruda): 1.25 mg/kg (up to a maximum dose of 125 mg) on Days 1 and 8 of a 21-day cycle until disease progression or unacceptable toxicity

CONTINUATION THERAPY

Continuation of treatment with enfortumab vedotin-ejfv (Padcev) is considered medically necessary and, therefore, covered for adult individuals with bladder cancer when **both** of the following criteria listed below are met:

- Currently treated with enfortumab vedotin-ejfv (Padcev) and continues to meet initial criteria above
- Demonstrated continued clinical benefit on enfortumab vedotin-ejfv (Padcev) therapy as defined by tumor response or lack of disease progression, and an acceptable toxicity profile

Duration of authorization: 12 months

Version Effective Date: 04/02/2025

Title: Enzyme Replacement for the Treatment of Gaucher's Disease

MEDICALLY NECESSARY:

Imiglucerase (Cerezyme®), taliglucerase alfa (ElELYso®) and velaglucerase alfa (VPRIV®) are considered medically necessary and, therefore, covered, as long-term enzyme replacement therapy (ERT) for pediatric and adult individuals with a confirmed diagnosis of Type 1 Gaucher's disease or those with clinical non-neuropathic manifestations of Type 3 Gaucher's disease, when all of the following criteria are met, including dosing and frequency:

- Diagnosis is confirmed by one of the following:
 - Deficiency of glucosylceramidase in peripheral blood leukocytes or other nucleated cells
 - Confirmation of biallelic pathogenic variant(s) in the GBA gene and resulting in one or more of the following conditions
 - Anemia
 - Bone disease
 - Hepatomegaly or splenomegaly
 - Thrombocytopenia
- Dosing and frequency for imiglucerase (Cerezyme®): initial dosages range from 2.5 U/kg of body weight 3 times a week to 60 U/kg once every 2 weeks. Maintenance dosages 30-60 U/kg every 2 weeks.
- Dosing and frequency for taliglucerase alfa (ElELYso®): initial dose 60 units/kg every 2 weeks, then dosing is individualized based on achievement and maintenance of therapeutic goals. If switching from imiglucerase therapy, use the same unit/kg dose in stable individuals.
- Dosing and frequency for velaglucerase alfa (VPRIV®): initial dosage for VPRIV in naïve adults and naïve pediatric individuals 4 years of age and older is 60 Units/kg administered every other week. Dosages are further individualized.

Duration of authorization: 12 months

Version Effective Date: 05/28/2025

Title: Epcoritamab-bysp (EPKINLY®)

MEDICALLY NECESSARY:

INITIAL THERAPY

Epcoritamab-bysp (Epkinly) is considered medically necessary and, therefore, covered as a single agent in adult individuals with partial response, no response, progressive, relapsed or refractory (including disease progression posttransplant or chimeric antigen receptor [CAR] T-cell therapy) when any of the following criteria are met:

Diffuse Large B-Cell Lymphoma (DLBCL)

Third-line and subsequent therapy in one of the following conditions (National Comprehensive Cancer Network [NCCN]-preferred):

- Diffuse large B-cell lymphoma, not otherwise specified (DLBCL, NOS)
- High-grade B-cell lymphoma

Histologic Transformation of Indolent Lymphomas to Diffuse Large B-Cell Lymphoma

- Third-line therapy (NCCN-preferred therapy) in individuals who have been previously treated with an anthracycline-based regimen and no intention to proceed to transplant for all subtypes of transformed indolent lymphomas
- Third-line and subsequent therapy in individuals with DLBCL arising from indolent lymphoma

Human Immunodeficiency Virus (HIV)-Related B-Cell Lymphomas

Third-line and subsequent therapy in one of the following conditions:

- HIV-related diffuse large B-cell lymphoma
- Primary effusion lymphoma
- Human herpesvirus 8 (HHV8)-positive diffuse large B-cell lymphoma, not otherwise specified

Post-Transplant Lymphoproliferative Disorders (PTLD)

Third-line and subsequent therapy in individuals with monomorphic PTLD (B-cell type)

Classic Follicular Lymphoma

Third-line and subsequent therapy in individuals with classic follicular lymphoma

CONTINUATION THERAPY

Epcoritamab-bysp (Epkinly) is considered medically necessary and, therefore, covered for continuation therapy when there is documentation of no evidence of unacceptable toxicity or disease progression while on the current regimen.

INPATIENT ADMISSION

When the medical necessity criteria has been met, the inpatient admission for administration of epcoritamab-bysp (Epkinly), as recommended by the US Food and Drug Administration (FDA), is covered in accordance with the following timeframes*:

- First Cycle - day 15 of therapy individuals are hospitalized for 24 hours after administration of 48-mg dosage due to the risk of cytokine-release syndrome (CRS) and immune effector cell–associated neurotoxicity syndrome (ICANS)

*Inpatient hospital stays that are longer than the preceding timeframes must be re-evaluated for medical necessity.

Duration of authorization: 12 months

Version Effective Date: 03/24/2025

Title: Eptinezumab-jjmr (VYEPTI™)

MEDICALLY NECESSARY:

Eptinezumab-jjmr (VYEPTI™) is considered medically necessary and, therefore, covered for the preventive treatment of migraine in adult individuals when all of the following criteria are met:

INITIAL CRITERIA

- A neurologist, headache specialist, or pain specialist has established a diagnosis of episodic (4 to 14 headache days per month) or chronic (15 or more headache days per month) migraine
- The individual is 18 years of age or older
- The individual had inadequate response or inability to tolerate a 4-week trial of TWO of the following prophylactic medications:
 - Topiramate
 - Divalproex sodium/valproic acid
 - Beta-blocker: metoprolol, propranolol, timolol, atenolol, nadolol
 - Tricyclic antidepressants: amitriptyline, nortriptyline
 - Serotonin-norepinephrine reuptake inhibitor (SNRI) antidepressants: venlafaxine, duloxetine
 - Onabotulinumtoxin-A (Botox) for chronic migraines
- Medication will not be used in combination with another calcitonin gene-related peptide (CGRP) inhibitor (e.g., for episodic or chronic migraines: erenumab [Aimovig], fremanezumab [Ajovy], or galcanezumab [Emgality]; or oral CGRP antagonist for episodic migraines: rimegepant [Nurtec ODT] or atogepant [Qulipta])

CONTINUATION CRITERIA

Documentation of response to therapy as defined by 50 percent reduction in migraine days per month from baseline (defined as at least 4 hours' duration and moderate intensity).

Duration of authorization: 12 months

Version Effective Date: 05/28/2025

Title: Eptinezumab-jjmr (VYEPTI™)

MEDICALLY NECESSARY:

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

G43.001 Migraine without aura, not intractable, with status migrainosus

G43.009 Migraine without aura, not intractable, without status migrainosus

G43.011 Migraine without aura, intractable, with status migrainosus

G43.019 Migraine without aura, intractable, without status migrainosus

G43.101 Migraine with aura, not intractable, with status migrainosus

G43.109 Migraine with aura, not intractable, without status migrainosus

G43.111 Migraine with aura, intractable, with status migrainosus

G43.119 Migraine with aura, intractable, without status migrainosus

G43.401 Hemiplegic migraine, not intractable, with status migrainosus

G43.409 Hemiplegic migraine, not intractable, without status migrainosus

G43.411 Hemiplegic migraine, intractable, with status migrainosus

G43.419 Hemiplegic migraine, intractable, without status migrainosus

G43.501 Persistent migraine aura without cerebral infarction, not intractable, with status migrainosus

G43.509 Persistent migraine aura without cerebral infarction, not intractable, without status migrainosus

G43.511 Persistent migraine aura without cerebral infarction, intractable, with status migrainosus

G43.519 Persistent migraine aura without cerebral infarction, intractable, without status migrainosus

G43.601 Persistent migraine aura with cerebral infarction, not intractable, with status migrainosus

G43.609 Persistent migraine aura with cerebral infarction, not intractable, without status migrainosus

G43.611 Persistent migraine aura with cerebral infarction, intractable, with status migrainosus

G43.619 Persistent migraine aura with cerebral infarction, intractable, without status migrainosus

G43.701 Chronic migraine without aura, not intractable, with status migrainosus

G43.709 Chronic migraine without aura, not intractable, without status migrainosus

G43.711 Chronic migraine without aura, intractable, with status migrainosus

G43.719 Chronic migraine without aura, intractable, without status migrainosus

G43.801 Other migraine, not intractable, with status migrainosus

G43.809 Other migraine, not intractable, without status migrainosus

G43.811 Other migraine, intractable, with status migrainosus

G43.819 Other migraine, intractable, without status migrainosus

G43.821 Menstrual migraine, not intractable, with status migrainosus

G43.829 Menstrual migraine, not intractable, without status migrainosus

G43.831 Menstrual migraine, intractable, with status migrainosus

G43.839 Menstrual migraine, intractable, without status migrainosus

G43.901 Migraine, unspecified, not intractable, with status migrainosus

G43.909 Migraine, unspecified, not intractable, without status migrainosus

G43.911 Migraine, unspecified, intractable, with status migrainosus

G43.919 Migraine, unspecified, intractable, without status migrainosus

G43.E01 Chronic migraine with aura, not intractable, with status migrainosus

G43.E09 Chronic migraine with aura, not intractable, without status migrainosus

G43.E11 Chronic migraine with aura, intractable, with status migrainosus

G43.E19 Chronic migraine with aura, intractable, without status migrainosus

Duration of authorization: 12 months

Version Effective Date: 05/28/2025

Title: Enzyme Replacement Therapy for Adenosine Deaminase Severe Combined Immune Deficiency (e.g., elapegademase-lvlr [Revcovi])

MEDICALLY NECESSARY:

Elapegademase-lvlr (Revcovi™) is considered medically necessary and, therefore, covered for the treatment of individuals with adenosine deaminase deficiency with severe combined immunodeficiency (ADA-SCID), when all of the following criteria, including Dosing and Frequency Requirements, are met:

- Diagnosis of adenosine deaminase deficiency (ADA) is confirmed by one of the following:
 - Molecular genetic testing that reveals biallelic pathogenic variation(s) of the ADA gene
 - Deficiency or absence of ADA catalytic activity (<1% of normal) in hemolysates (in untransfused individuals) or in extracts of dried blood spots or other cells (e.g., blood mononuclear cells, fibroblasts)
 - An increase above laboratory standard (0.2 ± 0.1 pmol/ 10^6 cells) in deoxyadenosine triphosphate (dATP) levels in erythrocytes
- Individual is not a candidate for, or has failed, bone marrow transplantation
- Absence of severe thrombocytopenia
- Dosing and Frequency: Administered as an intramuscular injection. The starting weekly dose is 0.4 mg/kg based on ideal body weight or actual weight whichever is greater, divided into two doses (0.2 mg/kg twice a week), for a minimum of 12 to 24 weeks until immune reconstitution is achieved. After that, the dose may be gradually adjusted down to maintain trough ADA activity over 30 mmol/hr/L, trough deoxyadenosine nucleotides (dAXP) level under 0.02 mmol/L, and/or to maintain adequate immune reconstitution based on clinical assessment of the individual. Further monitoring of levels is required with the possibility of further dosage adjustment.

Duration of authorization: 12 months

Version Effective Date: 07/24/2024

Title: Enzyme Replacement Therapy for Mucopolysaccharidosis (e.g., Aldurazyme®, Elaprase®, Vimizim®, Naglazyme®, Mepsevii™, etc.)

MEDICALLY NECESSARY:

Laronidase (Aldurazyme®) is considered medically necessary and, therefore, covered for use in individuals aged 6 months or older, when all of the following criteria are met, including dosing and frequency:

- Diagnosis of Hurler or Hurler-Scheie forms of mucopolysaccharidosis I (MPS I) or Scheie form of MPS I with moderate-to-severe symptoms, confirmed by one of the following:
 - Demonstrated deficiency of the lysosomal alpha-L-iduronidase (e.g., in peripheral blood leukocytes, plasma, or cultured fibroblasts)
 - Confirmation of biallelic pathogenic variant(s) in the IDUA gene
- Dosing and frequency: 0.58 mg/kg of body weight administered once weekly as an intravenous infusion

Idursulfase (Elaprase®) is considered medically necessary and, therefore, covered for use for individuals aged at least 16 months when all of the following criteria are met, including dosing and frequency:

- Diagnosis of Hunter syndrome (MPS II) confirmed by one of the following:
 - Deficiency of iduronate 2-sulfatase in leukocytes, fibroblasts, or plasma, and documentation of normal enzymatic activity of at least one other sulfatase in the same tissue type
 - Confirmation of a hemizygous pathogenic variant(s) in the IDS gene
- Dosing and frequency: 0.5 mg/kg of body weight administered once weekly as an intravenous infusion

Elosulfase alfa (Vimizim®) is considered medically necessary and, therefore, covered for use in individuals aged at least 5 years, when all of the following criteria are met, including dosing and frequency:

- Diagnosis of MPS Type IVA (MPS IVA), also called Morquio A syndrome, has been confirmed by one of the following:
 - Deficiency of N-acetylgalactosamine-6-sulphatase (GALNS) in cultured fibroblasts or leukocytes
 - Confirmation of biallelic pathogenic variant(s) in the GALNS gene
- Dosing and frequency: 2 mg/kg given intravenously once every week

Galsulfase (Naglazyme®) is considered medically necessary and, therefore, covered for use in individuals aged at least 5 years when all of the following criteria are met, including dosing and frequency:

- Diagnosis of MPS type VI (MPS VI, Maroteaux-Lamy syndrome) has been confirmed by one of the following:
 - Deficiency of N-acetylgalactosamine 4-sulfatase [ARSB] in leukocytes, fibroblasts, and dried blood spots

- Confirmation of biallelic pathogenic variant(s) in the ARSB gene
- Dosing and frequency: 1 mg/kg of body weight, administered once weekly as an intravenous infusion

Vestronidase alfa-vjbk (Mepsevii™) is considered medically necessary and, therefore, covered for use in infants aged at least 5 months, children, and adult individuals when all of the following criteria are met, including dosing and frequency:

- Diagnosis of MPS type VII (MPS VII, Sly syndrome) has been confirmed by one of the following:
 - Deficiency of beta-glucuronidase in peripheral blood leukocytes or cultured fibroblasts
 - Genetic testing confirming pathogenic variant(s) in the GUSB gene
- Dosing and frequency: 4 mg/kg administered by intravenous infusion every 2 weeks

Duration of authorization: 12 months

Version Effective Date: 08/21/2024

Title: Erythropoiesis-Stimulating Agents (ESAs)

MEDICALLY NECESSARY:

ANEMIA ASSOCIATED WITH CANCER AND RELATED ONCOLOGIC CONDITIONS

MEDICALLY NECESSARY CRITERIA FOR EPOETIN ALFA (EPOGEN[®], PROCRIT[®]), DARBEPOETIN ALFA (ARANESP[®]) AND RELATED BIOSIMILARS (e.g., EPOETIN ALFA-EPBX [RETACRIT[™]])

Initiation Criteria for Erythropoiesis-Stimulating Agents (ESAs) Therapy for Cancer and Related Oncologic Conditions

Erythropoiesis-stimulating agents such as epoetin alfa (Epogen[®], Procrit[®]), darbepoetin alfa (Aranesp[®]), or related biosimilars (e.g., epoetin alfa-epbx [Retacrit[™]]) are considered medically necessary and, therefore, covered when any of the following criteria are met:

- The individual has anemia secondary to a regimen of myelosuppressive anticancer chemotherapy for non-myeloid malignancies and has no other identifiable cause of anemia, and upon initiation, there is a minimum of two additional months of planned chemotherapy.
 - The hemoglobin (Hb) level immediately prior to the first administration of ESA is less than 10 g/dL (or hematocrit [HCT] is less than 30 percent).
- The individual is undergoing palliative treatment.

Treatment of Chemotherapy-Induced Anemia

- As treatment of symptomatic chemotherapy-Induced anemia in individuals with cancer with any of the following:
 - Have moderate to severe chronic kidney disease
 - Are undergoing palliative treatment
 - Are receiving myelosuppressive chemotherapy and have no other identifiable cause of anemia
 - Refuse blood transfusions in select cases

National Comprehensive Cancer Network (NCCN) note: Erythropoiesis-stimulating agents are not recommended when myelosuppressive chemotherapy is given with curative intent (except for individuals who refuse blood transfusions), for individuals with cancer who are not receiving therapy, or for individuals receiving non-myelosuppressive therapy

Myelodysplastic Syndrome

For individuals with symptomatic anemia related to myelodysplastic syndrome, as treatment of lower risk[†] disease, when all of the following criteria are met:

- Individuals with one of the following:
 - As an alternative to lenalidomide, for individuals, with del(5q), with or without one other cytogenetic abnormality (except those involving chromosome 7) and serum erythropoietin ≤500 mU/mL

- For individuals with no del(5q), with or without one other cytogenetic abnormalities ring sideroblasts <15 percent (or ring sideroblasts <5% with an SF3B1 mutation) with serum erythropoietin ≤500 mU/mL
 - As a single agent (NCCN preferred regimen)
 - In combination with lenalidomide or a granulocyte-colony stimulating factor (G-CSF) following no response (despite adequate iron stores) to an erythropoiesis-stimulating agent (ESA) alone or luspatercept-aamt
- For individuals with no del(5q), with or without one other cytogenetic abnormalities ring sideroblasts ≥15 percent (or ring sideroblasts ≥5% with an SF3B1 mutation), with serum erythropoietin ≤500 mU/mL following no response to luspatercept-aamt
 - As a single agent
 - In combination with a granulocyte-colony stimulating factor (G-CSF)
- Hb is less than 10 g/dL (or HCT is less than 30 percent) at the initiation of therapy.
- The intent of therapy is to maintain a Hb/HCT level no greater than 10-12 g/dL (Hb) or 30-36 percent (HCT).

†Lower risk defined as IPSS-R (Very Low, Low, Intermediate), IPSS (Low/Intermediate-1), WPSS (Very Low, Low, Intermediate).

There are three main prognostic scoring systems. See Guidelines Section for more details.

Myelofibrosis

For individuals with anemia related to myelofibrosis when all both of the following criteria are met:

- Endogenous serum erythropoietin level less than 500mU/mL
- Hb is less than 10 g/dL (or HCT is less than 30 percent) at the initiation of therapy and one of the following:
 - With presence of symptomatic splenomegaly and/or constitutional symptoms currently controlled on a JAK inhibitor, to be given in combination with ruxolitinib
 - With no symptomatic splenomegaly and/or constitutional symptoms

Continuation of ESA Therapy for Cancer and Related Oncologic Conditions

Professional providers should use the lowest dose of ESA required to avoid red blood cell (RBC) transfusions. ESA treatment is considered medically necessary and, therefore, covered for eight weeks after the final dose of a myelosuppressive chemotherapy regimen.

NOT MEDICALLY NECESSARY CRITERIA FOR EPOETIN ALFA (EPOGEN®, PROCRIT®), RELATED BIOSIMILARS (e.g., EPOETIN ALFA-EPBX [RETACRIT™]), AND DARBEPOETIN ALFA (ARANESP®) An ESA such as epoetin alfa (Epogen®, Procrit®), related biosimilars (e.g., epoetin alfa-epbx [Retacrit™]), or darbepoetin alfa (Aranesp®) is considered not medically necessary and, therefore, not covered for any of the following indications because the available published peer-reviewed literature does not support its use:

- Anemia of cancer not related to cancer treatment
- Prophylactic use to prevent chemotherapy-induced anemia

- Prophylactic use to reduce tumor hypoxia
- Individuals with erythropoietin-type resistance due to neutralizing antibodies
- Anemia in individuals who have cancer or are undergoing cancer treatment, when anemia is due to folate deficiency, vitamin B12 deficiency, iron deficiency, hemolysis, bleeding, or bone marrow fibrosis
- Anemia associated with the treatment of acute or chronic myelogenous leukemia (AML, CML) or erythroid cancers
- Any anemia associated only with radiotherapy
- For individuals receiving non-myelosuppressive therapy
- For individuals with pure red cell aplasia that begins following treatment with epoetin alfa or other erythropoietin protein drugs

ANEMIA ASSOCIATED WITH NON-ONCOLOGIC CONDITIONS

MEDICALLY NECESSARY CRITERIA FOR EPOETIN ALFA (EPOGEN®, PROCRIT®), RELATED BIOSIMILARS (e.g., EPOETIN ALFA-EPBX [RETACRIT™]), AND DARBEPOETIN ALFA (ARANESP®). Epoetin alfa (Epogen®, Procrit®), related biosimilars (e.g., epoetin alfa-epbx [Retacrit™]), or darbepoetin alfa (Aranesp®) are considered medically necessary and, therefore, covered for the treatment of anemia associated with the following indications when the following criteria for each indication are met:

Acquired Immunodeficiency Syndrome (HIV/AIDS)

For individuals who have HIV/AIDS and anemia when all of the following criteria are met:

- Endogenous serum erythropoietin level of 500mU/mL or less that is induced by treatment with zidovudine (AZT) administered at 4,200 mg/week or less.
- Hb is less than 10g/dL or Hct is less than 30 percent at the initiation of therapy.

Chronic Kidney Disease (CKD)

For individuals who have anemia related to CKD when all of the following criteria are met:

- Hb is less than 10 g/dL (or HCT is less than 30 percent) at the initiation of therapy.
- Glomerular filtration rate (GFR) is less than 60 mL/min/1.73 m² for 3 or more months.

MEDICALLY NECESSARY CRITERIA FOR EPOETIN ALFA (EPOGEN®, PROCRIT®) AND RELATED BIOSIMILARS (e.g., EPOETIN ALFA-EPBX [RETACRIT™])

Epoetin alfa (Epogen®, Procrit®) and related biosimilars (e.g., epoetin alfa-epbx [Retacrit™]) are considered medically necessary and, therefore, covered for the treatment of anemia associated with the following indication when the following criteria are met:

Perisurgical Adjuvant Therapy

For individuals with anemia who are undergoing elective, nonvascular, noncardiac, nonvascular surgery, when all of the following criteria are met:

- Hb is between 10-13 g/dL (or HCT is between 30-39 percent).
- The individual is at high risk for perioperative blood loss.
- The individual is not a candidate for autologous blood transfusion.
- The individual is expected to lose two or more units of blood.
- The individual has been evaluated to ensure that anemia is due to chronic disease.

CONTINUATION OF ESA THERAPY WITH EPOETIN ALFA (EPOGEN®, PROCRIT®) AND RELATED BIOSIMILARS (e.g., EPOETIN ALFA-EPBX [RETACRIT™])

During ESA therapy, many individuals eventually require supplemental iron. In order to guide appropriate supplementation, iron stores should be regularly monitored to ensure a transferrin saturation greater than 20 percent and/or serum ferritin levels greater than 100 ng/mL.

MEDICALLY NECESSARY CRITERIA FOR METHOXYPOLYETHYLENE GLYCOL-EPOETIN BETA (MIRCERA®)

Methoxypolyethylene glycol-epoetin beta (Mircera®) is considered medically necessary and, therefore, covered for the treatment of the following indications when the following criteria are met:

- Anemia associated with chronic kidney disease in adults on hemodialysis and adults not on hemodialysis
- Anemia associated with chronic kidney disease in pediatric individuals 5 to 17 years of age on hemodialysis who are converting from another ESA after their hemoglobin level was stabilized with an ESA

CONTINUATION OF ESA THERAPY WITH METHOXYPOLYETHYLENE GLYCOL-EPOETIN BETA (MIRCERA®)

Methoxypolyethylene glycol-epoetin beta (Mircera®) is considered medically necessary and, therefore, covered for continuation of the treatment when the following criteria are met:

- Professional providers use the lowest dose of ESA required to avoid red blood cell (RBC) transfusions. During therapy, evaluation of iron status and correction or exclusion of other causes of anemia is required.
- If Hb does not rise adequately over a 12-week escalation period: Additional dose increase is unlikely to improve response and may increase risk. Evaluate other causes of anemia and discontinue therapy if responsiveness does not improve.

NOT MEDICALLY NECESSARY CRITERIA FOR METHOXYPOLYETHYLENE GLYCOL-EPOETIN BETA (MIRCERA®)

Methoxypolyethylene glycol-epoetin beta (Mircera®) is considered not medically necessary and, therefore, not covered for any of the following indications because the available published peer-reviewed literature does not support its use:

- Treatment of anemia due to cancer chemotherapy or radiation
- Substitute for RBC transfusions in individuals who require immediate correction of anemia

NOT ELIGIBLE FOR REIMBURSEMENT

Peginesatide (Omontys®) is no longer manufactured and has been withdrawn from the market, as of February 23, 2013; therefore, it is not eligible for reimbursement. This drug was withdrawn from the market due to serious hypersensitivity reactions, which can be life-threatening.

Duration of authorization: 12 months

Version Effective Date: 04/22/2024

Title: Etranacogene dezaparvovec-drlb (Hemgenix®)

MEDICALLY NECESSARY:

Etranacogene dezaparvovec-drlb (Hemgenix®) is considered medically necessary and, therefore, covered for the treatment of hemophilia B in individuals 18 years of age and older when they meet ALL of the following criteria:

- Documentation of the diagnosis of moderately severe or severe hemophilia B as evidenced by a baseline (without Factor IX replacement therapy) Factor IX level of less than or equal to 2% of normal.
- ONE of the following:
 - Documentation of BOTH of the following:
 - Receiving routine prophylaxis with Factor IX therapy continuously for at least 2 months
 - According to the prescriber, has at least a 150 exposure-day history of Factor IX therapy
 - Documentation of BOTH of the following:
 - History of life-threatening hemorrhage
 - On-demand use of Factor IX therapy was required for this life-threatening hemorrhage
 - Documentation of BOTH of the following:
 - History of repeated, serious spontaneous bleeding episodes
 - On-demand use of Factor IX therapy was required for these serious spontaneous bleeding episodes
- Documentation of ALL of the following:
 - BOTH of the following:
 - Factor IX inhibitor titer testing performed within 30 days before receiving etranacogene dezaparvovec-drlb (Hemgenix)
 - No current, or history of, Factor IX inhibitors
 - Adequate hepatic function as evidenced by ALL of the following:
 - Alanine aminotransferase is less or equal to 2 times the upper limit of normal
 - Aspartate aminotransferase is less or equal to 2 times the upper limit of normal
 - Total bilirubin levels are less or equal to 2 times the upper limit of normal
 - Alkaline phosphatase levels are less or equal to 2 times the upper limit of normal
 - No evidence of advanced liver impairment and/or advanced fibrosis. For example, liver elastography (e.g., greater than or equal to 9 kPa) suggestive of or equal to METAVIR stage 3 disease.
 - Adequate renal function as evidenced by BOTH of the following:
 - Estimated creatinine clearance of at least 30 mL/min
 - Creatinine levels are less or equal to 2 times the upper limit of normal

- Platelet count of at least $50 \times 10^9/L$ performed within the last 30 days
- Prior to receiving etranacogene dezaparvovec-drlb (Hemgenix), BOTH of the following:
 - Screening for hepatitis B and C is negative
 - Is not currently receiving antiviral therapy for a prior hepatitis B virus or C virus exposure
- If positive for human immunodeficiency virus (HIV), is controlled on antiviral therapy as evidenced by adequate CD4+ counts of at least 200/ μ L or by a viral load of less than or equal to 200 copies/mL
- If positive for HIV, is controlled on antiviral therapy as evidenced by adequate CD4+ counts of at least 200/ μ L or by a viral load of less than or equal to 200 copies/mL
- Prescriber attestation of no other coagulation disorders, besides hemophilia B
- No prior history of receiving gene therapy
- Prescriber attestation that prophylactic therapy with Factor IX will not be given once adequate Factor IX levels have been achieved. Use of episodic Factor IX therapy is acceptable for the treatment of bleeds and for surgery/procedures if needed as determined by the hemophilia specialist physician.
- Prescriber attestation that, following etranacogene dezaparvovec-drlb (Hemgenix) infusion, ALL of the following will be performed:
 - Liver enzyme testing to monitor for liver enzyme elevations will be done at least weekly for the first 3 months and periodically thereafter
 - Implementing a course of corticosteroids will be considered if there are clinically relevant increases in alanine aminotransferase levels
 - Individual will undergo monitoring for Factor IX activity at least weekly for the first 3 months and periodically thereafter
 - If the individual has preexisting risk factors for hepatocellular carcinoma, they will receive abdominal ultrasound screenings and be monitored at least annually with alpha-fetoprotein elevations in the 5 years following receipt of etranacogene dezaparvovec-drlb (Hemgenix). Risk factors include a patient with prior history of hepatitis B and/or C, non-alcoholic fatty liver disease, chronic alcohol consumption, nonalcoholic steatohepatitis, and advanced age.
- Gene replacement therapy is prescribed by a hemophilia specialist.

Duration of authorization: 12 months

Version Effective Date: 05/28/2025

Title: Evinacumab-dgnb (Evkeeza®)

MEDICALLY NECESSARY:

INITIAL THERAPY

Evinacumab-dgnb (Evkeeza) is considered medically necessary and, therefore, covered for the treatment of individuals 5 years of age or older with homozygous familial hypercholesterolemia (HoFH) when all of the following criteria, including dosing and frequency, are met:

- Documented diagnosis of HoFH confirmed by **one** of the following:
 - Documentation of the presence of pathogenic variations at two alleles at the low-density lipoprotein receptor (LDL-R), apolipoprotein B (APO-B), proprotein convertase subtilisin-kexin type 9 (PCSK9) or low-density lipoprotein receptor adaptor protein-1 (*LDLRAP1*) gene locus.
 - Untreated low-density lipoprotein cholesterol (LDL-C) greater than 500 mg/dL **or** treated LDL-C greater than or equal to 300 mg/dL and **one** of the following:
 - Cutaneous or tendinous xanthomas before 10 years of age
 - Documentation of untreated total cholesterol greater than 250 mg/dL in both parents
- Individual currently has elevated LDL-C levels and meets the criteria for each age group:
 - Individuals 10 years of age and older: LDL-C 100 mg/dL or greater despite receiving all of the following therapies for at least 12 weeks, unless documented failure, contraindication, or intolerance, and will continue these therapies while on evinacumab-dgnb (Evkeeza):
 - Maximally tolerated moderate- or high-intensity statin therapy (e.g., atorvastatin, rosuvastatin, simvastatin)
 - Ezetimibe (Zetia)
 - PCSK9 inhibitor (e.g., alirocumab [Praluent], evolocumab [Repatha]), unless individual has two LDLR-negative alleles
 - Individuals 5 to less than 10 years of age: LDL-C 100 mg/dL or greater (no prior therapies required)
- Dosing and frequency: 15 mg/kg administered by intravenous (IV) infusion once monthly (every 4 weeks)

CONTINUATION THERAPY

Continuation of evinacumab-dgnb (Evkeeza) is considered medically necessary and, therefore, covered when the individual continues to receive other lipid-lowering therapy (unless documented failure, contraindication, or intolerance) and has a documented reduction in LDL-C of at least 30% since initiation of therapy.

Duration of authorization: 12 months

Version Effective Date: 05/28/2024

Title: Exon Skipping Drugs for Duchenne Muscular Dystrophy (DMD) (Eteplirsen (Exondys 51), Golodirsen (Vyondys 53), Viltolarsen (Viltepso)), Casimersen (Amondys 45)

MEDICALLY NECESSARY:

BENEFIT EXCLUSION

Exon-skipping drugs eteplirsen (Exondys 51), golodirsen (Vyondys 53), viltolarsen (Viltepso), and casimersen (Amondys 45) are a benefit contract exclusion for most plans, and, therefore, not eligible for reimbursement consideration. Individual benefits must be verified.

Duration of authorization: 12 months

Version Effective Date: 01/01/2025

Title: Fam-trastuzumab deruxtecan-nxki (Enhertu®)

MEDICALLY NECESSARY:

FAM-TRASTUZUMAB DERUXTECAN-NXKI (ENHERTU)

Fam-trastuzumab deruxtecan-nxki (Enhertu) injection is considered medically necessary and, therefore, covered as monotherapy when the following criteria are met, including human epidermal growth factor receptor 2 (HER2) protein overexpression verified by one of the US Food and Drug Administration (FDA)-approved diagnostic tests as listed in the policy guidelines, left ventricular ejection fraction of 50% or greater, and dosing and frequency requirements for the following indications:

Ampullary Adenocarcinoma

- Therapy for disease progression as a single agent (if HER2 positive [IHC3+, or IHC2+ with FISH HER2 amplified]) in individuals with good performance status (ECOG 0-1, with good biliary drainage and adequate nutritional intake)
- Dosing and frequency for fam-trastuzumab deruxtecan-nxki (Enhertu): 5.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle)

Biliary Tract Cancers

Gallbladder Cancer, Intrahepatic Cholangiocarcinoma, Extrahepatic Cholangiocarcinoma

- As subsequent therapy for progression on or after systemic therapy for unresectable or resected gross residual (R2) disease or metastatic disease that is HER2-positive (IHC 3+)
- Dosing and frequency for fam-trastuzumab deruxtecan-nxki (Enhertu): 5.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle)

Bladder Cancer

- As second-line systemic therapy (if a first-line therapy containing both platinum chemotherapy and an immune checkpoint inhibitor was used, including maintenance checkpoint inhibitor), or as subsequent-line systemic therapy (individuals should have already received platinum and a checkpoint inhibitor, if eligible) or HER2 positive, IHC 3+ for any of the following:
 - stage II (cT2, N0) disease or stage IIIA (cT3, N0; cT4a, N0; cT1-T4a, N1) disease if tumor is present following reassessment of tumor status 2 to 3 months after primary treatment with concurrent bladder-preserving chemoradiotherapy and maximal transurethral resection of bladder tumor (TURBT)
 - stage IIIB (cT1-T4a, N2,3) disease following partial response or progression after primary treatment with downstaging systemic therapy or concurrent chemoradiotherapy
 - stage IVA (cT4b, any N, M0) disease if tumor is present following reassessment of tumor status after primary treatment with first-line systemic therapy or concurrent chemoradiotherapy
 - stage IVA (any T, any N, M1a) disease if stable disease or progression following reassessment of tumor status after primary treatment with first-line systemic therapy

- metastatic stage IVB (any T, any N, M1b) disease
 - muscle invasive local recurrence or persistent disease in a preserved bladder treated with curative intent
 - metastatic or local recurrence postcystectomy treated with curative intent
- Dosing and frequency for fam-trastuzumab deruxtecan-nxki (Enhertu): 5.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle)

Upper GU Tract Tumors

- As treatment for metastatic disease for HER2-positive, IHC 3+ for one of the following:
 - as second-line systemic therapy if a first-line therapy containing both platinum chemotherapy and an immune checkpoint inhibitor was used, including maintenance checkpoint inhibitor
 - as subsequent-line systemic therapy (individuals should have already received a platinum and a checkpoint inhibitor, if eligible)
- Dosing and frequency for fam-trastuzumab deruxtecan-nxki (Enhertu): 5.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle)

Urothelial Carcinoma of the Prostate

- Therapy for metastatic disease for HER2-positive, IHC 3+ for one of the following:
 - second-line systemic therapy if a first-line therapy containing both platinum chemotherapy and an immune checkpoint inhibitor was used, including maintenance checkpoint inhibitor
 - subsequent-line systemic therapy (individuals should have already received a platinum and a checkpoint inhibitor, if eligible)
- Dosing and frequency for fam-trastuzumab deruxtecan-nxki (Enhertu): 5.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle)

Primary Carcinoma of the Urethra

- Treatment for recurrent or metastatic disease for HER2-positive, IHC 3+ (except for recurrence of clinical stage T3-4 disease or palpable inguinal lymph nodes) for one of the following:
 - second-line systemic therapy if a first-line therapy containing both platinum chemotherapy and an immune checkpoint inhibitor was used, including maintenance checkpoint inhibitor
 - subsequent-line systemic therapy (individuals should have already received a platinum and a checkpoint inhibitor, if eligible)
- Dosing and frequency for fam-trastuzumab deruxtecan-nxki (Enhertu): 5.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle)

Breast Cancer

Unresectable or Metastatic Breast Cancer

- For adult individuals with unresectable or metastatic HER2-positive (IHC 3+ or ISH positive) breast cancer who have received a prior anti-HER2–based regimen either in the metastatic setting, or in the neoadjuvant or adjuvant setting and have developed disease recurrence during or within 6 months of completing therapy.

- For adult individuals with hormone receptor (HR)-positive, HER2-low (IHC 1+ or IHC 2+/ISH-) or HER2-ultralow (IHC 0 with membrane staining) breast cancer, as determined by an FDA-approved test, that has progressed on one or more endocrine therapies in the metastatic setting
- For adult individuals with unresectable or metastatic HER2-low (IHC 1+ or IHC 2+/ISH-) breast cancer, as determined by an FDA-approved test, who have received prior chemotherapy in the metastatic setting or developed disease recurrence during or within 6 months of completing adjuvant chemotherapy.
- Dosing and frequency for fam-trastuzumab deruxtecan-nxki (Enhertu): 5.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle)

Inflammatory Breast Cancer

- First-line therapy as a single agent for recurrent unresectable (local or regional) or stage IV (M1) HER2-negative, hormone receptor positive with visceral crisis or endocrine therapy refractory disease if no germline BRCA 1/2 mutation and/or HER2 IHC 0+, 1+, or 2+/ISH negative
- National Comprehensive Cancer Network (NCCN) preferred as second-line therapy as a single agent for recurrent unresectable (local or regional) or stage IV (M1) HER2 IHC 0+, 1+ or 2+/ISH negative disease that is:
 - hormone receptor negative if no germline BRCA 1/2 mutation (may be considered in a later line if not used in second line or may be considered first-line therapy when disease has progressed during or within 6 months after completing adjuvant therapy)
 - hormone receptor positive with visceral crisis or endocrine therapy refractory (may be used for previously treated disease with at least one line of endocrine-based therapy in the metastatic setting)
- As a single agent for individuals with no response to preoperative systemic therapy, or recurrent unresectable (local or regional) or stage IV (M1) HER2-positive disease that is hormone receptor negative, or hormone receptor positive with or without endocrine therapy for any of the following indications:
 - as second-line therapy (NCCN preferred)
 - as first-line therapy for select individuals (i.e., those with rapid progression within 6 months of neoadjuvant or adjuvant therapy [12 months for pertuzumab-containing regimens])
- Dosing and frequency for fam-trastuzumab deruxtecan-nxki (Enhertu): 5.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle)

Invasive Breast Cancer

- First-line therapy as a single agent for recurrent unresectable (local or regional) or stage IV (M1) HER2-negative, hormone receptor positive with visceral crisis or endocrine therapy refractory disease if no germline BRCA 1/2 mutation and/or HER2 IHC 0+, 1+, or 2+/ISH negative
- As second-line therapy (NCCN preferred) as a single agent for recurrent unresectable (local or regional) or stage IV (M1) HER2 IHC 0+ 1+ or 2+ and ISH-negative disease that is:
 - hormone receptor negative if no germline BRCA 1/2 mutation (may be considered in a later line if not used in second line or may be considered first-line therapy when disease has progressed during or within 6 months after completing adjuvant chemotherapy)
 - hormone receptor positive with visceral crisis or endocrine therapy refractory (may be used for previously treated disease with at least one line of endocrine-based therapy in the metastatic setting)

- As a single agent for recurrent unresectable (local or regional) or stage IV (M1) HER2-positive disease that is hormone receptor negative, or hormone receptor positive with or without endocrine therapy for any of the following indications:
 - as second-line therapy (NCCN preferred)
 - as first-line therapy for select individuals (i.e., those with rapid progression within 6 months of neoadjuvant or adjuvant therapy [12 months for pertuzumab-containing regimens])
- Dosing and frequency for fam-trastuzumab deruxtecan-nxki (Enhertu): 5.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle)

Central Nervous System Cancers

Limited Brain Metastases

- As a single-agent treatment for limited brain metastases in individuals with HER2-positive breast cancer for any of the following indications:
 - as initial treatment in select individuals (e.g., individuals with small asymptomatic brain metastases)
 - as treatment for recurrent brain metastases
 - treatment of relapsed disease with either stable systemic disease or reasonable systemic treatment options
- Dosing and frequency for fam-trastuzumab deruxtecan-nxki (Enhertu): 5.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle)

Extensive Brain Metastases

- Used as a single-agent treatment for extensive brain metastases in individuals with HER2-positive breast cancer for any of the following indications:
 - as primary treatment in select individuals (e.g., individuals with small asymptomatic brain metastases)
 - as treatment for recurrent disease with stable systemic disease or reasonable systemic treatment options
- Dosing and frequency for fam-trastuzumab deruxtecan-nxki (Enhertu): 5.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle)

Cervical Cancer

- As second-line or subsequent therapy for HER2-positive tumors (IHC 3+ or 2+) and one of the following:
 - local/regional recurrence
 - stage IVB or recurrence with distant metastases
- Dosing and frequency for fam-trastuzumab deruxtecan-nxki (Enhertu): 5.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle)

Colon Cancer

- Adjuvant treatment for unresectable metachronous metastases (HER2-amplified, IHC 3+) that converted to resectable disease after initial treatment. Biologic therapy is only appropriate for continuation of favorable response from conversion therapy (proficient mismatch repair/microsatellite-stable [pMMR/MSS] or ineligible for or progressed on checkpoint inhibitor immunotherapy for deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] or polymerase epsilon/delta [POLE/POLD1] mutation with ultrahypermutated phenotype [e.g., TMB >50 mut/Mb])
- Initial treatment as in individuals (HER2-amplified, IHC 3+) (pMMR/MSS-deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] or polymerase epsilon/delta [POLE/POLD1] mutation with ultrahypermutated phenotype [e.g., TMB >50 mut/Mb] and individual is not a candidate for immunotherapy) for individuals with unresectable metachronous metastases and previous FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin) within the past 12 months
- Second-line and subsequent therapy (biomarker-directed), if not previously given, for progression of advanced or metastatic disease (pMMR/MSS or ineligible for or progressed on checkpoint inhibitor immunotherapy for dMMR/MSI-H or POLE/POLD1 mutation with ultrahypermutated phenotype [e.g., TMB >50 mut/Mb]) (HER2-amplified, IHC 3+)
- Dosing and frequency for fam-trastuzumab deruxtecan-nxki (Enhertu): 5.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle)

Appendiceal Adenocarcinoma

- Second-line and subsequent therapy (biomarker-driven), if not previously given, for progression of advanced or metastatic disease (pMMR/MSS or ineligible for or progressed on dMMR/MSI-H or POLE/POLD1 mutation with ultrahypermutated phenotype [e.g., TMB >50 mut/Mb]) (HER2-amplified, IHC 3+)
- Dosing and frequency for fam-trastuzumab deruxtecan-nxki (Enhertu): 5.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle)

Esophageal, Esophagogastric Junction and Gastric Cancers

- Palliative therapy for individuals with HER2 overexpression–positive adenocarcinoma and Karnofsky performance score greater than or equal to 60% or Eastern Cooperative Oncology Group (ECOG) performance score less than or equal to 2 as (NCCN preferred) second-line or subsequent for one of the following conditions:
 - for individuals who are not surgical candidates
 - for individuals who have unresectable locally advanced, recurrent, or metastatic disease
- Adult individuals with locally advanced or metastatic HER2-positive (IHC 3+ or IHC 2+/ISH positive) gastric or gastroesophageal junction adenocarcinoma who have received a prior trastuzumab-based regimen
- Dosing and frequency for fam-trastuzumab deruxtecan-nxki (Enhertu): 6.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle)

Gastric Cancer

- Palliative therapy for HER2 overexpression–positive individuals who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease (including peritoneal-only metastatic disease, including positive cytology) and Karnofsky performance score greater than or equal to 60% or ECOG performance

score less than or equal to 2 as preferred second-line or subsequent therapy

- Dosing and frequency for fam-trastuzumab deruxtecan-nxki (Enhertu): 6.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle)

Head and Neck Cancers

Salivary Gland Tumors

- As single-agent systemic therapy for HER2-positive recurrent disease with one of the following:
 - distant metastases in individuals with a performance status (PS) of 0 to 3
 - unresectable locoregional recurrence or second primary with prior radiation therapy
- Dosing and frequency for fam-trastuzumab deruxtecan-nxki (Enhertu): 6.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle)

Non-Small Cell Lung Cancer

- NCCN preferred as subsequent therapy for ERBB2 (HER2) mutation–positive recurrent, advanced, or metastatic disease (except for locoregional recurrence or symptomatic local disease [excluding mediastinal lymph node recurrence with prior radiation therapy] with no evidence of disseminated disease
- Subsequent systemic therapy for recurrent, advanced, or metastatic disease in those with PS 0–2 whose tumors have HER2 overexpression (IHC 3+) (except for locoregional recurrence or symptomatic local disease [excluding mediastinal lymph node recurrence with prior radiation therapy] with no evidence of disseminated disease
- Adult individuals with unresectable or metastatic non-small cell lung cancer (NSCLC) whose tumors have activating HER2 (ERBB2) mutations, as detected by an FDA-approved test, and who have received a prior systemic therapy
- Dosing and frequency for fam-trastuzumab deruxtecan-nxki (Enhertu): 5.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle)

Occult Primary Cancers

- For individuals with HER2-positive [IHC 3+] tumors who are symptomatic with PS 1 to 2 or asymptomatic individuals with PS 0 and aggressive disease that is metastatic or where surgical resection is likely to result in severe morbidity, and that has progressed on or following prior systemic treatment and has no satisfactory alternative treatment options for any of the following:
 - axillary involvement in those with a prostate or postprostatectomy if clinically indicated
 - lung nodules or breast marker–negative pleural effusion
 - resectable liver disease
 - peritoneal mass or ascites with nonovarian histology
 - retroperitoneal mass of non–germ cell histology in selected individuals
 - unresectable liver disease or disseminated metastases
- For individuals with HER2-positive [IHC 3+] tumors who are symptomatic with PS 1 to 2 or asymptomatic individuals with PS 0 and aggressive disease for systemic therapy in individuals with multiple lung

nodules, pleural effusion, or disseminated metastases that progressed on or following prior systemic treatment and have no satisfactory alternative treatment options

- Dosing and frequency for fam-trastuzumab deruxtecan-nxki (Enhertu): 5.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle)

Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer

Epithelial Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer; Carcinosarcoma (Malignant Mixed Müllerian Tumors); Clear Cell Carcinoma of the Ovary; Mucinous Neoplasms of the Ovary; Grade 1 Endometrioid Carcinoma

- For platinum-resistant persistent disease or recurrence in HER2-positive tumors [IHC 3+ or 2+] (except for immediate treatment of biochemical relapse)
 - as immediate treatment for serially rising CA-125 in individuals who previously received chemotherapy
 - for progression on primary, maintenance, or recurrence therapy
 - for stable or persistent disease (if not on maintenance therapy)
 - for complete remission and relapse less than 6 months after completing chemotherapy
- Dosing and frequency for fam-trastuzumab deruxtecan-nxki (Enhertu): 5.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle)

Low-Grade Serous Carcinoma

- For platinum-resistant recurrence in HER2-positive tumors [IHC 3+ or 2+]
- Dosing and frequency for fam-trastuzumab deruxtecan-nxki (Enhertu): 5.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle)

Pancreatic Adenocarcinoma

- Subsequent therapy if HER2 positive (IHC3+) for locally advanced or metastatic disease and disease progression if good PS (defined as ECOG PS 0–1, with good biliary drainage and adequate nutritional intake) or intermediate PS (ECOG 2)
- Therapy as a single agent* if HER2 positive (IHC3+, or IHC2+ with FISH HER2 amplified) if good PS (ECOG PS 0–1) for one of the following:
 - local recurrence in the pancreatic operative bed after resection
 - recurrent metastatic disease with or without local recurrence after resection
- Dosing and frequency for fam-trastuzumab deruxtecan-nxki (Enhertu®): 5.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle)

NCCN note: *as alternate systemic therapy not previously used.

Rectal Cancer

- Initial treatment in individuals (HER2-amplified, IHC 3+) for individuals with unresectable metachronous metastases (pMMR/MSS) or deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] and are not candidates for immunotherapy) and previous FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin) within the past 12 months
- Second-line and subsequent therapy, if not previously given, for progression of advanced or metastatic disease (HER2-amplified, IHC 3+) (pMMR/MSS or ineligible for or progressed on checkpoint inhibitor immunotherapy for dMMR/MSI-H or POLE/POLD1 mutation with ultrahypermutated phenotype [e.g., TMB >50 mut/Mb])
- Dosing and frequency for fam-trastuzumab deruxtecan-nxki (Enhertu): 5.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle)

Small Bowel Adenocarcinoma

- Second-line and subsequent therapy for advanced or metastatic disease that is HER2-amplified (IHC 3+) (if not previously given)
- Dosing and frequency for fam-trastuzumab deruxtecan-nxki (Enhertu): 5.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle)

Solid Tumors

- For solid tumor, unresectable or metastatic, HER2-positive (IHC 3+), in individuals who have received prior systemic therapy and have no satisfactory alternative treatment options
- Dosing and frequency for fam-trastuzumab deruxtecan-nxki (Enhertu): 5.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle)

Uterine Neoplasms

Endometrial Carcinoma

- Second-line or subsequent therapy for recurrent disease that is HER2-positive tumor (IHC 3+ or 2+) for any of the following:
 - isolated metastases
 - disseminated metastases with or without sequential palliative external beam radiation therapy (EBRT)
 - with sequential EBRT and with or without brachytherapy for locoregional recurrence in individuals with no prior radiotherapy to site of recurrence, or previous vaginal brachytherapy only
 - after surgical exploration, with sequential EBRT for locoregional recurrence in individuals with disease confined to the vagina or paravaginal soft tissue, or in pelvic or para-aortic lymph nodes
 - after surgical exploration, with or without sequential EBRT for locoregional recurrence in individuals with upper abdominal or peritoneal disease
 - with or without sequential palliative EBRT or brachytherapy for locoregional recurrence in individuals who have received prior EBRT to site of recurrence

- Dosing and frequency for fam-trastuzumab deruxtecan-nxki (Enhertu): 5.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle)

Vaginal Cancer

- Second-line or subsequent therapy for HER2-positive tumors (IHC 3+ or 2+) and one of the following:
 - locoregional recurrence
 - stage IVB or recurrent distant metastases
- Dosing and frequency for fam-trastuzumab deruxtecan-nxki (Enhertu): 5.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle)

Vulvar Cancer

- Second-line or subsequent therapy for advanced or recurrent/metastatic disease for HER-2 positive (IHC 3+ or 2+) tumors
- Dosing and frequency for fam-trastuzumab deruxtecan-nxki (Enhertu): 5.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle)

CONTINUATION THERAPY

Fam-trastuzumab deruxtecan-nxki (Enhertu) is considered medically necessary and, therefore, covered for continuation therapy until disease progression, drug intolerance, or unacceptable toxicity.

Duration of authorization: 12 months

Version Effective Date: 06/16/2025

Title: Fam-trastuzumab deruxtecan-nxki (Enhertu®)

MEDICALLY NECESSARY:

Dosing and frequency

1.Biliary Tract Cancers 2.Bladder Cancer 3.Upper GU Tract Tumors 4. Urothelial Carcinoma of the Prostate 5. Primary Carcinoma of the Urethra 6. Breast Cancer 7. Central Nervous System Cancers 8. Cervical Cancer 9. Colon Cancer 10. Head and Neck Cancers (Salivary gland or non-nasopharyngeal) 11. Appendiceal Adenocarcinoma 12. Non-Small Cell Lung Cancer 13. Occult Primary Cancers 14. Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer 15. Pancreatic Adenocarcinoma 16. Rectal Cancer 17. Small Bowel Adenocarcinoma 18. Solid Tumors 19. Uterine Neoplasms 20. Vaginal Cancer 21. Vulvar Cancer	5.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle)
1.Esophageal, Esophagogastric Junction and Gastric Cancers 2. Gastric Cancer 3. Head and Neck Cancers(Salivary gland)	6.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle)

Duration of authorization: 12 months

Version Effective Date: 06/16/2025

Title: Fidanacogene elaparovect-dzkt (Beqvez™)

MEDICALLY NECESSARY:

Fidanacogene elaparovect-dzkt (Beqvez™) is considered medically necessary and, therefore, covered for the one-time (per lifetime) single dose treatment of hemophilia B for adult (≥18 years of age) individuals when ALL of the following criteria are met:

- Individual has moderately severe or severe hemophilia B as evidenced by a baseline (without Factor IX replacement therapy) Factor IX level ≤2% of normal
- Individual meets ONE of the following (i, ii, or iii):

i. According to the prescribing physician, the individual has a history of use of Factor IX therapy for ≥ 150 exposure days; OR

ii. Individual meets BOTH of the following (a and b):

a) Individual has a history of life-threatening hemorrhage; AND

b) On-demand use of Factor IX therapy was required for this life-threatening hemorrhage; OR

iii. Individual meets BOTH of the following (a and b):

1. Individual has a history of repeated, serious spontaneous bleeding episodes;

AND

b) On-demand use of Factor IX therapy was required for these serious spontaneous bleeding episodes;

- Individual does not have neutralizing antibodies to adeno-associated virus serotype Rh74var (AAVRh74var) capsid by an approved test
- Individual meets ALL of the following (i, ii, and iii):

i. Factor IX inhibitor titer testing has been performed within 30 days; AND

ii. Individual is negative for Factor IX inhibitors; AND

iii. Individual does not have a history of Factor IX inhibitors;

- Individual meets BOTH of the following:

i. Individual does not have an active infection with hepatitis B virus or hepatitis C virus; AND

ii. Individual is not currently receiving antiviral therapy for a prior hepatitis B virus or hepatitis C virus exposure;

- According to the prescribing physician, the individual does not have uncontrolled human immunodeficiency virus infection;
- Individual has undergone liver function testing within 30 days of administration of biologic and meets ALL of the following (i, ii, iii, and iv):

i. Alanine aminotransferase level is ≤ two times the upper limit of normal; AND

ii. Aspartate aminotransferase level is ≤ two times the upper limit of normal; AND

iii. Total bilirubin level is ≤ 1.5 times the upper limit of normal;

AND

iv. Alkaline phosphatase level is $\leq$ two times the upper limit of normal;

- Individual does not have evidence of advanced liver impairment and/or advanced fibrosis (e.g., liver elastography [e.g., ≥ 9 kPA] suggestive of or equal to METAVIR Stage 3 disease).
- Within the past 30 days, the platelet count for the individual was $\geq 100 \times 10^9/L$;
- Within the past 30 days, individual's creatinine was ≤ 2.0 mg/dL;
- Individual has not received a gene therapy for hemophilia B in the past; AND
- The medication is prescribed by a hemophilia specialist physician.

Duration of authorization: 12 months

Version Effective Date: 05/28/2025

Title: Filgrastim (Neupogen®) and Related Biosimilars, and tbo-filgrastim (Granix®)

MEDICALLY NECESSARY:

COMPANY-DESIGNATED PREFERRED PRODUCTS

Although there are many filgrastim products on the market (e.g., filgrastim [Neupogen], filgrastim-aafi [Nivestym], filgrastim-sndz [Zarxio], filgrastim-txid (Nypozi), tbo-filgrastim [Granix], filgrastim-ayow [Releuko]), there is no reliable evidence of the superiority of any one product of filgrastim compared to other products. The Company has designated the following filgrastim products as its preferred products:

- Filgrastim-aafi (Nivestym)
- Filgrastim-sndz (Zarxio)

These products are less costly and at least as likely to produce equivalent therapeutic results as the non-preferred products, which include, but are not limited to, filgrastim (Neupogen), tbo-filgrastim (Granix), any other nonpreferred filgrastim biosimilars.

According to the US Food and Drug Administration (FDA), “a biosimilar is a biological product that has no clinically meaningful differences from the existing FDA-approved reference product. All biosimilar products meet the FDA’s rigorous standards for approval for the indications described in the product labeling. Once a biosimilar has been approved by the FDA, the safety and effectiveness of these products have been established, just as they have been for the reference product.” Coverage of a biosimilar product as an alternate to a reference product is not considered a form of step therapy by the Company.

NON-PREFERRED PRODUCTS

Use of the non-preferred filgrastim products, which include, but are not limited to, filgrastim (Neupogen), tbo-filgrastim (Granix), filgrastim-ayow (Releuko) and any other non-preferred filgrastim biosimilars is considered medically necessary and, therefore, covered only for individuals who are currently receiving or have previously received a non-preferred product for the specified filgrastim indication.

If the individual has not previously received filgrastim (Neupogen), tbo-filgrastim (Granix), or any other non-preferred filgrastim biosimilars to treat the specified indication, these non-preferred products are only eligible for coverage when the individual has contraindication(s) or intolerance(s) to the Company-designated preferred products.

FILGRASTIM (NEUPOGEN) AND RELATED BIOSIMILARS

Filgrastim (Neupogen) and related biosimilars (e.g., filgrastim-aafi [Nivestym], filgrastim-sndz [Zarxio], filgrastim-txid (Nypozi), filgrastim-ayow [Releuko]) are considered medically necessary and, therefore, covered when used as recommended by the then-current National Comprehensive Cancer Network (NCCN) and American Society of Clinical Oncology (ASCO) guidelines for any of the following indications:

- Prophylaxis of myelosuppressive chemotherapy–induced febrile neutropenia or other dose-limiting neutropenic events in high-risk* (>20% overall risk of febrile neutropenia) individuals with solid tumors and nonmyeloid malignancies receiving treatment in the curative/adjuvant or palliative settings
- Prophylaxis of myelosuppressive chemotherapy–induced febrile neutropenia or other dose-limiting neutropenic events in intermediate-risk* (10%–20% overall risk of febrile neutropenia) individuals with solid tumors and nonmyeloid malignancies receiving treatment in the curative/adjuvant or palliative settings who have one or more of the following risk factors:
 - Prior chemotherapy or radiation therapy
 - Persistent neutropenia
 - Bone marrow involvement by tumor
 - Recent surgery and/or open wounds
 - Liver dysfunction (bilirubin >2 mg/dL)
 - Renal dysfunction (creatinine clearance <50 mL/min)
 - Age greater than 65 years receiving full chemotherapy dose intensity
 - Poor performance status (Eastern Cooperative Oncology Group [ECOG] Performance Status 3–4)
 - Human immunodeficiency virus (HIV) infection with low CD4 counts (≤ 450 cells/mm³ or less)
 - Chronic immunosuppression in the posttransplant setting, including organ transplant
- Prophylaxis of chemotherapy-induced febrile neutropenia in individuals with acute myeloid leukemia (AML) who are receiving induction chemotherapy for any of the following:
 - As a component of repeating the initial successful induction regimen if late relapse (≥ 12 months since induction regimen)
 - For relapsed or refractory disease in combination with cladribine and cytarabine, with or without mitoxantrone or idarubicin
 - For relapsed or refractory disease in combination with fludarabine and cytarabine, with or without idarubicin
- Prophylaxis of chemotherapy-induced febrile neutropenia in individuals with AML who are receiving consolidation chemotherapy for any of the following:
 - In combination with fludarabine, cytarabine, and idarubicin with or without gemtuzumab ozogamicin (preferred only if given during induction) for patients with poor-risk AML with and without TP53-mutation or del17p abnormality, therapy-related AML other than core-binding factor acute myeloid leukemia (CBF-AML), antecedent myelodysplastic syndromes (MDS) or chronic myelomonocytic leukemia (CMML).
- Prophylaxis of chemotherapy-induced febrile neutropenia or other dose-limiting neutropenic events in low-risk (<10% overall risk of febrile neutropenia) individuals with solid tumors and nonmyeloid malignancies receiving treatment in the curative/adjuvant or palliative settings who have two or more individual-related risk factors.
- Treatment of chemotherapy-induced febrile neutropenia

- In individuals who have been receiving prophylactic filgrastim
 - Consider in individuals who have not received prophylactic granulocyte colony-stimulating factors but who have risk factors for an infection-associated complication
- For hematopoietic cell transplantation for any of the following:
 - In combination with plerixafor
 - In combination with cyclophosphamide with or without plerixafor
 - As a single agent
 - In combination with disease-specific chemotherapy with or without plerixafor
 - In combination with motixafortide (Aphexda) in individuals with multiple myeloma
- Additional therapy for an insufficient collection of stem cells in combination with plerixafor following treatment with filgrastim alone or filgrastim and disease-specific chemotherapy
- Treatment for hematopoietic cell mobilization for allogeneic donors as a single agent
- Treatment for hematopoietic cell mobilization for autologous donors
 - In combination with plerixafor
 - In combination with cyclophosphamide with or without plerixafor
 - As a single agent
 - In combination with disease-specific chemotherapy with or without plerixafor
 - In combination with motixafortide (Aphexda) in individuals with multiple myeloma
- Therapeutic use in acute lymphoblastic leukemia (ALL) in adult individuals with relapsed/refractory (R/R) Philadelphia chromosome–negative B-ALL, T-ALL, and Philadelphia chromosome–positive B-ALL if refractory to tyrosine kinase inhibitors as a component of:
 - FLAG: induction/consolidation (fludarabine, cytarabine, granulocyte colony-stimulating factor)
 - FLAG-IDA: induction/consolidation (fludarabine, cytarabine, granulocyte colony-stimulating factor; with idarubicin)
- ALL or AML in pediatric individuals who have relapsed disease and have serious/life-threatening neutropenic infection
- Prophylaxis of chemotherapy-induced febrile neutropenia in individuals with Wilms tumor (nephroblastoma), when administered with Regimen M and Regimen I for courses of either:
 - Cyclophosphamide and etoposide
 - Cyclophosphamide, doxorubicin, and vincristine
- Diffuse aggressive lymphoma in individuals age 65 years and older treated with curative chemotherapy regimen cyclophosphamide, doxorubicin, vincristine, prednisone, and rituximab (R-CHOP)
- In pediatric individuals where dose-intense chemotherapy is administered for an indication that is known to have a survival benefit (e.g., Ewing sarcoma)

- Dose-dense therapy (standard doses given more frequently) for the adjuvant treatment of high-risk breast cancer or for the use of high-dose intensity methotrexate, vinblastine, doxorubicin, and cisplatin (HD-M-VAC) in urothelial cancer
- Secondary prophylaxis in individuals who have experienced a neutropenic event from a prior cycle of chemotherapy (for which primary prophylaxis was not received), in which a reduced dose or treatment delay may compromise disease-free or overall survival or treatment outcome
- Therapeutic use in individuals with cancer who have fever and neutropenia and are at high risk for infection-associated complications or who have prognostic factors that are predictive of poor clinical outcomes. High-risk features include the following factors:
 - Expected prolonged (>10 days) and profound ($<0.1 \times 10^9/L$) neutropenia
 - Age greater than 65 years
 - Pneumonia
 - Hypotension and multiorgan dysfunction (sepsis syndrome)
 - Invasive fungal infection
 - Hospitalization at the time of fever development
 - Other clinically documented infections
 - Prior episode of febrile neutropenia
- Prophylaxis of neutropenia and neutropenia-related clinical sequelae, e.g., febrile neutropenia, in individuals with nonmyeloid malignancies undergoing myeloablative chemotherapy followed by bone marrow transplantation (BMT)
- Mobilize autologous hematopoietic progenitor cells into the peripheral blood for collection by leukapheresis
- Prophylaxis of sequelae of severe neutropenia (e.g., fever, infections, oropharyngeal ulcers) in symptomatic individuals with congenital neutropenia, cyclic neutropenia, or idiopathic neutropenia
- Prophylaxis of neutropenia in individuals, undergoing hematopoietic cell transplant for any of the following indications:
 - Mobilization of hematopoietic progenitor cells in combination with plerixafor in the autologous setting for individuals with non-Hodgkin lymphoma or multiple myeloma
 - Mobilization of donor hematopoietic progenitor cells or for granulocyte transfusion in the allogeneic setting
 - As supportive care in the posttransplant setting
- Mobilization of hematopoietic progenitor cells in hematopoietic cell transplant in the autologous setting for any of the following:
 - As a single agent
 - Following combination chemotherapy
 - In combination with sargramostim
 - In combination with plerixafor for individuals with non-Hodgkin lymphoma or multiple myeloma
- Hematopoietic cell transplant for mobilization of donor hematopoietic progenitor cells or for granulocyte transfusion in the allogeneic setting
- Supportive care for hematopoietic cell transplant in the posttransplant setting

- Treatment of chemotherapy-induced febrile neutropenia for one of the following conditions:
 - In individuals who have been receiving prophylactic tbo-filgrastim
 - In individuals who have not received prophylactic granulocyte colony-stimulating factors but who have risk factors for an infection-associated complication
- Treatment for individuals with radiation-induced myelosuppression following a radiological or nuclear incident (hematopoietic acute radiation syndrome [H-ARS]):
- Management of CAR T-Cell-Related toxicities as additional supportive care for neutropenic individuals
- Treatment of individuals with lower risk^{†,††} MDS associated with symptomatic anemia with no del(5q), with or without other cytogenetic abnormalities with serum erythropoietin ≤500 mU/mL for any of the following:
 - With ring sideroblasts <15% (or ring sideroblasts <5% with an SF3B1 mutation) in combination with an erythropoiesis-stimulating agent (ESA) following no response (despite adequate iron stores) to either an ESA alone or luspatercept-aamt (REBLOZYL)
 - With ring sideroblasts ≥15% (or ring sideroblasts ≥5% with an SF3B1 mutation), in combination with an erythropoiesis-stimulating agent (ESA) following no response to luspatercept-aamt (REBLOZYL)

TBO-FILGRASTIM (GRANIX)

Tbo-filgrastim (Granix) is considered medically necessary and, therefore, covered for any of the following indications:

- May be used as a substitute for filgrastim
- Prophylaxis of severe neutropenia in adult and pediatric individuals 1 month and older with nonmyeloid malignancies receiving myelosuppressive anticancer therapy associated with a clinically significant incidence of febrile neutropenia
- Prophylaxis of chemotherapy-induced febrile neutropenia or other dose-limiting neutropenic events in high-risk (>20% overall risk of febrile neutropenia[†]) individuals with solid tumors and nonmyeloid malignancies receiving treatment in the curative/adjvant or palliative settings
- Prophylaxis of chemotherapy-induced febrile neutropenia or other dose-limiting neutropenic events in intermediate-risk (10% to 20% overall risk of febrile neutropenia[†]) individuals with solid tumors and nonmyeloid malignancies receiving treatment in the curative/adjvant or palliative settings who have one or more risk factors
- Prophylaxis of chemotherapy-induced febrile neutropenia or other dose-limiting neutropenic events in low-risk (<10% overall risk of febrile neutropenia) individuals with solid tumors and nonmyeloid malignancies receiving treatment in the curative/adjvant or palliative settings who have two or more individual-related risk factors.
- Treatment for individuals with radiation-induced myelosuppression following a radiological/nuclear incident (hematopoietic acute radiation syndrome [H-ARS])

- Treatment of chemotherapy-induced febrile neutropenia for one of the following conditions:
 - In individuals who have been receiving prophylactic tbo-filgrastim
 - In individuals who have not received prophylactic granulocyte colony-stimulating factors but who have risk factors for an infection-associated complication
- Treatment of individuals with lower risk^{†,††} MDS associated with symptomatic anemia with no del(5q), with or without other cytogenetic abnormalities with serum erythropoietin ≤500 mU/mL and any of the following:
 - In combination with an erythropoiesis-stimulating agent (ESA) following no response (despite adequate iron stores) to either an ESA alone or luspatercept-aamt (REBLOZYL) in individuals with ring sideroblasts <15% (or ring sideroblasts <5% with an SF3B1 mutation)
 - In combination with an ESA following no response to luspatercept-aamt (REBLOZYL) in individuals with ring sideroblasts ≥15% (or ring sideroblasts ≥5% with an SF3B1 mutation)

See Attachment A for examples of disease settings and chemotherapy regimens with a high (>20%) or intermediate (10%-20%) risk for febrile neutropenia (Note: These are not all-inclusive lists**).*

^{†,††}Lower risk defined as IPSS-R (Very Low, Low, Intermediate), IPSS (Low/Intermediate-1), WPSS (Very Low, Low, Intermediate).

Duration of authorization: 12 months

Version Effective Date: 04/01/2025

EXAMPLES OF DISEASE SETTINGS AND CHEMOTHERAPY REGIMENS WITH A HIGH (>20%) OR INTERMEDIATE (10-20%) RISK FOR FEBRILE NEUTROPENIA

Note: These are not all-inclusive lists.

Chemotherapy regimens and associated incidence of febrile neutropenia (FN) are based on the clinical trial(s) according to the grade based on The National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) criteria. Note: These are not all-inclusive lists. For those regimens not included in this list, assess febrile neutropenia risk based on published peer-reviewed clinical trials.

Per The National Comprehensive Cancer Network (NCCN) Guidelines, the decision for use of Filgrastim (Neupogen) and related biosimilars during the first chemotherapy cycle is based on the disease, type of chemotherapy regimen (i.e., high-dose, dose-dense, or standard-dose therapy), patient risk factors, and treatment intent (i.e., curative or palliative).

The decision for use of Filgrastim (Neupogen) and related biosimilars during the second and subsequent chemotherapy cycles is based on whether there was prior febrile neutropenia or a dose-limiting neutropenic event (e.g., a nadir count or day of treatment count that could otherwise impact the planned chemotherapy dose). If there was prior use of a granulocyte-colony stimulating factor (G-CSF), NCCN Guidelines recommend a dose reduction in chemotherapy or a change in the treatment regimen. If there was no prior use of a G-CSF, The NCCN Guidelines indicate to consider using a G-CSF.

EXAMPLES OF DISEASE SETTINGS AND CHEMOTHERAPY REGIMENS WITH A HIGH RISK FOR FEBRILE NEUTROPENIA (>20%)

Note: This is not an all-inclusive list

Acute Lymphoblastic Leukemia (ALL)

Select ALL regimens as directed by treatment protocol (see NCCN guidelines for ALL)

Bladder Cancer

Dose-dense MVAC (methotrexate, vinblastine, doxorubicin, cisplatin)

Bone Cancer

VAIA (vincristine, doxorubicin, dactinomycin, and ifosfamide)

VDC-IE (vincristine, doxorubicin or dactinomycin, and cyclophosphamide alternating with ifosfamide and etoposide)

Cisplatin/doxorubicin

VDC (cyclophosphamide, vincristine, doxorubicin or dactinomycin)

VIDE (vincristine, ifosfamide, doxorubicin or dactinomycin, etoposide)

Breast Cancer

Dose-dense AC followed by dose-dense paclitaxel (doxorubicin, cyclophosphamide, paclitaxel)

TAC (docetaxel, doxorubicin, cyclophosphamide)

TC* (docetaxel, cyclophosphamide)

TCH* (docetaxel, carboplatin, trastuzumab)

Head and Neck Squamous Cell Carcinoma

TPF (docetaxel, cisplatin, 5- fluorouracil)

Hodgkin's Lymphoma

Brentuximab vedotin + AVD (doxorubicin, vinblastine, dacarbazine)

Escalated BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone)

Kidney Cancer

Doxorubicin/gemcitabine

Non-Hodgkin's Lymphomas

CHP (cyclophosphamide, doxorubicin, prednisone) + brentuximab vedotin

Dose-adjusted EPOCH* (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)

ICE* (ifosfamide, carboplatin, etoposide)

Dose-dense CHOP-14* (cyclophosphamide, doxorubicin, vincristine, prednisone)

MINE* (mesna, ifosfamide, mitoxantrone, etoposide)

DHAP* (dexamethasone, cisplatin, cytarabine)

ESHAP* (etoposide, methylprednisolone, cisplatin, cytarabine)

HyperCVAD* (cyclophosphamide, vincristine, doxorubicin, dexamethasone + rituximab)

Pola-R-CHP (polatuzumab vedotin-piiq, rituximab, cyclophosphamide, doxorubicin, prednisone)

Melanoma

Dacarbazine-based combination with IL-2, interferon alpha (dacarbazine, cisplatin, vinblastine, IL-2, interferon alpha)

Multiple Myeloma

DT-PACE (dexamethasone/thalidomide/cisplatin/doxorubicin/cyclophosphamide/etoposide) with or without bortezomib (VTD-PACE)

Ovarian Cancer

Topotecan*

Docetaxel

Soft Tissue Sarcoma

MAID (mesna, doxorubicin, ifosfamide, dacarbazine)

Doxorubicin*

Ifosfamide/doxorubicin

Small Cell Lung Cancer

Topotecan

Testicular Cancer

VeIP (vinblastine, ifosfamide, cisplatin)

VIP (etoposide, ifosfamide, cisplatin)

TIP (paclitaxel, ifosfamide, cisplatin)

EXAMPLES OF DISEASE SETTINGS AND CHEMOTHERAPY REGIMENS WITH AN INTERMEDIATE RISK FOR FEBRILE NEUTROPENIA (10-20%)

Note: This is not an all-inclusive list.

Occult Primary – Adenocarcinoma

Gemcitabine/docetaxel

Breast Cancer

Docetaxel*

AC* (doxorubicin, cyclophosphamide) + sequential docetaxel (during taxane portion only)

Paclitaxel* every 21 days

Cervical Cancer

Cisplatin/topotecan

Paclitaxel/cisplatin*

Topotecan

Irinotecan

Colorectal Cancer

FOLFIRINOX (fluorouracil, leucovorin, irinotecan, oxaliplatin)

Esophageal and Gastric Cancers

Irinotecan/cisplatin*

Epirubicin/cisplatin/5-fluorouracil

Epirubicin/cisplatin/capecitabine

Non-Hodgkin's Lymphomas

GDP* (gemcitabine, dexamethasone, cisplatin/carboplatin)

CHOP* (cyclophosphamide, doxorubicin, vincristine, prednisone) including regimens with pegylated liposomal doxorubicin

Bendamustine*

Non-Small Cell Lung Cancer

Cisplatin/paclitaxel

Cisplatin/vinorelbine

Cisplatin/docetaxel

Cisplatin/etoposide

Carboplatin/paclitaxel*

Docetaxel

Ovarian Cancer

Carboplatin/docetaxel

Prostate Cancer

Cabazitaxel

Small Cell Lung Cancer

Etoposide/carboplatin

Testicular Cancer

BEP (bleomycin, etoposide, cisplatin)

Etoposide/cisplatin

Uterine Sarcoma

Docetaxel

Version Effective Date: 04/01/2025

Title: Givosiran (Givlaari) and Panhematin (Hemin)

MEDICALLY NECESSARY:

GIVOSIRAN (GIVLAARI)

Initial Therapy

Initiation of givosiran (Givlaari) is considered medically necessary and, therefore, covered if the following criteria are met:

- Individual is 18 years of age or older
 - Individual has a diagnosis of acute hepatic porphyria, and confirmation of one of the following subtypes:
 - Acute intermittent porphyria (AIP)
 - Hereditary coproporphyria (HCP)
 - Variegate porphyria (VP)
 - Alanine aminotransferase (ALT) dehydratase-deficiency porphyria (ADP)
- Individual has documentation of elevated urinary or plasma porphobilinogen (PBG) or delta-aminolevulinic acid (ALA) within the past year
- Individual meets one of the following criteria:
 - Individual has active symptomatic disease, with at least two documented porphyria attacks within the last 6 months
 - Individual is currently on prophylactic hemin treatment due to history of severe or frequent porphyria attacks

Dosing and Frequency

The recommended dosing for givosiran (Givlaari) by the US Food and Drug Administration (FDA) is 2.5 mg/kg given subcutaneously (SC) once every month by a healthcare provider, and injections are administered in a facility that is equipped and staffed to handle any anaphylactic reactions that may occur.

Continuation Therapy

Continuation of givosiran (Givlaari) is considered medically necessary and, therefore, covered if the following criteria are met:

- Individual has experienced a clinical response to therapy (e.g., a reduction in the number of porphyria attacks, or a reduction in hemin requirements for acute attacks)
- Individual does not have severe or clinically significant transaminase elevations, defined as ALT greater than five times the upper limit of normal.

PANHEMATIN (HEMIN)

Panhematin (Hemin) is considered medically necessary and, therefore, covered for individuals with acute hepatic porphyria when all of the following criteria are met:

- The individual is 16 years of age or older

- The individual has a diagnosis of acute hepatic porphyria, and confirmation of one of the following subtypes:
 - Acute intermittent porphyria (ACP)
 - Hereditary coproporphyria (HCP)
 - Variegate porphyria (VP)
 - ALA dehydratase-deficiency porphyria (ADP)
- The individual has documentation of elevated urinary or plasma PBG, ALA, or total porphyrin prior to receiving treatment
- The individual has presence of clinical symptoms suggestive of acute porphyric attack (e.g., unremitting abdominal pain, neuropathy, paresis, tachycardia)

If the individual has recurrent porphyria attacks (≥ 4 per year), prophylactic use—with or without the presence of symptoms—is considered medically necessary.

Dosing and Frequency

The recommended dosing for panhematin (Hemin) is 1 to 4 mg/kg/d intravenous (IV) for 3 to 14 days based on the clinical signs. In more severe cases, this dose may be repeated no earlier than every 12 hours.

Duration of authorization: 12 months**Version Effective Date: 05/19/2025**

Title: Glofitamab-gxbm (Columvi)

MEDICALLY NECESSARY:

GLOFITAMAB-GXBM (COLUMVI)

Glofitamab-gxbm (Columvi) is considered medically necessary and, therefore, covered as a single agent for the treatment of adult individuals for any of the following indications:

Diffuse Large B-Cell Lymphoma, Large B-cell lymphoma (LBCL)

- For the treatment of individuals with relapsed or refractory diffuse large B-cell lymphoma, not otherwise specified (DLBCL, NOS) or large B-cell lymphoma (LBCL) arising from follicular lymphoma, after two or more lines of systemic therapy.
- As National Comprehensive Cancer Network (NCCN) preferred third-line and subsequent therapy (only after at least two lines of systemic therapy) as a single agent for partial response, progressive, relapsed, or refractory disease including individuals with disease progression after transplant or chimeric antigen receptor (CAR) T-cell therapy.

Diffuse Large B-Cell Lymphoma, High-Grade B-Cell Lymphomas

- As a third-line and subsequent therapy (only after at least two lines of systemic therapy) for the treatment of individuals with partial response, no response, progressive, relapsed, or refractory disease, including individuals with disease progression after transplant or chimeric antigen receptor (CAR) T-cell therapy.

Histologic Transformation of Indolent Lymphomas to Diffuse Large B-Cell Lymphoma

- As a treatment of histologic transformation of follicular or marginal zone lymphoma to diffuse large B-cell lymphoma (only after at least two lines of systemic therapy) for partial response, no response, progressive, or relapsed disease including individuals with disease progression after transplant or CAR T-cell therapy

High-Grade B-Cell Lymphomas

- As NCCN-preferred third-line and subsequent therapy (only after at least two lines of systemic therapy) as for partial response, no response, progressive, relapsed, or refractory disease including individuals with disease progression after transplant or CAR T-cell therapy.

Human Immunodeficiency Virus (HIV)-Related B-Cell Lymphomas

- As NCCN-preferred third-line and subsequent therapy (only after at least two lines of systemic therapy) for HIV-related diffuse large B-cell lymphoma, primary effusion lymphoma, and human herpesvirus 8 (HHV8)-positive diffuse large B-cell lymphoma, not otherwise specified for partial response, no response, relapsed, progressive or refractory disease including individuals with disease progression after transplant or CAR T-cell therapy.

Post-Transplant Lymphoproliferative Disorders (PTLD)

- As NCCN-preferred third-line and subsequent therapy (only after at least two lines of systemic therapy) for monomorphic PTLD (B-cell type) for partial response, no response, relapsed, progressive or refractory disease including individuals with disease progression after transplant or CAR T-cell therapy.

Duration of authorization: 12 months

Version Effective Date: 10/01/2024

Title: Golimumab (Simponi Aria®) Intravenous (IV) Injection

MEDICALLY NECESSARY:

INITIAL THERAPY

Ankylosing Spondylitis (AS)

Golimumab (Simponi Aria) is considered medically necessary and, therefore, covered for the treatment of active AS when all of the following criteria are met:

- The individual is at least 18 years old.
- Documentation of failure, contraindication, or intolerance to either of the following:
 - At least a 4-week trial of two nonsteroidal anti-inflammatory drugs (NSAIDs) at maximum recommended or tolerated anti-inflammatory dose
 - At least a 3-month trial of one disease-modifying antirheumatic drug (DMARD) (e.g., sulfasalazine, methotrexate, hydroxychloroquine)
- Active or latent tuberculosis (TB) has been ruled out.

Immune Checkpoint Inhibitor–Related Toxicities

Golimumab (Simponi Aria) is considered medically necessary and, therefore, covered for the management of moderate or severe immunotherapy-related inflammatory arthritis when all of the following criteria are met:

- If no improvement after holding immunotherapy and treating with oral corticosteroids, or if unable to taper corticosteroids, or no response to conventional synthetic DMARDs (e.g., methotrexate, sulfasalazine, leflunomide, hydroxychloroquine)
- Active or latent TB has been ruled out.

Polyarticular Juvenile Idiopathic Arthritis (pJIA)

Golimumab (Simponi Aria) is considered medically necessary and, therefore, covered for the treatment of active pJIA when all of the following criteria are met:

- The individual is at least 2 years old.
- Documentation of failure, contraindication, or intolerance to at least 2 months of one DMARD (e.g., methotrexate)
- Active or latent TB has been ruled out.

Psoriatic Arthritis (PsA)

Golimumab (Simponi Aria) is considered medically necessary and, therefore, covered for the treatment of active PsA when all of the following criteria are met:

- The individual is at least 2 years old.
- Documentation of failure, contraindication, or intolerance to either of the following:
 - At least a 4-week trial of any NSAIDs at maximum recommended or tolerated anti-inflammatory dose

- At least a 3-month trial of one DMARD (e.g., methotrexate, hydroxychloroquine, leflunomide, or sulfasalazine)
- Active or latent TB has been ruled out.

Rheumatoid Arthritis (RA)

Golimumab (Simponi Aria) is considered medically necessary and, therefore, covered for the treatment of moderately to severely active RA in combination with methotrexate (MTX) (or a different DMARD when MTX is contraindicated or the individual is intolerant [e.g., sulfasalazine, hydroxychloroquine, and leflunomide]) when all of the following criteria are met:

- The individual is at least 18 years old.
- The individual has persistent disease despite at least 3 months of MTX.
 - In individuals in whom MTX is contraindicated or the individual is intolerant to MTX, a 3-month trial of a different DMARD (e.g., sulfasalazine, hydroxychloroquine, and leflunomide) is acceptable.
- Active or latent TB has been ruled out.

CONTINUATION THERAPY

Golimumab (Simponi Aria) is considered medically necessary and, therefore, covered for the continuation therapy when the individual meets all of the following:

- Individual has met the medical necessity criteria for Initial Therapy
- There is documentation of positive clinical response or stabilization to therapy (e.g., improvement in total active [swollen and tender] joint count from baseline, or improvement in symptoms [e.g., pain, stiffness, inflammation] from baseline)

Duration of authorization: 12 months

Version Effective Date: 07/10/2024

Title: Golimumab (Simponi Aria®) Intravenous (IV) Injection

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

MEDICALLY NECESSARY

L40.50 Arthropathic psoriasis, unspecified

L40.51 Distal interphalangeal psoriatic arthropathy

L40.52 Psoriatic arthritis mutilans

L40.53 Psoriatic spondylitis

L40.54 Psoriatic juvenile arthropathy

L40.59 Other psoriatic arthropathy

M05.7A Rheumatoid arthritis with rheumatoid factor of other specified site without organ or systems involvement

M05.8A Other rheumatoid arthritis with rheumatoid factor of other specified site

M05.00 Felty's syndrome, unspecified site

M05.011 Felty's syndrome, right shoulder

M05.012 Felty's syndrome, left shoulder

M05.021 Felty's syndrome, right elbow

M05.022 Felty's syndrome, left elbow

M05.031 Felty's syndrome, right wrist

M05.032 Felty's syndrome, left wrist

M05.041 Felty's syndrome, right hand

M05.042 Felty's syndrome, left hand

M05.051 Felty's syndrome, right hip

M05.052 Felty's syndrome, left hip

M05.061 Felty's syndrome, right knee

M05.062 Felty's syndrome, left knee

M05.071 Felty's syndrome, right ankle and foot

M05.072 Felty's syndrome, left ankle and foot

M05.09 Felty's syndrome, multiple sites

M05.10 Rheumatoid lung disease with rheumatoid arthritis of unspecified site

M05.111 Rheumatoid lung disease with rheumatoid arthritis of right shoulder

M05.112 Rheumatoid lung disease with rheumatoid arthritis of left shoulder

M05.121 Rheumatoid lung disease with rheumatoid arthritis of right elbow

M05.122 Rheumatoid lung disease with rheumatoid arthritis of left elbow

M05.131 Rheumatoid lung disease with rheumatoid arthritis of right wrist

M05.132 Rheumatoid lung disease with rheumatoid arthritis of left wrist

M05.141 Rheumatoid lung disease with rheumatoid arthritis of right hand

M05.142 Rheumatoid lung disease with rheumatoid arthritis of left hand

M05.151 Rheumatoid lung disease with rheumatoid arthritis of right hip

M05.152 Rheumatoid lung disease with rheumatoid arthritis of left hip

M05.161 Rheumatoid lung disease with rheumatoid arthritis of right knee

M05.162 Rheumatoid lung disease with rheumatoid arthritis of left knee

M05.171 Rheumatoid lung disease with rheumatoid arthritis of right ankle and foot

M05.172 Rheumatoid lung disease with rheumatoid arthritis of left ankle and foot

M05.19 Rheumatoid lung disease with rheumatoid arthritis of multiple sites

M05.20 Rheumatoid vasculitis with rheumatoid arthritis of unspecified site

M05.211 Rheumatoid vasculitis with rheumatoid arthritis of right shoulder

M05.212 Rheumatoid vasculitis with rheumatoid arthritis of left shoulder

M05.221 Rheumatoid vasculitis with rheumatoid arthritis of right elbow

M05.222 Rheumatoid vasculitis with rheumatoid arthritis of left elbow

M05.231 Rheumatoid vasculitis with rheumatoid arthritis of right wrist

M05.232 Rheumatoid vasculitis with rheumatoid arthritis of left wrist

M05.241 Rheumatoid vasculitis with rheumatoid arthritis of right hand

M05.242 Rheumatoid vasculitis with rheumatoid arthritis of left hand

M05.251 Rheumatoid vasculitis with rheumatoid arthritis of right hip

M05.252 Rheumatoid vasculitis with rheumatoid arthritis of left hip

M05.261 Rheumatoid vasculitis with rheumatoid arthritis of right knee

M05.262 Rheumatoid vasculitis with rheumatoid arthritis of left knee

M05.271 Rheumatoid vasculitis with rheumatoid arthritis of right ankle and foot

M05.272 Rheumatoid vasculitis with rheumatoid arthritis of left ankle and foot

M05.29 Rheumatoid vasculitis with rheumatoid arthritis of multiple sites

M05.30 Rheumatoid heart disease with rheumatoid arthritis of unspecified site

M05.311 Rheumatoid heart disease with rheumatoid arthritis of right shoulder

M05.312 Rheumatoid heart disease with rheumatoid arthritis of left shoulder

M05.321 Rheumatoid heart disease with rheumatoid arthritis of right elbow

M05.322 Rheumatoid heart disease with rheumatoid arthritis of left elbow

M05.331 Rheumatoid heart disease with rheumatoid arthritis of right wrist

M05.332 Rheumatoid heart disease with rheumatoid arthritis of left wrist

M05.341 Rheumatoid heart disease with rheumatoid arthritis of right hand

M05.342 Rheumatoid heart disease with rheumatoid arthritis of left hand

M05.351 Rheumatoid heart disease with rheumatoid arthritis of right hip

M05.352 Rheumatoid heart disease with rheumatoid arthritis of left hip

M05.361 Rheumatoid heart disease with rheumatoid arthritis of right knee

M05.362 Rheumatoid heart disease with rheumatoid arthritis of left knee

M05.371 Rheumatoid heart disease with rheumatoid arthritis of right ankle and foot

M05.372 Rheumatoid heart disease with rheumatoid arthritis of left ankle and foot

M05.39 Rheumatoid heart disease with rheumatoid arthritis of multiple sites

M05.40 Rheumatoid myopathy with rheumatoid arthritis of unspecified site

M05.411 Rheumatoid myopathy with rheumatoid arthritis of right shoulder

M05.412 Rheumatoid myopathy with rheumatoid arthritis of left shoulder

M05.421 Rheumatoid myopathy with rheumatoid arthritis of right elbow

M05.422 Rheumatoid myopathy with rheumatoid arthritis of left elbow

M05.431 Rheumatoid myopathy with rheumatoid arthritis of right wrist

M05.432 Rheumatoid myopathy with rheumatoid arthritis of left wrist

M05.441 Rheumatoid myopathy with rheumatoid arthritis of right hand

M05.442 Rheumatoid myopathy with rheumatoid arthritis of left hand

M05.451 Rheumatoid myopathy with rheumatoid arthritis of right hip

M05.452 Rheumatoid myopathy with rheumatoid arthritis of left hip

M05.461 Rheumatoid myopathy with rheumatoid arthritis of right knee

M05.462 Rheumatoid myopathy with rheumatoid arthritis of left knee

M05.471 Rheumatoid myopathy with rheumatoid arthritis of right ankle and foot

M05.472 Rheumatoid myopathy with rheumatoid arthritis of left ankle and foot

M05.49 Rheumatoid myopathy with rheumatoid arthritis of multiple sites

M05.50 Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified site

M05.511 Rheumatoid polyneuropathy with rheumatoid arthritis of right shoulder

M05.512 Rheumatoid polyneuropathy with rheumatoid arthritis of left shoulder

M05.521 Rheumatoid polyneuropathy with rheumatoid arthritis of right elbow

M05.522 Rheumatoid polyneuropathy with rheumatoid arthritis of left elbow

M05.531 Rheumatoid polyneuropathy with rheumatoid arthritis of right wrist

M05.532 Rheumatoid polyneuropathy with rheumatoid arthritis of left wrist

M05.541 Rheumatoid polyneuropathy with rheumatoid arthritis of right hand

M05.542 Rheumatoid polyneuropathy with rheumatoid arthritis of left hand

M05.551 Rheumatoid polyneuropathy with rheumatoid arthritis of right hip

M05.552 Rheumatoid polyneuropathy with rheumatoid arthritis of left hip

M05.561 Rheumatoid polyneuropathy with rheumatoid arthritis of right knee

M05.562 Rheumatoid polyneuropathy with rheumatoid arthritis of left knee

M05.571 Rheumatoid polyneuropathy with rheumatoid arthritis of right ankle and foot

M05.572 Rheumatoid polyneuropathy with rheumatoid arthritis of left ankle and foot

M05.59 Rheumatoid polyneuropathy with rheumatoid arthritis of multiple sites

M05.60 Rheumatoid arthritis of unspecified site with involvement of other organs and systems

M05.611 Rheumatoid arthritis of right shoulder with involvement of other organs and systems

M05.612 Rheumatoid arthritis of left shoulder with involvement of other organs and systems

M05.621 Rheumatoid arthritis of right elbow with involvement of other organs and systems

M05.622 Rheumatoid arthritis of left elbow with involvement of other organs and systems

M05.631 Rheumatoid arthritis of right wrist with involvement of other organs and systems

M05.632 Rheumatoid arthritis of left wrist with involvement of other organs and systems

M05.641 Rheumatoid arthritis of right hand with involvement of other organs and systems

M05.642 Rheumatoid arthritis of left hand with involvement of other organs and systems

M05.651 Rheumatoid arthritis of right hip with involvement of other organs and systems

M05.652 Rheumatoid arthritis of left hip with involvement of other organs and systems

M05.661 Rheumatoid arthritis of right knee with involvement of other organs and systems

M05.662 Rheumatoid arthritis of left knee with involvement of other organs and systems

M05.671 Rheumatoid arthritis of right ankle and foot with involvement of other organs and systems

M05.672 Rheumatoid arthritis of left ankle and foot with involvement of other organs and systems

M05.69 Rheumatoid arthritis of multiple sites with involvement of other organs and systems

M05.70 Rheumatoid arthritis with rheumatoid factor of unspecified site without organ or systems involvement

M05.711 Rheumatoid arthritis with rheumatoid factor of right shoulder without organ or systems involvement

M05.712 Rheumatoid arthritis with rheumatoid factor of left shoulder without organ or systems involvement

M05.721 Rheumatoid arthritis with rheumatoid factor of right elbow without organ or systems involvement

M05.722 Rheumatoid arthritis with rheumatoid factor of left elbow without organ or systems involvement

M05.731 Rheumatoid arthritis with rheumatoid factor of right wrist without organ or systems involvement

M05.732 Rheumatoid arthritis with rheumatoid factor of left wrist without organ or systems involvement

M05.741 Rheumatoid arthritis with rheumatoid factor of right hand without organ or systems involvement

M05.742 Rheumatoid arthritis with rheumatoid factor of left hand without organ or systems involvement

M05.751 Rheumatoid arthritis with rheumatoid factor of right hip without organ or systems involvement

M05.752 Rheumatoid arthritis with rheumatoid factor of left hip without organ or systems involvement

M05.761 Rheumatoid arthritis with rheumatoid factor of right knee without organ or systems involvement

M05.762 Rheumatoid arthritis with rheumatoid factor of left knee without organ or systems involvement

M05.771 Rheumatoid arthritis with rheumatoid factor of right ankle and foot without organ or systems involvement

M05.772 Rheumatoid arthritis with rheumatoid factor of left ankle and foot without organ or systems involvement

M05.79 Rheumatoid arthritis with rheumatoid factor of multiple sites without organ or systems involvement

M05.80 Other rheumatoid arthritis with rheumatoid factor of unspecified site

M05.811 Other rheumatoid arthritis with rheumatoid factor of right shoulder

M05.812 Other rheumatoid arthritis with rheumatoid factor of left shoulder

M05.821 Other rheumatoid arthritis with rheumatoid factor of right elbow

M05.822 Other rheumatoid arthritis with rheumatoid factor of left elbow

M05.831 Other rheumatoid arthritis with rheumatoid factor of right wrist

M05.832 Other rheumatoid arthritis with rheumatoid factor of left wrist

M05.841 Other rheumatoid arthritis with rheumatoid factor of right hand

M05.842 Other rheumatoid arthritis with rheumatoid factor of left hand

M05.851 Other rheumatoid arthritis with rheumatoid factor of right hip

M05.852 Other rheumatoid arthritis with rheumatoid factor of left hip

M05.861 Other rheumatoid arthritis with rheumatoid factor of right knee

M05.862 Other rheumatoid arthritis with rheumatoid factor of left knee

M05.871 Other rheumatoid arthritis with rheumatoid factor of right ankle and foot

M05.872 Other rheumatoid arthritis with rheumatoid factor of left ankle and foot

M05.89 Other rheumatoid arthritis with rheumatoid factor of multiple sites

M05.9 Rheumatoid arthritis with rheumatoid factor, unspecified

M06.0A Rheumatoid arthritis without rheumatoid factor, other specified site

M06.8A Other specified rheumatoid arthritis, other specified site

M06.00 Rheumatoid arthritis without rheumatoid factor, unspecified site

M06.011 Rheumatoid arthritis without rheumatoid factor, right shoulder

M06.012 Rheumatoid arthritis without rheumatoid factor, left shoulder

M06.021 Rheumatoid arthritis without rheumatoid factor, right elbow

M06.022 Rheumatoid arthritis without rheumatoid factor, left elbow

M06.031 Rheumatoid arthritis without rheumatoid factor, right wrist

M06.032 Rheumatoid arthritis without rheumatoid factor, left wrist

M06.041 Rheumatoid arthritis without rheumatoid factor, right hand

M06.042 Rheumatoid arthritis without rheumatoid factor, left hand

M06.051 Rheumatoid arthritis without rheumatoid factor, right hip

M06.052 Rheumatoid arthritis without rheumatoid factor, left hip

M06.061 Rheumatoid arthritis without rheumatoid factor, right knee

M06.062 Rheumatoid arthritis without rheumatoid factor, left knee

M06.071 Rheumatoid arthritis without rheumatoid factor, right ankle and foot

M06.072 Rheumatoid arthritis without rheumatoid factor, left ankle and foot

M06.08 Rheumatoid arthritis without rheumatoid factor, vertebrae

M06.09 Rheumatoid arthritis without rheumatoid factor, multiple sites

M06.4 Inflammatory polyarthropathy

M06.80 Other specified rheumatoid arthritis, unspecified site

M06.811 Other specified rheumatoid arthritis, right shoulder

M06.812 Other specified rheumatoid arthritis, left shoulder

M06.821 Other specified rheumatoid arthritis, right elbow

M06.822 Other specified rheumatoid arthritis, left elbow

M06.831 Other specified rheumatoid arthritis, right wrist

M06.832 Other specified rheumatoid arthritis, left wrist

M06.841 Other specified rheumatoid arthritis, right hand

M06.842 Other specified rheumatoid arthritis, left hand

M06.851 Other specified rheumatoid arthritis, right hip

M06.852 Other specified rheumatoid arthritis, left hip

M06.861 Other specified rheumatoid arthritis, right knee

M06.862 Other specified rheumatoid arthritis, left knee

M06.871 Other specified rheumatoid arthritis, right ankle and foot

M06.872 Other specified rheumatoid arthritis, left ankle and foot

M06.88 Other specified rheumatoid arthritis, vertebrae

M06.89 Other specified rheumatoid arthritis, multiple sites

M06.9 Rheumatoid arthritis, unspecified

M08.3 Juvenile rheumatoid polyarthritis (seronegative)

M45.0 Ankylosing spondylitis of multiple sites in spine

M45.1 Ankylosing spondylitis of occipito-atlanto-axial region

M45.2 Ankylosing spondylitis of cervical region

M45.3 Ankylosing spondylitis of cervicothoracic region

M45.4 Ankylosing spondylitis of thoracic region

M45.5 Ankylosing spondylitis of thoracolumbar region

M45.6 Ankylosing spondylitis lumbar region

M45.7 Ankylosing spondylitis of lumbosacral region

M45.8 Ankylosing spondylitis sacral and sacrococcygeal region

M45.9 Ankylosing spondylitis of unspecified sites in spine

Duration of authorization: 12 months

Version Effective Date: 07/10/2024

Title: Guselkumab (Tremfya®) Injection for Intravenous Use

MEDICALLY NECESSARY:

ULCERATIVE COLITIS

Guselkumab (Tremfya) for intravenous (IV) infusion is considered medically necessary and, therefore, covered for the treatment of individuals with moderate-to-severe active ulcerative colitis when both of the following criteria and the Dosing and Frequency Requirements listed below are met:

- The individual is at least 18 years of age.
- There is documentation of inadequate response, lost response, or intolerance to a trial of one of the following:
 - Immunomodulators (e.g., azathioprine, 6-mercaptopurine, methotrexate)
 - Demonstrated dependence on corticosteroids (e.g., budesonide [Entocort EC], prednisone, hydrocortisone, methylprednisolone)
 - Tumor necrosis factor (TNF) blocker (e.g., adalimumab Humira®)
 - Biologics for the treatment of UC (e.g., ustekinumab (Stelara), risankizumab (Skyrizi), Golimumab (Simponi®)
 - JAK Inhibitors (e.g., tofacitinib [Xeljanz], Upadacitinib [Rinvoq])
- No concurrent use with any other biologic therapy (i.e., tumor necrosis factor antagonists)
- Prescribed by or in consultation with a gastroenterologist
- Dosing and frequency: IV infusion will be used as an induction dose, followed by maintenance dosing with subcutaneous (SC) injection
 - Induction: IV: 200 mg on weeks 0, 4, and 8 followed by maintenance (Tremfya SC)

Note: The duration of Guselkumab (Tremfya) IV infusion is limited to 3 doses.

Duration of authorization: 12 months

Version Effective Date: 03/24/2025

Title: Imetelstat (Rytelo™)

MEDICALLY NECESSARY:

INITIAL THERAPY

Imetelstat (Rytelo™) is considered medically necessary and, therefore, covered for the treatment of adult individuals with low- to intermediate-1 risk myelodysplastic syndromes (MDS) with transfusion-dependent anemia when dosing and frequency requirements and **ALL** of the following criteria are met:

- Diagnosis of MDS confirmed by bone marrow aspirate and/or biopsy
- Individual has required transfusion of 4 or more red blood cell (RBC) units over 8 weeks **AND** pretransfusion hemoglobin is 9.0 g/dL or less
- Individual with lower risk disease (i.e., very low, low, intermediate) as assessed by validated rating index/scale (e.g., International Prognostic Scoring System-revised [IPSS-R]) and **ONE** of the following:
 - Disease associated with symptomatic anemia **WITH** del(5q), with or without one other cytogenetic abnormality (except those involving chromosome 7) and **ONE** of the following:
 - Following no response to or relapse after lenalidomide if poor probability to respond to immunosuppressive therapy (IST) (e.g., older age, high-risk mutations)
 - Following no response to or relapse after an erythropoiesis-stimulating agent (ESA) if poor probability to respond to IST (e.g., older age, high-risk mutations)
 - Following no response to or relapse after lenalidomide, followed by no response to or intolerance or relapse after IST
 - Following no response to or relapse after an ESA with serum erythropoietin 500 mU/mL or less, followed by no response to or intolerance or relapse after IST
 - Disease associated with symptomatic anemia **WITHOUT** del(5q), with or without other cytogenetic abnormalities and **ONE** of the following:
 - With ring sideroblasts less than 15 percent (or ring sideroblasts less than 5 percent with an SF3B1 mutation) and **ONE** of the following:
 1. With serum erythropoietin 500 mU/mL or less following no response to or relapse after an ESA alone, followed by no response to or relapse after an ESA with or without a G-CSF or lenalidomide
 2. With serum erythropoietin 500 mU/mL or less following no response to or relapse after an ESA alone, followed by no response to or relapse after luspatercept-aamt
 3. With serum erythropoietin 500 mU/mL or less following no response to or relapse after luspatercept-aamt, followed by no

response to or relapse after an ESA with or without a G-CSF or lenalidomide

4. With serum erythropoietin greater than 500 mU/mL and a poor probability to respond to IST (e.g., older age, high-risk mutations)
 5. With serum erythropoietin greater than 500 mU/mL following no response to or intolerance or relapse after IST
- With ring sideroblasts 15 percent or greater (or ring sideroblasts 5 percent or greater with an SF3B1 mutation) and **ONE** of the following:
 1. Following no response to or relapse after luspatercept-aamt (National Comprehensive Cancer Network [NCCN] preferred)
 2. With serum erythropoietin 500 mU/mL or less following no response to or relapse after luspatercept-aamt, followed by no response to or relapse after an ESA with or without a G-CSF if a poor probability to respond to IST (e.g., older age, high-risk mutations)
 3. With serum erythropoietin 500 mU/mL or less following no response to or relapse after luspatercept-aamt, followed by no response to or relapse after an ESA with or without a G-CSF, followed by no response to or intolerance or relapse after IST
 4. As initial treatment if serum erythropoietin greater than 500 mU/mL (ineligible for ESAs)
 5. With serum erythropoietin greater than 500 mU/mL following no response to or relapse after luspatercept-aamt, followed by no response to or relapse after lenalidomide if a poor probability to respond to IST (e.g., older age, high-risk mutations)
 6. With serum erythropoietin greater than 500 mU/mL following no response to or relapse after luspatercept-aamt, followed by no response to or relapse after lenalidomide, followed by no response to or intolerance or relapse after IST
- Dosing and frequency: 7.1 mg/kg administered as an intravenous infusion over 2 hours every 4 weeks

CONTINUATION THERAPY

Continuation of imetelstat (Rytelo) is considered medically necessary and, therefore, covered for individuals who have demonstrated **BOTH** of the following, compared to baseline:

- Individual experiences a decrease in RBC transfusion burden after 24 weeks of treatment (administration of 6 doses)
- No unacceptable toxicity occurs at any time

Duration of authorization: 12 months

Version Effective Date: 05/19/2025

Title: Immune Globulin Intravenous (IVIG), Subcutaneous (SCIG)

MEDICALLY NECESSARY:

SUBCUTANEOUS IMMUNE GLOBULIN (SCIG)

Company-Designated Preferred Products

Cutaquig, Cuvitru, Hizentra, HyQvia, and Xembify are brand names of SCIG products that are currently on the market. There are also certain IVIG products (e.g., Gammagard Liquid, Gammaked, Gamunex-C) that can be administered intravenously or subcutaneously. Although there are several brands of IVIG and SCIG on the market approved for the treatment of PIDD or CIDP, there is no reliable evidence of the superiority of any one brand compared to others. The Company has designated Gammagard Liquid, Gammaked, and Gamunex-C as its preferred subcutaneous products. These products are less costly and at least as likely to produce equivalent therapeutic results as the non-preferred products, which include, but are not limited to: Cutaquig, Cuvitru, Hizentra, HyQvia, and Xembify.

SCIG (e.g., Cutaquig, Cuvitru, Hizentra, HyQvia, and Xembify) products are considered medically necessary and, therefore, covered for the following indications when the dosing and frequency requirements listed in Attachment A and the following criterion is met:

- The individual has had a documented failure, contraindication* or intolerance to the subcutaneous administration of one or more of the Company's preferred subcutaneous products (i.e., Gammagard Liquid, Gammaked, or Gamunex-C)

*Contraindications to IG products may include factors such as, but not limited to: volume load, sugar content, sodium content, osmolality, IgA content, or pH.

Immunodeficiency Syndromes

- HIES (Hyper-IgE syndromes, Job syndrome) when all of the following signs and symptoms are present:
 - The individual has eosinophilia (500 or more eosinophils/ μ L)
 - The individual has elevated serum IgE (>2000 IU/mL), with normal IgG, IgA, and IgM levels
 - The individual has eczema, recurrent staphylococcal lung infections, and/or skin abscesses documented in office or hospital charts
 - The individual has had a documented failure, contraindication* or intolerance to the subcutaneous administration of one or more of the Company's preferred subcutaneous products (i.e., Gammagard Liquid, Gammaked, or Gamunex-C) (See "Company-Designated Preferred Products section above and "NOT MEDICALLY NECESSARY USES FOR SCIG" section below).
- PIDD[†] when the individual has a confirmed genetic diagnosis or laboratory evidence of PIDD **or** the individual meets both of the following criteria:
 - The individual has a personal history of recurrent, antibiotic-refractory, bacterial infections of the ear (e.g., otitis media) or sinopulmonary infections (e.g.,

sinusitis, bronchitis/bronchiectasis, pneumonia), which are documented in office or hospital charts

- The individual has a deficiency of antibody response to at least **one** of the following antigens (e.g., proteins, polysaccharides, or viral antigens)
 - Polyvalent pneumococcal polysaccharide vaccine (e.g., Pneumovax 23), measured at the time of immunization and 4 to 8 weeks after vaccination
 - A protective (normal) response to each pneumococcal serotype is defined as a titer equal to or greater than 1.3 µg/mL antibody.
 1. For individuals ages 6 to 65 years, a normal response is defined as conversion of 70% of the serotypes tested with at least a twofold increase in the titers.
 2. For children 24 months through 5 years of age, a normal response is defined as the conversion of 50% or more of the serotypes tested with at least a twofold increase in the titers.
 3. (Note: When reported, the conversion factor for nanograms of antibody nitrogen per milliliter (ng N/mL) to antibody micrograms per milliliter is as follows: 160 ng N/mL = 1 µg/mL)
 - Protein antigens, tetanus/diphtheria vaccine measured at the time of immunization and 3 to 4 weeks after vaccination:
 - A protective (normal) response is defined as any of the following:
 1. At least a fourfold increase for protein antigens
 2. A serum diphtheria antitoxin level of 0.01 International Units (IU)/mL is the lowest level giving some degree of protection, and levels of at least 0.1 IU/mL are generally regarded as protective
 3. A protective level for tetanus is 0.15 IU/mL
- The individual has had a documented failure, contraindication* or intolerance to the subcutaneous administration of one or more of the Company's preferred subcutaneous products (i.e., Gammagard Liquid, Gammaked, or Gamunex-C) (See "Company-Designated Preferred Products section above and "NOT MEDICALLY NECESSARY USES FOR SCIG" section below).

*The list of PIDDs includes but is not limited to:

1. Activated Phosphoinositide 3-kinase Delta Syndrome (APDS)
2. Ataxia-telangiectasia
3. Autosomal recessive agammaglobulinemia
4. Caspase-8 deficiency
5. Combined immunodeficiencies
6. Common variable immunodeficiency (including TACI and ICOS mutation)
7. DiGeorge syndrome
8. DOCK (dedicator of cytokinesis 8) deficiency

9. Griscelli syndrome
10. Hereditary hypogammaglobulinemia
11. Hypogammaglobulinemia, persistent (IgG $\leq$ 400 mg/dL or less than two standard deviations [SD] from normal)
12. IgG-subclass deficiency (deficiency of one or more IgG subclasses to levels less than 2 SD below the age-specific mean, in the presence of normal or near-normal total IgG levels). (These levels must be assessed on at least two occasions while the individual is free of acute infections.)
13. Immunodeficiency with increased IgM
14. Major histocompatibility complex class I or II deficiency
15. Nezelof's syndrome
16. NEMO (mutations in IKK-gamma) deficiency
17. Nijmegen breakage syndrome
18. Purine nucleoside phosphorylase [PNP] deficiency
19. Selective IgA deficiency with IgG subclass deficiency (reduced serum IgA levels [<7 mg/dL] and normal IgG and IgM levels)
20. Severe combined immunodeficiency (SCID)
21. SCID due to adenosine deaminase deficiency
22. Specific antibody deficiency (selective antibody deficiency) with normal immunoglobulins
 1. Individual has impaired production of specific antibodies to polysaccharide antigens after vaccination and normal responses to protein antigens
23. Transient hypogammaglobulinemia of infancy
24. WHIM (warts, hypogammaglobulinemia, immunodeficiency, and myelokathexis) syndrome
25. Wiskott-Aldrich syndrome
26. X-linked agammaglobulinemia (Bruton's agammaglobulinemia, congenital agammaglobulinemia)
27. X-linked and autosomal recessive hyper-IgM syndromes
28. X-linked immunodeficiency
29. X-linked lymphoproliferative disease

Neurological and Musculoskeletal Disorders

- CIDP, when all of the following criteria are met:
 - The individual will begin treatment with SCIG after transitioning from IVIG.
 - The individual has progressive or relapsing motor or sensory impairment caused by neuropathy in more than one limb for at least 2 months
 - The individual has at least one of the following electrodiagnostic findings of demyelination:
 - Motor distal latency prolongation in two nerves
 - Reduction of motor conduction velocity in two nerves
 - Prolongation of F-wave latency in two nerves
 - Absence of F-waves in at least one nerve
 - Motor conduction block in at least one nerve

- Abnormal temporal dispersion in at least two nerves
- Distal compound muscle action potential (CMAP) duration increase in at least one nerve
- The individual has had a documented failure, contraindication* or intolerance to the subcutaneous administration of the Company's preferred subcutaneous products (i.e., Gammagard Liquid, Gammaked, or Gamunex-C) (See "Company-Designated Preferred Products" section above and "NOT MEDICALLY NECESSARY USES FOR SCIG" section below).

INTRAVENOUS IMMUNE GLOBULIN (IVIG)

Use of IVIG therapy (e.g., Alyglo, Asceniv, Bivigam, Flebogamma, Gammagard Liquid, Gammagard S/D, Gammaked, Gammaplex, Gamunex-C, Octagam, Panzyga, Privigen) is considered medically necessary and, therefore, covered for the following indications when the dosing and frequency requirements listed in Attachment A and the following criteria are met:

Dermatologic

- Autoimmune mucocutaneous blistering disease for the following biopsy-proven conditions: pemphigus vulgaris, pemphigus foliaceus, bullous pemphigoid, mucous membrane pemphigoid (cicatrical pemphigoid), epidermolysis bullosa acquisita when one of the following criteria is met (IVIG for the treatment of autoimmune mucocutaneous blistering disease must be used for short-term therapy, not maintenance therapy):
 - The individual failed conventional therapy (e.g., steroids, methotrexate, immunosuppressive therapy) or conventional therapy is contraindicated.
 - The individual has a rapidly progressive disease in which a clinical response could not be effected quickly enough using conventional agents. In this case, IVIG is given along with conventional treatments, and IVIG would be used only until conventional therapy could take effect.
- Stevens-Johnson syndrome or toxic epidermal necrolysis
- Scleromyxedema

Hematologic

- ITP when one of the following criteria is met:
 - The individual requires a rapid platelet count increase (e.g., prior to surgical procedures, to control excessive bleeding, to defer or avoid a splenectomy).
 - The individual has acute bleeding due to severe thrombocytopenia (platelet counts usually less than 30,000/mm³).
 - The individual has severe thrombocytopenia (platelet counts less than 20,000/mm³) and is considered at risk for intracerebral hemorrhage.
- AIHA when the following criterion is met:
 - The individual has had prior treatment with corticosteroids and/or splenectomy, unless contraindicated.
- Anemia due to parvovirus B19 infection:
 - In individuals with chronic parvovirus B19 infection and severe anemia associated with bone marrow suppression

- Chronic refractory ITP when all of the following criteria are met:
 - The individual has a disease duration of greater than 6 months.
 - The individual has no concurrent illness or disease to explain the thrombocytopenia.
 - The individual has platelet counts that remain persistently $\leq 20,000/\text{mm}^3$.
 - The individual has had splenectomy and/or prior treatment with corticosteroids, unless documented failure, contraindication, or intolerance to corticosteroids exists.
- Evans syndrome when one of the following criteria is met:
 - The individual requires a rapid platelet count increase
 - The individual has severe thrombocytopenia (platelet counts $< 30,000/\text{mm}^3$)
 - The individual has had prior treatment with corticosteroids, unless contraindicated.
- ITP during pregnancy when one of the following criteria is met:
 - The individual has previously delivered infants with autoimmune thrombocytopenia.
 - The individual's platelet counts are less than $50,000/\text{mm}^3$ during the current pregnancy.
 - The individual has a history of splenectomy.
- Fetal/neonatal alloimmune thrombocytopenia
- Rh and ABO incompatibility (moderate to severe) as treatment in addition to phototherapy to prevent or delay exchange transfusion in neonates
- SCLS or Clarkson disease when associated with monoclonal gammopathy

Immunodeficiency Syndromes, Primary and Secondary

- Acquired (secondary) hypogammaglobulinemia in oncologic conditions:
 - CAR T cell (anti-CD19) therapy (e.g., axicabtagene ciloleucel [Yescarta], brexucabtagene autoleucel [Tecartus], lisocabtagene maraleucel [Breyanzi], tisagenlecleucel [Kymriah®]) **for one of the following:**
 - Acquired hypogammaglobulinemia when the individual has an IgG level of less than 400 to 600 mg/dL and serious or recurrent infections (particularly bacterial) until serum IgG levels normalize and infections resolve
 - Used for management of the following immunotherapy-related toxicities
 - Further intervention for myocarditis if no improvement within 24 to 48 hours of starting high-dose methylprednisolone
 - Adjunct to rituximab for severe (Grade 3) or life-threatening (Grade 4) bullous dermatitis
 - Stevens-Johnson syndrome, or toxic epidermal necrolysis
 - Moderate, severe, or life-threatening (G2-4) steroid-refractory myositis (proximal muscle weakness, neck flexor weakness, with or without myalgias) for significant dysphagia, life-threatening situations, or cases refractory to corticosteroids

- Severe (G3-4) myasthenia gravis
 - Moderate (G2) or severe (G3-4) Guillain-Barré syndrome or severe (G3-4) peripheral neuropathy in combination with high-dose methylprednisolone
 - Encephalitis in combination with high-dose methylprednisolone if severe or progressing symptoms (strongly consider if progressing over 24 hours)
 - Demyelinating disease (optic neuritis, transverse myelitis, acute demyelinating encephalomyelitis)
 - Moderate (G3) pneumonitis if no improvement after 48 to 72 hours of corticosteroids or severe (G3-4) pneumonitis if no improvement after 48 hours of methylprednisolone
 - Life-threatening (G4) cytokine release syndrome that is refractory to high-dose corticosteroids and anti-IL-6 therapy
- Chronic lymphocytic leukemia with associated hypogammaglobulinemia when one of the following criteria is met:
 - The individual has an IgG level of less than 600 mg/dL.
 - The individual presents evidence of a specific antibody deficiency.
 - The individual presents with serious, recurrent bacterial infections.
- Multiple myeloma with associated hypogammaglobulinemia in an individual who has a high risk of recurrent infections despite prophylactic antibiotic therapy
- Other malignant diseases with associated hypogammaglobulinemia in an individual who has a high risk of serious, recurrent bacterial infections
- Acquired von Willebrand disease associated with IgG-MGUS or antibody-mediated acquired von Willebrand disease in individuals in life-threatening situations or prior to surgery when treatment of the underlying condition is not possible.
 - Documented failure, contraindication, or intolerance to standard treatment (e.g., desmopressin and von Willebrand factor replacement)
- ANCA-associated vasculitides (Wegener's granulomatosis, microscopic polyangiitis [MPA], Churg-Strauss syndrome):
 - The individual is unresponsive/refractory to, intolerant of, or has a contraindication to other standard therapies (e.g., corticosteroids, immunosuppressants).
- Autoimmune neutropenia
- Bone marrow transplantation when both of the following criteria are met:
 - The individual is 20 years of age or older and has had a transplant for a covered indication.
 - The individual received the transplant within the past 90 days.
- Catastrophic antiphospholipid syndrome (CAPS) when all of the following criteria are met:
 - The condition is life-threatening.
 - The individual has severe thrombocytopenia and features of microangiopathy (e.g., thrombocytopenia, microangiopathic hemolytic anemia).

- The individual is unresponsive/refractory to, intolerant of, or has a contraindication to other standard therapies (i.e., corticosteroids and anticoagulants).
 - IVIG must be used in combination with plasma exchange.
- Coagulopathy due to acquired inhibitor of clotting factor VIII
- Hematopoietic stem cell transplant (HSCT) for an adult, adolescent, or pediatric allogeneic stem cell transplant recipient who experiences severe hypogammaglobulinemia (IgG $\leq$ 400 mg/dL)
- HIES (Hyper-IgE syndromes, Job syndrome) when all of the following signs and symptoms are present:
 - Individual has eosinophilia (500 or more eosinophils/ μ L).
 - Individual has elevated serum IgE (>2000 IU/mL), with normal IgG, IgA, and IgM levels.
 - Individual has eczema, recurrent staphylococcal lung infections, and/or skin abscesses documented in office or hospital charts.
- Human immunodeficiency virus (HIV)-infected individuals to reduce significant bacterial infection when all of the following criteria are met:
 - The individual is younger than 14 years of age.
 - The individual has entry CD4 lymphocyte counts greater than or equal to 200/ mm^3 .
 - The individual is clinically symptomatic or asymptomatic, but is immunologically abnormal.
 - The individual has severe hypogammaglobulinemia (serum IgG level <400 mg/dL) and/or functional antibody deficiency demonstrated by either poor specific antibody titers or recurrent bacterial infections.
 - The individual has recurrent serious bacterial infections, (i.e., two or more infections such as bacteremia, meningitis, or pneumonia in a 1-year period).
- Immune checkpoint inhibitor–related toxicities, management (Note: examples of immune checkpoint inhibitors include, but are not limited to: ipilimumab [Yervoy], PD-1/PD-L1 inhibitors [e.g., atezolizumab [Tecentriq], nivolumab [Opdivo], pembrolizumab [Keytruda])
 - Myocarditis if no improvement within 24 to 48 hours of starting pulse-dose methylprednisolone
 - Adjunct to rituximab for severe (Grade 3) or life-threatening (Grade 4) bullous dermatitis
 - Stevens-Johnson syndrome, or toxic epidermal necrolysis
 - Moderate or severe (G2-3) steroid-refractory myalgias or myositis (muscle weakness), or life-threatening (G4) steroid-refractory myositis
 - Severe (Grade 3-4) myasthenia gravis
 - Moderate (Grade 2) or severe (Grade 3-4) Guillain-Barré syndrome or severe (Grade 3-4) peripheral neuropathy in combination with pulse-dose methylprednisolone

- Encephalitis in combination with pulse-dose methylprednisolone if severe or progressing symptoms, or if oligoclonal bands present (strongly consider if progressing over 24 hours)
- Transverse myelitis
- Moderate (G3) pneumonitis if no improvement after 48 to 72 hours of corticosteroids or severe (G3-4) pneumonitis if no improvement after 48 hours of methylprednisolone
- Kawasaki disease (mucocutaneous lymph node syndrome)
- Neonatal hemochromatosis (neonatal alloimmune hepatitis):
 - Administration to pregnant women with history of pregnancy ending in documented neonatal hemochromatosis who are at risk for subsequent pregnancies ending in documented neonatal hemochromatosis
 - Administration to the neonate with documented neonatal hemochromatosis, combined with exchange transfusion
- PIDD[‡] when the individual has a confirmed genetic diagnosis or laboratory evidence of PIDD **or** the individual meets both of the following criteria:
 - Individual has a personal history of recurrent, antibiotic-refractory, bacterial infections of the ear (e.g., otitis media) or sinopulmonary infections (e.g., sinusitis, bronchitis/bronchiectasis, pneumonia), which are documented in office or hospital charts.
 - Individual has a deficiency of antibody response to at least **one** of the following antigens (e.g., proteins, polysaccharides, or viral antigens):
 - Polyvalent pneumococcal polysaccharide vaccine (e.g., Pneumovax 23), measured at the time of immunization and 4 to 8 weeks after vaccination.
 - A protective (normal) response to each pneumococcal serotype is defined as a titer equal to or greater than 1.3 mcg/mL antibody.
 1. For individuals ages 6 to 65 years, a normal response is defined as conversion of 70% of the serotypes tested with at least a twofold increase in the titers.
 2. For children 24 months through 5 years of age, a normal response is defined as the conversion of 50% or more of the serotypes tested with at least a twofold increase in the titers.
 3. (Note: When reported, the conversion factor for nanograms of antibody nitrogen per milliliter (ng N/mL) to antibody micrograms per milliliter is as follows: 160 ng N/mL = 1 µg/mL)
 - Protein antigens, tetanus/diphtheria vaccine measured at the time of immunization and 3 to 4 weeks after vaccination
 - A protective (normal) response is defined as any of the following:
 1. At least a fourfold increase for protein antigens

2. A serum diphtheria antitoxin level of 0.01 International Units (IU)/mL is the lowest level giving some degree of protection, and levels of at least 0.1 IU/mL are generally regarded as protective
3. A protective level for tetanus is 0.15 IU/mL

[†]The list of PIDDs includes, but is not limited to:

1. APDS
2. Ataxia-telangiectasia
3. Autosomal recessive agammaglobulinemia
4. Caspase-8 deficiency
5. Combined immunodeficiencies
6. Common variable immunodeficiency (including TACI and ICOS mutation)
7. DiGeorge syndrome
8. DOCK (dedicator of cytokinesis-8) deficiency
9. Griscelli syndrome
10. Hereditary hypogammaglobulinemia
11. Hypogammaglobulinemia, persistent (IgG $\leq$ 400 mg/dL or less than two SD from normal)
12. IgG-subclass deficiency (deficiency of one or more IgG subclasses to levels less than 2 SD below the age-specific mean, in the presence of normal or near-normal total IgG levels). (These levels must be assessed on at least two occasions while the individual is free of acute infections.)
13. Immunodeficiency with increased immunoglobulin M [IgM]
14. Major histocompatibility complex class I or II deficiency
15. Nezelof syndrome
16. NEMO (mutations in IKK-gamma) deficiency
17. Nijmegen breakage syndrome
18. PNP deficiency
19. Selective IgA deficiency with IgG subclass deficiency (reduced serum IgA levels [<7 mg/dL] and normal IgG and IgM levels)
20. SCID
21. SCID due to adenosine deaminase deficiency
22. Specific antibody deficiency (selective antibody deficiency) with normal immunoglobulins
 1. Individual has impaired production of specific antibodies to polysaccharide antigens after vaccination and normal responses to protein antigens
23. Transient hypogammaglobulinemia of infancy
24. WHIM syndrome
25. Wiskott-Aldrich syndrome
26. X-linked agammaglobulinemia (aka, Bruton's agammaglobulinemia, congenital agammaglobulinemia)
27. X-linked and autosomal recessive hyper-IgM syndromes

- 28. X-linked immunodeficiency
- 29. X-linked lymphoproliferative disease

- Preterm and/or low-birth-weight neonates as prevention for serious infections (including sepsis, urinary tract infection, soft-tissue infections or cellulitis) when severe hypogammaglobulinemia (IgG $\leq$ 400 mg/dL) is present
- Solid organ transplant amongst sensitized transplant candidates, and AMR when the individual has had a transplant

Infectious Disease

- Toxic shock syndrome
 - IVIG may be considered an adjunct in the treatment of staphylococcal or streptococcal toxic shock syndrome.

Neurological and Musculoskeletal Disorders

- ADEM
 - Rescue therapy for individuals unresponsive/refractory to, intolerant of, or who have a contraindication to, corticosteroids.
- CIDP, when all of the following criteria are met:
 - The individual has progressive or relapsing motor or sensory impairment caused by neuropathy in more than one limb for at least 2 months
 - The individual has at least one of the following electrodiagnostic findings of demyelination:
 - Motor distal latency prolongation in two nerves
 - Reduction of motor conduction velocity in two nerves
 - Prolongation of F-wave latency in two nerves
 - Absence of F-waves in at least one nerve
 - Motor conduction block in at least one nerve
 - Abnormal temporal dispersion in at least two nerves
 - Distal CMAP duration increase in at least one nerve
- DM or PM when all of the following criteria are met:
 - There must be clinical evidence to support the diagnosis, as well as a biopsy (or unequivocal diagnostic features through history, examination, and electromyography/nerve conduction studies [EMG/NCS]) performed to verify the diagnosis of dermatomyositis or polymyositis.
 - The individual has impaired function (such as a decrease in muscle strength and/or electromyography abnormalities measured by a standard clinical scale at the time of initial therapy) and/or elevated serum creatine kinase (CK) levels.

- The individual is unresponsive/refractory to, intolerant of, or has a contraindication to, a 4-month trial of steroids and/or immunosuppressants.
- Guillain-Barré syndrome
 - The individual's function is impaired (e.g., unable to stand or walk without aid), measured by a standard clinical scale and/or objective findings on a physical examination at the time of initial therapy.
- Intractable seizures and epilepsies in infants and children
 - The individual is unresponsive/refractory to, intolerant of, or has a contraindication to, all standard therapies (e.g., antiepileptic drugs and corticosteroids).
- Lambert-Eaton myasthenic syndrome
 - The individual is unresponsive/refractory to, intolerant of, or has a contraindication to, other standard therapies (e.g., plasma exchange, corticosteroids or other immunosuppressants, cholinesterase inhibitors, or 3,4-diaminopyridine [DAP]).
- MMN
 - The individual has progressive, symptomatic MMN that has been diagnosed on the basis of electrophysiologic findings that rule out other possible conditions that may not respond to IVIG.
- Myasthenia gravis syndrome when all of the following criteria are met:
 - The individual has severely impaired function (such as a risk of respiratory failure) measured by a standard clinical scale and/or objective findings on a physical examination at the time of initial therapy.
 - The individual is refractory to other standard therapies (e.g., plasmapheresis) or to standard pharmacological therapies (e.g., corticosteroids, azathioprine, cyclosporine, cyclophosphamide, cholinesterase inhibitors) given in therapeutic doses over at least 8 weeks or is intolerant of, or has a contraindication to, standard therapies.
- Myasthenic crisis (i.e., an acute episode of respiratory muscle weakness) in individuals with contraindication to plasma exchange
- NMO (Devic syndrome)
 - The individual is unresponsive/refractory to, intolerant of, or has a contraindication to other standard therapies (e.g., corticosteroids and azathioprine).
- Rasmussen encephalitis
 - In individuals with intractable focal motor seizures and progressive neurologic deterioration (dementia, hemiparesis)
- Relapsing-remitting MS when all of the following criteria are met:
 - The individual has impaired function measured by a standard clinical scale and/or objective findings on a physical examination at the time of initial therapy.
 - The individual is refractory to other standard therapies (e.g., interferons) given in therapeutic doses over at least 3 months, or is intolerant of, or has a contraindication to, standard therapies.
 - The individual has an acute relapse of the disease.

- Stiff Person Syndrome
 - The individual is refractory to other standard therapies (e.g., muscle relaxants, benzodiazepines, and gabapentin-related medications)
- SLE in an individual who failed previous treatment such as corticosteroids and immunosuppressive agents, or treatment was ineffective or contraindicated

CONTINUATION OF THERAPY FOR IVIG, SCIG

Once treatment with immune globulin (IVIG, SCIG) is initiated, documentation of the individual's progress is required. If there is initial improvement and continued treatment is necessary, then objective clinical assessment to monitor the progress is required. Objective monitoring may be done with any accepted clinical method such as the Medical Research Council (MRC) scale, Rankin score, Activities of Daily Living (ADL) scores, and/or objective findings on physical examination. Changes in these measures and the relationship of the change to immune globulin use are expected to be documented clearly. Subjective improvement is insufficient to continue immune globulin treatment. Clinical monitoring takes clear precedence over laboratory monitoring. If clinical improvement is evident, then laboratory monitoring solely to guide immune globulin therapy is not necessary.

Duration of authorization: 12 months

Version Effective Date: 01/02/2025

Title: Immune Globulin Intravenous (IVIG), Subcutaneous (SCIG)

MEDICALLY NECESSARY:

DOSING AND FREQUENCY REQUIREMENTS FOR INTRAVENOUS IMMUNE GLOBULIN (IVIG) AND SUBCUTANEOUS IMMUNE GLOBULIN (SCIG)

The Company reserves the right to modify the Dosing and Frequency Requirements listed in this Policy to ensure consistency with the most recently published recommendations for the use of IVIG and SCIG. Changes to these guidelines are based on a consensus of information obtained from resources such as, but not limited to: the US Food and Drug Administration (FDA), drug manufacturers' guidelines, Company-recognized authoritative pharmacology compendia, or published peer-reviewed clinical research. The professional provider must supply supporting documentation (i.e., published peer-reviewed literature) in order to request coverage for an amount of IVIG and SCIG outside of the Dosing and Frequency Requirements listed in this policy. For a list of Company-recognized pharmacology compendia and criteria for peer-reviewed clinical research, view our policy on off-label coverage for prescription drugs and biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of these drugs. If the member's dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider **must** submit those changes to the Company for a new approval based on those changes as part of the precertification process. The Company reserves the right to conduct post-payment review and audit procedures for any claims submitted for IVIG and SCIG.

DOSING AND FREQUENCY REQUIREMENTS FOR INTRAVENOUS IMMUNE GLOBULIN (IVIG)

Examples of IVIG therapy include Alyglo, Asceniv, Bivigam, Flebogamma, Gammagard Liquid, Gammagard S/D, Gammaked, Gammaplex, Gamunex-C, Octagam, Panzyga, Privigen

DERMATOLOGIC

Indication	Dosing and Frequency
Autoimmune mucocutaneous blistering disease for the following biopsy-proven conditions: pemphigus vulgaris, pemphigus foliaceus, bullous pemphigoid, mucous membrane pemphigoid (cicatrical pemphigoid), epidermolysis bullosa acquisita	Induction and Maintenance: 2 g/kg per cycle (total dose divided equally, each given on 2 to 5 consecutive days). Initial frequency is generally 1 cycle every 3 to 4 weeks (or every 2 weeks for ocular cicatricial pemphigoid ²¹⁴). The frequency or dose may be slowly reduced after there is effective control of the disease (eg, increase intervals to 6, 8, 10, 12, 14, and 16 weeks. Last cycle given after a 16-week interval). ^{3, 86, 95, 97, 127, 140, 179} IVIG must be used only for short-term therapy. ⁷⁹

Stevens-Johnson syndrome and toxic epidermal necrolysis	Induction: Adults: 2-3 g/kg over a period of 2 to 5 days. ^{4, 87, 172, 179, 180} Pediatric: 1.5-2 g/kg per day for 3 days. ^{5, 180} Maintenance: Maintenance therapy is not warranted. ¹⁷⁹
Scleromyxedema	Induction and Maintenance: 2 g/kg (total dose, divided over 2-5 days) and repeated every 4-12 weeks. Reassess after 6 months of therapy. ^{6, 7, 8, 70, 102, 179, 182, 197}

HEMATOLOGIC

Indication	Dosing and Frequency
Acute idiopathic thrombocytopenic purpura (ITP)	Induction: Adult: 1-2 g/kg administered over 1 to 5 days. ^{12, 183, 184} Pediatric: 1 g/kg/day for 1 to 2 days. ^{12, 80, 184} Maintenance: Maintenance therapy is not warranted.
Anemia, autoimmune hemolytic (AIHA)	Induction and Maintenance: 0.4-1 g/kg per day for 5 days, and may repeat every 3 weeks. ^{14, 18, 88}
Anemia due to parvovirus B19 infection	Induction: In individuals with chronic infections with anemia, administer 0.4 g/kg for 5-10 days or 1 g/kg for 3 days. ^{25, 42} In HIV-infected individuals with pure red cell aplasia related to B19 coinfection, administer 1-2 g/kg/day for 2-5 days ^{25, 42} or 0.4 g/kg/day for 5-10 days. ⁴² Maintenance: 0.4 g/kg every 4 weeks. ^{25, 42}
Chronic refractory idiopathic thrombocytopenic purpura (ITP)	Induction: Adult: 400 mg/kg daily for 2 to 5 days. ¹ Alternatively, 1 to 2 g/kg divided into 2 doses and given over 2 consecutive days. ^{1, 81} Pediatric: 0.8-1 g/kg with a second dose given in 48 hours if platelet count has not increased to above $20 \times 10^9/L$. ¹² Maintenance: Maintenance therapy is not warranted. ²⁴² Retreatment: If the response is inadequate, 400 mg/kg may be administered as a single dose once every several weeks. In some individuals, it may be necessary to increase the dose to 800 mg/kg or 1 g/kg. ^{1, 81, 82}

Evans syndrome	Induction: 2 g/kg/day in divided doses over 2-5 days. ^{218, 219, 220, 221} May repeat 2 weeks later, if needed. ²²¹
Idiopathic thrombocytopenic purpura (ITP) during pregnancy	Induction: 400 mg/kg per day for three to five days. ^{11, 12, 168} Maintenance: Peer-reviewed literature does not speak to Maintenance therapy; therefore, dosing is not warranted.
Fetal/neonatal alloimmune thrombocytopenia	Induction and Maintenance: For antenatal treatment: 1 g/kg weekly. This treatment is initiated around 20 weeks of pregnancy and no later than 30 weeks. ^{12, 185} For neonatal treatment: 1 g/kg per day for 1 to 3 days. ¹³
Rh and ABO incompatibility (moderate to severe) as treatment in addition to phototherapy to prevent or delay exchange transfusion in neonates	Neonatal Induction: 500-1000 mg/kg over 2 to 4 hours, given every 12 hours, up to 2 doses. ^{44, 45, 46, 47, 48, 49, 131, 212} Neonatal Maintenance: There is an absence of peer-reviewed evidence and clinical consensus regarding Maintenance therapy; therefore, dosing is not warranted.
Systemic Capillary Leak Syndrome (SCLS) or Clarkson's Disease	Induction: 2 g/kg/month ^{188, 189, 190, 191} Maintenance: 0.4–2 g/kg/month ^{188, 189, 191} Taper to the lowest effective dose ¹⁷⁹ Retreatment: If relapse occurs, administer up to 2 g/kg ¹⁸⁸

IMMUNODEFICIENCY SYNDROMES

Indication	Dosing and Frequency
Acquired (secondary) hypogammaglobulinemia in oncologic conditions	Chimeric antigen receptor (CAR) T cell therapy acquired hypogammaglobulinemia Induction and Maintenance: - Adult: 400-600 mg/kg every 3 to 4 weeks to reach serum IgG levels greater than 400 mg/dL.^{203, 204, 213, 215, 223} - Pediatric: 400 mg/kg every 3-4 weeks to reach IgG greater than 400 mg/dL.²²³ Chronic lymphocytic leukemia (CLL) with associated hypogammaglobulinemia Induction and Maintenance: 200-400 mg/kg every 3 to 4 weeks for 1 year. After 1 year, treatment should be

	continued to maintain IgG trough levels >500 mg/dL. ^{1, 14, 18, 37, 121, 123, 133, 134, 152} Multiple myeloma • Induction and Maintenance: 0.4 g/kg every 3 to 4 weeks to reach serum IgG levels greater than 500 mg/dL. ^{35, 75, 139} Other malignant diseases with associated hypogammaglobulinemia in an individual who has a high risk of serious, recurrent bacterial infections • Induction: Single dose of 400 to 600 mg/kg. ^{18, 37} • Maintenance: 0.4 g/kg every 3-4 weeks with reevaluation every 4-6 months. ^{18, 37}
Acquired Von Willebrand disease associated with IgG-MGUS (monoclonal gammopathy of undetermined significance of the IgG Class) or antibody-mediated acquired Von Willebrand disease	Induction: 1 g/kg daily for two days. ^{12, 160, 161} Maintenance: Maintenance therapy is not warranted.
Antineutrophil cytoplasmic antibodies (ANCA)-associated vasculitides (Wegener's granulomatosis, microscopic polyangiitis [MPA], Churg-Strauss syndrome)	Induction: 2 g/kg (total dose, divided over 5 days). ^{165, 166, 186} Maintenance: There is an absence of peer-reviewed evidence and clinical consensus regarding Maintenance therapy; therefore, dosing is not warranted.
Autoimmune neutropenia	Induction: 0.4-1 g/kg/day for 2-5 days. ^{12, 15, 16, 89, 90, 92} Maintenance: There is an absence of peer-reviewed evidence and clinical consensus regarding Maintenance therapy; therefore, dosing is not warranted.
Bone marrow transplantation	Induction: 500 mg/kg weekly to day 90. ^{17, 118} Maintenance: If severely hypogammaglobulinemic (IgG levels less than

	400 mg/dL) after day 90, administer 500 mg/kg monthly to day 360 post-transplantation. ^{17, 93}
Catastrophic antiphospholipid syndrome (CAPS)	Induction: 0.4 g/kg daily for 4-5 days.^{144, 162, 163} Maintenance: Maintenance therapy is not warranted.
Coagulopathy due to acquired inhibitor of clotting factor VIII	Induction and Maintenance: 1 g/kg/day for 2 days or 0.4 g/kg/day for 5 days followed by maintenance doses at intervals as clinically indicated to reduce inhibitor titers.^{12, 18, 19, 96, 151}
Hematopoietic stem cell transplant (HSCT) for an adult, adolescent, or pediatric allogeneic stem cell transplant recipient who experiences severe hypogammaglobulinemia (IgG less than or equal to 400 mg/dL):	Within the first 100 days after transplant: Induction and Maintenance: Adult or adolescent: 500 mg/kg/week when serum IgG falls below 400 mg/dL.^{20, 94, 122} Pediatric: 400 mg/kg/month when serum IgG falls below 400 mg/dL.⁹⁴ Beyond the first 100 days after transplant: Induction and Maintenance: Adult: 500 mg/kg every 3-4 weeks when serum IgG falls below 400 mg/dL.^{94, 122}
Hyperimmunoglobulinemia E syndrome (HIES) ^{26, 27, 29}	Induction and Maintenance: 300-600 mg/kg every 3 weeks, or 400-800 mg/kg every 4 weeks. Dosing intervals will be dependent on the catabolic rate of the individual's IgG but will generally be no more frequently than every 3 to 5 weeks. Treatment should be continued to maintain IgG trough levels >500 mg/dL.^{1, 2, 14, 18, 142, 154, 177, 178}
Human immunodeficiency virus (HIV)--infected individuals to reduce significant bacterial infection	Induction and Maintenance in Pediatric Individuals: 400 mg/kg every 2 to 4 weeks.^{14, 18, 21, 75, 181}
Immune checkpoint inhibitor-related toxicities, management	• Bullous dermatitis, severe (Grade 3) or life-threatening (Grade 4), adjunct to rituximab ◦ Induction: 1 g/kg/day for 2 days, with monthly cycle until clear²¹⁵ • Stevens-Johnson syndrome, or toxic epidermal necrolysis:

	○ Induction: 1 g/kg/day in divided doses over 3-4 days ²¹⁵ • Myocarditis if no improvement within 24-48 hours of starting pulse-dose methylprednisolone • Myasthenia Gravis, severe (grade 3-4) • Moderate (G3) pneumonitis if no improvement after 48-72 hours of corticosteroids or severe (G3-4) pneumonitis if no improvement after 48 hours of methylprednisolone • Moderate (Grade 2) or severe (Grade 3-4) Guillain-Barré Syndrome or severe (Grade 3-4) peripheral neuropathy in combination with pulse-dose methylprednisolone • Encephalitis in combination with pulse-dose methylprednisolone if severe or progressing symptoms, or if oligoclonal bands present (strongly consider if progressing over 24 hours) • Demyelinating disease (optic neuritis, transverse myelitis, acute demyelinating encephalomyelitis) • moderate or severe steroid-refractory myalgias or myositis (muscle weakness), or life-threatening steroid-refractory myositis • moderate or severe or life-threatening steroid-refractory myalgias or myositis (proximal muscle weakness, neck flexor weakness, with or without myalgias) for significant dysphagia, life-threatening situations, or cases refractory to corticosteroids • G4 cytokine release syndrome that is refractory to high-dose corticosteroids and anti-IL-6 therapy ○ Induction: 2 g/kg/day in divided doses over 2-5 days ²¹⁵
Kawasaki disease (mucocutaneous lymph node syndrome)	Induction: Single dose of 2 g/kg or 400 mg/kg for 4 consecutive day, as soon as diagnosis is established.^{1, 15, 18, 22, 40, 224, 235} Children with

	persistent fever 36 hours after completion of an initial dose of IVIG can be treated with an additional single infusion of IVIG (2 g/kg) for a total cumulative IVIG dose of 4 g/kg.^{41, 142} Maintenance: Maintenance therapy is not warranted.
Neonatal hemochromatosis (neonatal alloimmune hepatitis)	Administration to the pregnant woman: Induction and Maintenance: 1 g/kg weekly from gestational week 18 until the end of gestation.^{74, 91, 156, 157, 158, 216} Administration to the neonate, combined with exchange transfusion: Induction: 1 g/kg birth weight daily in the immediate one to two days after birth.^{74, 159, 216} Maintenance: There is an absence of peer-reviewed evidence and clinical consensus regarding Maintenance therapy; therefore, dosing is not warranted.
Primary immunodeficiency disorders (PIDD) associated with defects in immunity ^{26, 27, 29}	Induction and Maintenance: 200-800 mg/kg every 3-4 weeks.¹ Dosing intervals will be dependent on the catabolic rate of the individual's IgG but will generally be no more frequently than every 3 to 5 weeks. Treatment should be continued to maintain IgG trough levels >500 mg/dL.^{1, 2, 14, 18, 142, 154, 177, 178}
Preterm and/or low-birth-weight neonates as prevention for serious infections when severe hypogammaglobulinemia is present ^{98, 120, 124, 126}	Induction and Maintenance: 500-900 mg/kg every 14 days to achieve a trough IgG level of 500-700 mg/dL.¹⁴ Administer 400-600 mg/kg every 3 to 4 weeks, titrating the dose based on maintaining trough IgG levels greater than 500 mg/dL.¹⁸
Solid organ transplant amongst sensitized transplant candidates ^{24, 119, 128, 129, 130, 135, 136, 137, 141, 145, 147, 148, 149} and Antibody-Mediated Rejection (AMR) (humoral/vascular rejection) ¹³⁸	High-dose IVIG protocol An in vitro PRA, crossmatch (CMX) test to identify patients most likely to benefit from IVIG therapy.³⁰ For responders on a deceased donor organ waiting list, administer 2 g/kg monthly up to 4 doses. Dose may be repeated at 12 and 24

	months. An additional 2 g/kg is given 1 month post-transplant.^{28, 30} For responders receiving positive CMX living donor organs, administer 1- 4 doses of 2 g/kg monthly with repeat CMX after each dose. An additional 2 g/kg is given 1 month post-transplant.^{30, 100} The endpoint of therapy is a negative enhanced CDC CMX. Plasmapheresis/low-dose IVIG protocol³⁰ Plasmapheresis (PP)/low dose IVIG and immunosuppressive agents prior to renal transplantation as follows: Every other day plasmapheresis (PP) followed by IVIG 100 mg/kg after each PP. In a study by Montgomery et al, a mean of 4 treatments were provided.¹⁰¹ Acute Antibody-Mediated Rejection (AMR) (Humoral/Vascular Rejection) High-dose IVIG alone (2 g/kg for one dose)^{23, 99, 129} OR Plasmapheresis daily or every other day followed by one of the following: ○ IVIG 100 mg/kg for 4-6 doses^{103, 104, 206, 207} ○ IVIG 100-500 mg/kg in divided doses up to a total maximum dose of 2g/kg over a 4 week period²⁰⁵ ○ IVIG 100 mg/kg for 4 doses. After last Plasmapheresis, high-dose IVIg 2 g/kg every 3 weeks for 4 doses, and two weekly doses of rituximab (375 mg/m²)¹³⁸ IVIG 0.5-2 g/kg total after the final PP treatment^{103, 206, 207} IVIG 2 g/kg, rituximab (375 mg/m² once), and Plasmapheresis²²²

	After the first year post-transplant, IVIG 200 mg/kg every two weeks for three doses. ²⁰⁶ Chronic Active AMR: One of the following regimens: ○ Plasmapheresis daily or every other day for 4-5 sessions followed by 2 g/kg IVIG (in one or two days), and intravenous rituximab 375 mg/m², one dose after IVIG. ²⁰⁸ ○ intravenous rituximab 375 mg/m² once on day 1, followed by IVIG 0.4 g/kg once daily for 4 days. ²⁰⁹ ○ IVIG 1.5 g/kg, bortezomib (1.3 mg/m² IV on days 1, 4, 8, and 11), and plasmapheresis (6x). ²¹⁰ ○ IVIG 1 g/kg weekly for 4 doses, followed by one dose of rituximab (375 mg/m²). ²²² Secondary immunodeficiency with hypogammaglobulinemia as a result of treatment with immunosuppressive agents: 500 mg/kg monthly ⁹⁹ In patients who have steroid-resistant rejection: IVIG 2-3 g/kg over a period of up to 10 consecutive days. ¹⁰³

INFECTIOUS DISEASE

Indication	Dosing and Frequency
Toxic shock syndrome	Induction: 1 g/kg on day 1, followed by 0.5 g/kg on days 2 and 3. ^{6, 38, 195} Alternatively, 2 g/kg for one dose and may repeat in 48 hours if the individual remains unstable. ^{36, 38} Maintenance: Maintenance therapy is not warranted.

NEUROLOGICAL AND MUSCULOSKELETAL DISORDERS

Indication	Dosing and Frequency
Acute disseminated encephalomyelitis (ADEM)	Induction: 2 g/kg divided over 2-5 days ^{73, 167, 181} Maintenance: Maintenance therapy is not warranted.
Chronic inflammatory demyelinating polyneuropathies (CIDP)	Induction: 2 g/kg divided over 2-5 days. ^{1, 18, 71, 72, 73, 85, 105, 142, 164} Maintenance Dosing: 1 or 2 g/kg divided over 1-5 days and administered every 2-8 weeks. ^{1, 18, 71, 72, 73, 85, 105, 164} Individualize the duration of any treatment beyond 6 months based upon the response and demonstrated need for continued therapy. ¹
Dermatomyositis and polymyositis	Induction and Maintenance: Adults: 2 g/kg in divided doses administered over 2-5 days and repeated each month for up to 3-6 months. The continued use of IVIG should be based on objective measures of its sustained effectiveness, as seen in improvements in at least one of the following: serum Creatine Kinase (CK) levels, muscle strength, electromyography testing, and/or improvement in rash (for dermatomyositis indication). ^{1, 31, 73, 153, 171, 230, 231} Pediatrics: 1-2 g/kg in divided doses administered over 2 days and repeated each month for up to 3-6 months. ^{32, 73} or 2 g/kg administered every 2 weeks for 3 doses, then each month for a total treatment period of 3-6 months. ^{32, 73, 143} The continued use of IVIG should be based on objective measures of its sustained effectiveness, as seen in improvements in at least one of the following: serum Creatine Kinase (CK) levels, muscle strength, electromyography testing, and/or improvement in rash (for dermatomyositis indication). ^{32, 73}
Guillain-Barre syndrome	Induction: Adults: One course of treatment of 400 mg/kg per day for 5 days. ^{14, 53, 56, 59, 61, 66, 67, 68, 75} Pediatrics: 2 g/kg in divided doses administered over 2-5 days ^{73, 75} Maintenance: There is an absence of peer-reviewed evidence

	and clinical consensus regarding Maintenance therapy; therefore, dosing is not warranted.
Intractable seizures and epilepsies in infants and children	Induction and Maintenance: 0.4 g/kg/day for 4-5 consecutive days. The cycle may be repeated every 2-6 weeks. ^{18, 61, 73, 76, 110, 111, 112, 113, 114, 115, 116, 117, 150}
Lambert-Eaton myasthenic syndrome	Induction: 2 g/kg divided over 2-5 days^{18, 50, 52, 53, 55, 58, 61, 62, 64, 68, 73, 155, 164, 170} Maintenance: Peer-reviewed literature and lack of clinical consensus for Maintenance is in the investigative state because low level evidence has demonstrated some sporadic clinical benefits.¹⁷⁰
Multifocal motor neuropathy (MMN)	Induction: 500 mg/kg per day for 5 days.^{14, 83, 164, 192, 225} Maintenance: 1 to 2 g/kg given over 2 or 5 days administered every 1 to 3 months to sustain improvement.^{14, 43, 61, 73, 164, 192, 225}
Myasthenia gravis syndrome	Induction: Adults: One course of treatment of 400 mg/kg per day for up to 5 consecutive days.^{33, 50, 51, 53, 54, 57, 60, 61, 63, 65, 68, 69, 73, 142, 179} Neonates, infants, children, adolescents: 2 g/kg in divided doses over 1-5 days.^{73, 181} Maintenance: Peer-reviewed literature and lack of clinical consensus for Maintenance is in the investigative state because low-level evidence has demonstrated some sporadic clinical benefits.^{61, 73, 181, 196, 236, 237, 238, 239, 240, 241} Retreatment: Retreatment with 400 mg/kg per day for 5 days may be considered in individuals with a future exacerbation or recurrent worsening of myasthenia gravis syndrome.^{33, 50, 51, 53, 54, 57, 60, 61, 63, 65, 68, 69}
Myasthenic crisis	Induction: One course of treatment of 400-600 mg/kg per day for 3 to 5 consecutive days.^{14, 50, 53, 55, 61, 68} Maintenance: Maintenance therapy is not warranted.
Neuromyelitis Optica (NMO) (Devic's Syndrome) ^{200, 201, 202}	Induction: 2 g/kg given over 5 days ^{198, 199}
Rasmussen's encephalitis ^{142, 169}	Induction: Adults: 2 g/kg given over 2 to 5 days.⁷³ Children: 2 g/kg given over 2 to 5 days.⁷³

	Maintenance: Peer-reviewed literature and lack of clinical consensus for Maintenance is in the investigative state because low level evidence has demonstrated some sporadic clinical benefits.
Relapsing-remitting multiple sclerosis ⁶¹	Induction: 2 g/kg in divided doses over 5 days.^{73, 75, 125, 173, 174, 193} Maintenance: 2 g/kg divided over 2 days administered monthly^{179, 196} Retreatment: Retreatment with 2 g/kg in divided doses over 5 days may be considered in individuals with an exacerbation of relapsing-remitting multiple sclerosis.^{18, 73, 173, 175}
Stiff-Person syndrome ^{106, 107, 108, 109, 142}	Induction: Adults: 2 g/kg over 2-5 days.^{61, 73, 132, 146} Children: 2 g/kg over 2 days.⁷³ Maintenance: IVIG maintenance therapy should be based on a systematic approach to determine the minimum effective dose. Continued use of IVIG should be based on objective measures of its sustained effectiveness. The maximum dose per treatment course should be 2 g/kg.^{73, 132}
Systemic lupus erythematosus (SLE)	Induction and Maintenance: 2 g/kg over a 5-day period given monthly. ^{34, 77, 78, 194, 217}

DOSING AND FREQUENCY REQUIREMENTS FOR SUBCUTANEOUS IMMUNE GLOBULIN (SCIG)

Examples of SCIG therapy include Cutaquig, Cuvitru, Hizentra, HyQvia and Xembify. Examples of IVIG products that may be administered via subcutaneous infusion for PIDD include Gammagard Liquid, Gammaked, Gamunex-C.

Indication	Dosing and Frequency
<u>Immunodeficiency Syndromes:</u> Hyperimmunoglobulinemia E syndrome (HIES) and Primary immunodeficiency disorders (PIDD) ¹⁵⁴	Induction: 100-200 mg/kg weekly^{176, 178, 196} <u>SCIG products administered via subcutaneous infusion</u> Cutaquig¹⁸⁷: Individuals previously on IVIG treatment should delay Cutaquig administration approximately 1 week after the last infusion of their previous treatment.

	When switching to Cutaquig from IVIG at regular intervals: Weekly dosing: Initial dose = 1.3 x previous IVIG (in grams)/number of weeks between IVIG doses. More frequent dosing: Provided the total weekly dose is maintained, any dosing interval from daily up to weekly can be used. Monitor serum trough IgG trough levels to guide subsequent dose adjustments and dosing intervals as needed. See prescribing information for more information. The target serum IgG trough levels are approximately 23% higher than the last IVIG trough level. Individuals previously on SCIG treatment: When switching to Cutaquig from SCIG at regular intervals: The weekly dose of Cutaquig is the same as other SCIG. Monitor serum trough IgG trough levels after 2-3 months of initiating Cutaquig to guide subsequent dose adjustments and dosing intervals as needed. See prescribing information for more information. Cuvitru⁹: Individuals previously on IVIG or HyQvia (SCIG) treatment should delay Cuvitru administration approximately 1 week after the last infusion of their previous treatment. Weekly dosing: Initial dose = 1.3 x previous IVIG or HyQvia (SCIG) dose (in grams)/number of weeks between IVIG or HyQvia (SCIG) doses. Bi-weekly dosing (every 2 weeks): Initial dose = Multiply the calculated weekly dose by two. Frequent dosing (2 to 7 times per week): Initial dose = Divide the calculated weekly dose by the

	desired number of times per week. Individuals switching from SCIG other than HyQvia: The weekly dose of Cuvitru is the same as other SCIG. See Bi-weekly and Frequent dosing (above) for more information. Monitor serum trough IgG trough levels to guide subsequent dose adjustments and dosing intervals as needed. See prescribing information for more information. Hizentra³⁹: The initial weekly dose of Hizentra is calculated to achieve a systemic serum IgG exposure (area under concentration-time curve [AUC]) not inferior to that of the previous IVIG treatment. Individuals previously on IVIG or SCIG treatment should delay Hizentra administration as follows: • For weekly or frequent dosing: Start Hizentra 1 week after the last infusion of their previous treatment. • For biweekly dosing: Start Hizentra 1-2 weeks after the last IVIG infusion, or 1 weeks after the last weekly SCIG infusion. Weekly dosing: Initial dose = $1.37 \times \text{previous IVIG dose (in grams) / number of weeks between IVIG doses}$. Bi-weekly dosing (every 2 weeks): Initial dose = Multiply the calculated weekly dose by two. Frequent dosing (2 to 7 times per week): Initial dose = Divide the calculated weekly dose by the desired number of times per week. Adjust the dose over time based on clinical response and serum IgG trough levels. Measure the IgG trough levels after 2 to 3 months of treatment with Hizentra. When switching from IVIG (for at least 3 months) to:

- Weekly Hizentra dosing: The target serum IgG trough levels are approximately 16% higher than the last IVIG trough level.
- Biweekly Hizentra dosing: The target serum IgG trough levels are approximately 10% higher than the last IVIG trough level.

When switching from weekly to biweekly Hizentra dosing: The target serum IgG trough levels are approximately 5% lower than the last IVIG trough level.

When switching from weekly to more frequent Hizentra dosing (2 to 7 times per week): The target serum IgG trough levels are approximately 3-4% higher than the last IVIG trough level.

Individuals switching from SCIG other than Hizentra:
The weekly dose of Hizentra is the same as other SCIG. See Bi-weekly and Frequent dosing (above) for more information.

HyQvia¹⁰:

Titrate dose and frequency from once-weekly dosing to once-every 3-4 weeks, as follows:

Week 1: 1st infusion (weekly dosing) at 25% of targeted dose

Week 2: 2nd infusion (every 2-week dosing) at 50% of targeted dose

Week 3: No infusion

Week 4: 3rd infusion (every 3-week dosing) at 75% of targeted dose

Week 5: No infusion

Week 6: No infusion

Week 7: 4th infusion (every 4-week dosing) at 100% of targeted dose (if required)

Individuals naïve to IgG treatment or switching from other SCIG: After initial titration, administer HyQvia at 300 to 600 mg/kg at 3-4 week intervals.

Individuals previously on another IgG treatment should delay HyQvia administration approximately 1 week after the last infusion of their previous treatment.

Individuals switching from IVIG: After initial titration,

	administer HyQvia at same dose and frequency as the previous IV treatment. Adjust dose by measuring serum trough IgG trough levels and calculating difference from baseline IVIG trough levels, then refer to dosage adjustment tables listed within prescribing information for particular product. Xembify²¹¹: Individuals previously on IVIG treatment should delay Xembify administration approximately 1 week after the last infusion of their previous treatment. Weekly dosing: Initial dose = $1.37 \times \text{previous IVIG dose (in grams)}/\text{number of weeks between IVIG doses}$. Frequent dosing (2 to 7 times per week): Initial dose = Divide the calculated weekly dose by the desired number of times per week. Individuals switching from another SCIG: The weekly dose of Xembify is the same as other SCIG. Adjust the dose over time based on clinical response and serum IgG trough levels. Measure the IgG trough levels after 2 to 3 months of treatment with Xembify. <u>IVIG products that may be administered via subcutaneous infusion</u> Gammagard Liquid⁸³: Initial dose = $1.37 \times \text{previous IVIG dose}/\text{number of weeks between IVIG doses}$. Maintenance dose is based on clinical response and target IgG trough level. Gammaked, Gamunex-C^{84, 85}: The initial weekly dose is calculated to achieve a systemic serum IgG exposure (area under concentration-time curve [AUC]) not inferior to that of the previous IVIG treatment. Initial dose = $1.37 \times \text{previous IVIG dose (in grams)}/\text{number}$

	of weeks between IVIG doses. Adjust the dose over time based on clinical response and serum IgG trough levels. Measure the IgG trough levels after two to three months of treatment with this drug.
<u>Neurological and Musculoskeletal Disorders</u> Chronic inflammatory demyelinating polyneuropathies (CIDP)	Hizentra³⁹: Initiate therapy 1 week after the last IGIV infusion. Weekly dosing: The recommended subcutaneous dose is 0.2 g/kg (1 mL/kg) per week, administered in 1 or 2 sessions over 1 or 2 consecutive days. • Individuals switching from IVIG: In the clinical study, a dose of 0.4 g/kg (2 mL/kg) per week was used. If CIDP symptoms worsen on 0.2 g/kg per week, increase dose to 0.4 g/kg (2 mL/kg) per week, administered in 2 sessions per week over 1 or 2 consecutive days. If CIDP symptoms worsen on 0.4 g/kg per week, consider re-initiating treatment with an IVIG product approved for the treatment of CIDP, while discontinuing Hizentra. Monitor clinical response and adjust the duration of therapy. Maintenance therapy has been studied for 12 months; therapy beyond this period should be individualized based upon the individual's response and need for continued therapy. HyQvia¹⁰: A dose ramp-up schedule over 9 weeks is recommended by gradually increasing the SC infusion volume until the full dose is reached to ensure tolerability. Doses less than or equal to 0.4 g/kg may be administered without a ramp-up provided acceptable tolerance by the individual. If switching from IVIG: The starting dose and dosing frequency of HyQvia is the same as the previous IGIV treatment. The typical dosing interval range in the clinical trial for HyQvia was 4 weeks. For patients with less frequent IGIV dosing (greater than 4 weeks), the dosing interval

	can be converted to 3 or 4 weeks while maintaining the same monthly equivalent IgG dose. Administer the calculated one-week dose (1st infusion) two weeks after the last IGIV infusion. One week after the first Hyqvia dose, administer another weekly equivalent dose.

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- .

Duration of authorization: 12 months

Version Effective Date: 01/02/2025

Title: Immune Globulin Intravenous (IVIG), Subcutaneous (SCIG)

MEDICALLY NECESSARY:

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

SUBCUTANEOUS IMMUNE GLOBULIN (SCIG)

C9399, J1555, J1558, J1559, J1561, J1569, J1575, AND J3590 are medically necessary when reported with the following diagnosis codes:

THIS IS NOT AN ALL INCLUSIVE LIST

D71 Functional disorders of polymorphonuclear neutrophils

D80.0 Hereditary hypogammaglobulinemia

D80.1 Nonfamilial hypogammaglobulinemia

D80.2 Selective deficiency of immunoglobulin A [IgA]

D80.3 Selective deficiency of immunoglobulin G [IgG] subclasses

D80.4 Selective deficiency of immunoglobulin M [IgM]

D80.5 Immunodeficiency with increased immunoglobulin M [IgM]

D80.6 Antibody deficiency with near-normal immunoglobulins or with hyperimmunoglobulinemia

D80.7 Transient hypogammaglobulinemia of infancy

D80.8 Other immunodeficiencies with predominantly antibody defects

D80.9 Immunodeficiency with predominantly antibody defects, unspecified

D81.0 Severe combined immunodeficiency [SCID] with reticular dysgenesis

D81.1 Severe combined immunodeficiency [SCID] with low T- and B-cell numbers

D81.2 Severe combined immunodeficiency [SCID] with low or normal B-cell numbers

D81.31 Severe combined immunodeficiency due to adenosine deaminase deficiency

D81.4 Nezelof's syndrome

D81.5 Purine nucleoside phosphorylase [PNP] deficiency

D81.6 Major histocompatibility complex class I deficiency

D81.7 Major histocompatibility complex class II deficiency

D81.82 Activated Phosphoinositide 3-kinase Delta Syndrome (APDS)

D81.89 Other combined immunodeficiencies

D81.9 Combined immunodeficiency, unspecified

D82.0 Wiskott-Aldrich syndrome

D82.1 Di George's syndrome

D82.3 Immunodeficiency following hereditary defective response to Epstein-Barr virus

D82.4 Hyperimmunoglobulin E [IgE] syndrome

D83.0 Common variable immunodeficiency with predominant abnormalities of B-cell numbers and function

D83.1 Common variable immunodeficiency with predominant immunoregulatory T-cell disorders

D83.2 Common variable immunodeficiency with autoantibodies to B- or T-cells

D83.8 Other common variable immunodeficiencies

D83.9 Common variable immunodeficiency, unspecified

D84.81 Immunodeficiency due to conditions classified elsewhere

D84.821 Immunodeficiency due to drugs

D84.822 Immunodeficiency due to external causes

D84.89 Other immunodeficiencies

D84.9 Immunodeficiency, unspecified

G11.3 Cerebellar ataxia with defective DNA repair

G61.81 Chronic inflammatory demyelinating polyneuritis

INTRAVENOUS IMMUNE GLOBULIN (IVIG)

J1459, J1556, J1557, J1561, J1566, J1568, J1569, J1572, AND J1599 are medically necessary when reported with the following diagnosis codes:

THIS IS NOT AN ALL INCLUSIVE LIST. REPORT THE MOST APPROPRIATE DIAGNOSIS CODE FOR TOXICITIES RELATED TO THE MANAGEMENT OF IMMUNE CHECKPOINT INHIBITOR TOXICITIES.

A48.3 Toxic shock syndrome

B20 Human immunodeficiency virus [HIV] disease

B97.6 Parvovirus as the cause of diseases classified elsewhere

C88.90 Malignant immunoproliferative disease, unspecified not having achieved remission

C88.91 Malignant immunoproliferative disease, unspecified, in remission

D47.2 Monoclonal gammopathy

D59.0 Drug-induced autoimmune hemolytic anemia

D59.10 Autoimmune hemolytic anemia, unspecified

D59.11 Warm autoimmune hemolytic anemia

D59.12 Cold autoimmune hemolytic anemia

D59.13 Mixed type autoimmune hemolytic anemia

D59.19 Other autoimmune hemolytic anemia

D63.8 Anemia in other chronic diseases classified elsewhere

D66 Hereditary factor VIII deficiency

D68.00 Von Willebrand's disease, unspecified

D68.01 Von Willebrand disease, type 1

D68.020 Von Willebrand disease, type 2A

D68.021 Von Willebrand disease, type 2B

D68.022 Von Willebrand disease, type 2M

D68.023 Von Willebrand disease, type 2N

D68.029 Von Willebrand disease, type 2, unspecified

D68.03 Von Willebrand disease, type 3

D68.04 Acquired Von Willebrand disease

D68.09 Other Von Willebrand disease

D68.311 Acquired hemophilia

D68.4 Acquired coagulation factor deficiency

D68.61 Antiphospholipid syndrome

D69.3 Immune thrombocytopenic purpura

D69.41 Evans syndrome

D70.8 Other neutropenia

D71 Functional disorders of polymorphonuclear neutrophils

D80.0 Hereditary hypogammaglobulinemia

D80.1 Nonfamilial hypogammaglobulinemia

D80.2 Selective deficiency of immunoglobulin A [IgA]

D80.3 Selective deficiency of immunoglobulin G [IgG] subclasses

D80.4 Selective deficiency of immunoglobulin M [IgM]

D80.5 Immunodeficiency with increased immunoglobulin M [IgM]

D80.6 Antibody deficiency with near-normal immunoglobulins or with hyperimmunoglobulinemia

D80.7 Transient hypogammaglobulinemia of infancy

D80.8 Other immunodeficiencies with predominantly antibody defects

D80.9 Immunodeficiency with predominantly antibody defects, unspecified

D81.0 Severe combined immunodeficiency [SCID] with reticular dysgenesis

D81.1 Severe combined immunodeficiency [SCID] with low T- and B-cell numbers

D81.2 Severe combined immunodeficiency [SCID] with low or normal B-cell numbers

D81.31 Severe combined immunodeficiency due to adenosine deaminase deficiency

D81.4 Nezelof's syndrome

D81.5 Purine nucleoside phosphorylase [PNP] deficiency

D81.6 Major histocompatibility complex class I deficiency

D81.7 Major histocompatibility complex class II deficiency

D81.82 Activated Phosphoinositide 3-kinase Delta Syndrome (APDS)

D81.89 Other combined immunodeficiencies

D81.9 Combined immunodeficiency, unspecified

D82.0 Wiskott-Aldrich syndrome

D82.1 Di George's syndrome

D82.3 Immunodeficiency following hereditary defective response to Epstein-Barr virus

D82.4 Hyperimmunoglobulin E [IgE] syndrome

D83.0 Common variable immunodeficiency with predominant abnormalities of B-cell numbers and function

D83.1 Common variable immunodeficiency with predominant immunoregulatory T-cell disorders

D83.2 Common variable immunodeficiency with autoantibodies to B- or T-cells

D83.8 Other common variable immunodeficiencies

D83.9 Common variable immunodeficiency, unspecified

D84.9 Immunodeficiency, unspecified

D84.81 Immunodeficiency due to conditions classified elsewhere

D84.821 Immunodeficiency due to drugs

D84.822 Immunodeficiency due to external causes

D84.89 Other immunodeficiencies

D89.834 Cytokine release syndrome, grade 4

E83.118 Other hemochromatosis

G04.00 Acute disseminated encephalitis and encephalomyelitis, unspecified

G04.01 Postinfectious acute disseminated encephalitis and encephalomyelitis (postinfectious ADEM)

G04.02 Postimmunization acute disseminated encephalitis, myelitis and encephalomyelitis

G04.81 Other encephalitis and encephalomyelitis

G04.89 Other myelitis

G04.90 Encephalitis and encephalomyelitis, unspecified

G04.91 Myelitis, unspecified

G11.3 Cerebellar ataxia with defective DNA repair

G25.82 Stiff-man syndrome

G35 Multiple sclerosis

G37.3 Acute transverse myelitis in demyelinating disease of central nervous system

G36.0 Neuromyelitis optica [Devic]

G40.011 Localization-related (focal) (partial) idiopathic epilepsy and epileptic syndromes with seizures of localized onset, intractable, with status epilepticus

G40.019 Localization-related (focal) (partial) idiopathic epilepsy and epileptic syndromes with seizures of localized onset, intractable, without status epilepticus

G40.111 Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with simple partial seizures, intractable, with status epilepticus

G40.119 Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with simple partial seizures, intractable, without status epilepticus

G40.211 Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with complex partial seizures, intractable, with status epilepticus

G40.219 Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with complex partial seizures, intractable, without status epilepticus

G40.311 Generalized idiopathic epilepsy and epileptic syndromes, intractable, with status epilepticus

G40.319 Generalized idiopathic epilepsy and epileptic syndromes, intractable, without status epilepticus

G40.A11 Absence epileptic syndrome, intractable, with status epilepticus

G40.A19 Absence epileptic syndrome, intractable, without status epilepticus

G40.B11 Juvenile myoclonic epilepsy, intractable, with status epilepticus

G40.B19 Juvenile myoclonic epilepsy, intractable, without status epilepticus

G40.C11 Lafora progressive myoclonus epilepsy, intractable, with status epilepticus

G40.C19 Lafora progressive myoclonus epilepsy, intractable, without status epilepticus

G40.411 Other generalized epilepsy and epileptic syndromes, intractable, with status epilepticus

G40.419 Other generalized epilepsy and epileptic syndromes, intractable, without status epilepticus

G40.803 Other epilepsy, intractable, with status epilepticus

G40.804 Other epilepsy, intractable, without status epilepticus

G40.813 Lennox-Gastaut syndrome, intractable, with status epilepticus

G40.814 Lennox-Gastaut syndrome, intractable, without status epilepticus

G40.823 Epileptic spasms, intractable, with status epilepticus

G40.824 Epileptic spasms, intractable, without status epilepticus

G40.843 KCNQ2-related epilepsy, intractable, with status epilepticus

G40.844 KCNQ2-related epilepsy, intractable, without status epilepticus

G40.911 Epilepsy, unspecified, intractable, with status epilepticus

G40.919 Epilepsy, unspecified, intractable, without status epilepticus

G61.0 Guillain-Barre syndrome

G61.81 Chronic inflammatory demyelinating polyneuritis

G61.82 Multifocal motor neuropathy

G70.00 Myasthenia gravis without (acute) exacerbation

G70.01 Myasthenia gravis with (acute) exacerbation

G70.80 Lambert-Eaton syndrome, unspecified

G70.81 Lambert-Eaton syndrome in disease classified elsewhere

G73.1 Lambert-Eaton syndrome in neoplastic disease

I77.82 Antineutrophilic cytoplasmic antibody (ANCA) vasculitis

I78.8 Other diseases of capillaries

J98.4 Other disorders of lung

L10.0 Pemphigus vulgaris

L10.2 Pemphigus foliaceus

L12.0 Bullous pemphigoid

L12.1 Cicatricial pemphigoid

L12.30 Acquired epidermolysis bullosa, unspecified

L12.31 Epidermolysis bullosa due to drug

L12.35 Other acquired epidermolysis bullosa

L13.9 Bullous disorder, unspecified

L51.1 Stevens-Johnson syndrome

L51.2 Toxic epidermal necrolysis [Lyell]

L51.3 Stevens-Johnson syndrome-toxic epidermal necrolysis overlap syndrome

L98.5 Mucinosis of the skin

M30.1 Polyarteritis with lung involvement [Churg-Strauss]

M30.3 Mucocutaneous lymph node syndrome [Kawasaki]

M31.30 Wegener's granulomatosis without renal involvement

M31.31 Wegener's granulomatosis with renal involvement

M31.7 Microscopic polyangiitis

M32.0 Drug-induced systemic lupus erythematosus

M32.10 Systemic lupus erythematosus, organ or system involvement unspecified

M32.11 Endocarditis in systemic lupus erythematosus

M32.12 Pericarditis in systemic lupus erythematosus

M32.13 Lung involvement in systemic lupus erythematosus

M32.14 Glomerular disease in systemic lupus erythematosus

M32.15 Tubulo-interstitial nephropathy in systemic lupus erythematosus

M32.19 Other organ or system involvement in systemic lupus erythematosus

M32.8 Other forms of systemic lupus erythematosus

M32.9 Systemic lupus erythematosus, unspecified

M33.00 Juvenile dermatomyositis, organ involvement unspecified

M33.01 Juvenile dermatomyositis with respiratory involvement

M33.02 Juvenile dermatomyositis with myopathy

M33.03 Juvenile dermatomyositis without myopathy

M33.09 Juvenile dermatomyositis with other organ involvement

M33.10 Other dermatomyositis, organ involvement unspecified

M33.11 Other dermatomyositis with respiratory involvement

M33.12 Other dermatomyositis with myopathy

M33.13 Other dermatomyositis without myopathy

M33.19 Other dermatomyositis with other organ involvement

M33.20 Polymyositis, organ involvement unspecified

M33.21 Polymyositis with respiratory involvement

M33.22 Polymyositis with myopathy

M33.29 Polymyositis with other organ involvement

M33.90 Dermatopolymyositis, unspecified, organ involvement unspecified

M33.91 Dermatopolymyositis, unspecified with respiratory involvement

M33.92 Dermatopolymyositis, unspecified with myopathy

M33.93 Dermatopolymyositis, unspecified without myopathy

M33.99 Dermatopolymyositis, unspecified with other organ involvement

M36.0 Dermato(poly)myositis in neoplastic disease

M60.80 Other myositis, unspecified site

M60.811 Other myositis, right shoulder

M60.812 Other myositis, left shoulder

M60.821 Other myositis, right upper arm

M60.822 Other myositis, left upper arm

M60.831 Other myositis, right forearm

M60.832 Other myositis, left forearm

M60.841 Other myositis, right hand

M60.842 Other myositis, left hand

M60.851 Other myositis, right thigh

M60.852 Other myositis, left thigh

M60.861 Other myositis, right lower leg

M60.862 Other myositis, left lower leg

M60.871 Other myositis, right ankle and foot

M60.872 Other myositis, left ankle and foot

M60.88 Other myositis, other site

M60.89 Other myositis, multiple sites

M60.9 Myositis, unspecified

O36.8210 Fetal anemia and thrombocytopenia, first trimester, not applicable or unspecified

O36.8211 Fetal anemia and thrombocytopenia, first trimester, fetus 1

O36.8212 Fetal anemia and thrombocytopenia, first trimester, fetus 2

O36.8213 Fetal anemia and thrombocytopenia, first trimester, fetus 3

O36.8214 Fetal anemia and thrombocytopenia, first trimester, fetus 4

O36.8215 Fetal anemia and thrombocytopenia, first trimester, fetus 5

O36.8219 Fetal anemia and thrombocytopenia, first trimester, other fetus

O36.8220 Fetal anemia and thrombocytopenia, second trimester, not applicable or unspecified

O36.8221 Fetal anemia and thrombocytopenia, second trimester, fetus 1

O36.8222 Fetal anemia and thrombocytopenia, second trimester, fetus 2

O36.8223 Fetal anemia and thrombocytopenia, second trimester, fetus 3

O36.8224 Fetal anemia and thrombocytopenia, second trimester, fetus 4

O36.8225 Fetal anemia and thrombocytopenia, second trimester, fetus 5

O36.8229 Fetal anemia and thrombocytopenia, second trimester, other fetus

O36.8230 Fetal anemia and thrombocytopenia, third trimester, not applicable or unspecified

O36.8231 Fetal anemia and thrombocytopenia, third trimester, fetus 1

O36.8232 Fetal anemia and thrombocytopenia, third trimester, fetus 2

O36.8233 Fetal anemia and thrombocytopenia, third trimester, fetus 3

O36.8234 Fetal anemia and thrombocytopenia, third trimester, fetus 4

O36.8235 Fetal anemia and thrombocytopenia, third trimester, fetus 5

O36.8239 Fetal anemia and thrombocytopenia, third trimester, other fetus

O36.8290 Fetal anemia and thrombocytopenia, unspecified trimester, not applicable or unspecified

O36.8291 Fetal anemia and thrombocytopenia, unspecified trimester, fetus 1

O36.8292 Fetal anemia and thrombocytopenia, unspecified trimester, fetus 2

O36.8293 Fetal anemia and thrombocytopenia, unspecified trimester, fetus 3

O36.8294 Fetal anemia and thrombocytopenia, unspecified trimester, fetus 4

O36.8295 Fetal anemia and thrombocytopenia, unspecified trimester, fetus 5

O36.8299 Fetal anemia and thrombocytopenia, unspecified trimester, other fetus

O99.111 Other diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism complicating pregnancy, first trimester

O99.112 Other diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism complicating pregnancy, second trimester

O99.113 Other diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism complicating pregnancy, third trimester

O99.119 Other diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism complicating pregnancy, unspecified trimester

P55.0 Rh isoimmunization of newborn

P55.1 ABO isoimmunization of newborn

P61.0 Transient neonatal thrombocytopenia

P78.84 Gestational alloimmune liver disease

T80.90XA Unspecified complication following infusion and therapeutic injection, initial encounter

T80.90XD Unspecified complication following infusion and therapeutic injection, subsequent encounter

T80.90XS Unspecified complication following infusion and therapeutic injection, sequela

T86.01 Bone marrow transplant rejection
T86.11 Kidney transplant rejection
T86.21 Heart transplant rejection
T86.31 Heart-lung transplant rejection
T86.41 Liver transplant rejection
T86.5 Complications of stem cell transplant
T86.810 Lung transplant rejection
T86.850 Intestine transplant rejection
T86.890 Other transplanted tissue rejection
Z94.0 Kidney transplant status
Z94.1 Heart transplant status
Z94.2 Lung transplant status
Z94.3 Heart and lungs transplant status
Z94.4 Liver transplant status
Z94.81 Bone marrow transplant status
Z94.82 Intestine transplant status
Z94.84 Stem cells transplant status

Duration of authorization: 12 months

Version Effective Date: 01/02/2025

Title: Inclisiran (Leqvio®)

MEDICALLY NECESSARY:

1. Criteria for Initial Approval

Inclisiran (Leqvio) is considered medically necessary and, therefore, covered for the treatment of primary hyperlipidemia in adults when *one* (A or B) of the following criteria are met:

A. Individual meets ALL of the following:

- Individual has a history of clinical atherosclerotic cardiovascular disease (ASCVD) (*see Section A in the GUIDELINES portion of this medical policy bulletin*); and
- Individual meets *one* of the following:
 - Current LDL-C level greater than or equal to 70 mg/dL after at least three months of treatment with a high-intensity statin. If the individual is unable to tolerate a high-intensity statin dose, a moderate-intensity statin dose may be used; *or*
 - Current LDL-C level greater than or equal to 70 mg/dL with a contraindication or intolerance to statins (*see SECTIONS B & C in the GUIDELINES portion of this medical policy bulletin*); and
- Individual will continue to receive concomitant statin therapy if no contraindication or intolerance (*see SECTIONS B & C in the GUIDELINES portion of this medical policy bulletin*); **OR**

B. Individual meets ALL of the following:

- Individual had an untreated (before any lipid-lowering therapy) LDL-C level greater than or equal to 190 mg/dL in the absence of a secondary cause; *and*
- Individual meets *one* of the following:
 - Current LDL-C level greater than or equal to 100 mg/dL after at least three months of treatment with a high-intensity statin. If the individual is unable to tolerate a high-intensity statin dose, a moderate-intensity statin dose may be used; *or*
 - Current LDL-C level greater than or equal to 100 mg/dL with a contraindication or intolerance to statins (*see SECTIONS B & C in the GUIDELINES portion of this medical policy bulletin*); and
- Individual will continue to receive concomitant statin therapy if no contraindication or intolerance (*see SECTIONS B & C in the GUIDELINES portion of this medical policy bulletin*).

2. Continuation of Therapy

Continuation of inclisiran (Leqvio) therapy is considered medically necessary in individuals who have an indication and associated factor(s) & presentation(s) listed in Section I above when ALL of the following criteria are met:

A. Individual has achieved or maintained an LDL-C reduction (e.g., LDL-C is now at goal, clinically acceptable lowering of LDL-C); *and*

B. Individual will continue to receive concomitant statin therapy if no contraindication or intolerance (*see SECTIONS B & C in the GUIDELINES portion of this medical policy bulletin*).

Guidelines

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, Inclisiran (Leqvio®) is covered under the medical benefits of the Company's products when the medical necessity criteria listed in this medical policy are met.

U.S. Food and Drug Administration (FDA)-Approved Indications

Initial Approval (December 22, 2021):

Leqvio is indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (ASCVD), who require additional lowering of low-density lipoprotein cholesterol (LDL-C).

Updated Label/Approval (July 2023):

Leqvio is indicated as an adjunct to diet and statin therapy for the treatment of adults with primary hyperlipidemia, including heterozygous familial hypercholesterolemia (HeFH), to reduce low-density lipoprotein cholesterol (LDL-C).

Section A - Clinical ASCVD

- Acute coronary syndromes
- Myocardial infarction
- Stable or unstable angina
- Coronary or other arterial revascularization procedure (e.g., percutaneous coronary intervention [PCI], coronary artery bypass graft [CABG] surgery)
- Stroke of presumed atherosclerotic origin
- Transient ischemic attack (TIA)
- Non-cardiac peripheral arterial disease (PAD) of presumed atherosclerotic origin (e.g., carotid artery stenosis, lower extremity PAD)
- Obstructive coronary artery disease (defined as fifty percent or greater stenosis on cardiac computed tomography angiogram or catheterization)
- Coronary Artery Calcium (CAC) Score ≥ 1000

Section B - Statin-Associated Muscle Symptoms (SAMS) and Statin Re-Challenge

- Score of 7 or higher on the Statin-Associated Muscle Symptom Clinical Index (SAMS-CI)

- Statin-associated elevation in creatine kinase (CK) level ≥ 10 times upper limit of normal (ULN)

Note: Statin re-challenge is NOT required for members who have experienced an elevation of CK level ≥ 10 times ULN after receiving lipid-lowering therapy (LLT) with a statin.

Section C - Contraindications to Statins

- Active liver disease, including unexplained persistent elevations in hepatic transaminase levels (e.g., alanine transaminase (ALT) level ≥ 3 times ULN)
- Pregnancy or planned pregnancy
- Breastfeeding

Duration of authorization: 12 months

Version Effective Date: 09/18/2024

Title: Inebilizumab-cdon (Uplizna)

MEDICALLY NECESSARY:

INITIAL CRITERIA

Inebilizumab-cdon (Uplizna) is considered medically necessary and, therefore, covered for the treatment of adult individuals with neuromyelitis optica spectrum disorder (NMOSD), when all of the following criteria are met, including dosing and frequency:

- The individual has a diagnosis of NMOSD.
- The individual is anti-aquaporin-4 (AQP4) antibody seropositive.
- The individual has a history of one or more relapses that required rescue therapy within the year or two or more relapses that required rescue therapy in the past two years.
- Dosing and frequency for inebilizumab-cdon (Uplizna):
 - Initial dose: 300 mg intravenous infusion followed two weeks later by a second 300 mg intravenous infusion
 - Subsequent doses (starting six months from the first infusion): single 300 mg intravenous infusion every six months

CONTINUATION CRITERIA

Inebilizumab-cdon (Uplizna) is considered medically necessary for continued use in adult individuals with a diagnosis of NMOSD when the initial criteria are met AND there is documentation of a positive clinical response (e.g., reductions in relapse or reduction in new onset of symptoms).

Duration of authorization: 12 months

Version Effective Date: 04/30/2025

Title: Interleukin-5 (IL-5) Antagonist (e.g., Cinqair®)

MEDICALLY NECESSARY:

INITIAL THERAPY

Reslizumab (Cinqair) is considered medically necessary and, therefore, covered for the treatment of severe eosinophilic asthma when all of the following criteria are met:

- The individual is 18 years of age or older
- Blood eosinophils of at least 400 cells/microliter* at the initiation of treatment (within 3-4 weeks of the first dose)
- The individual is currently receiving treatment that does not maintain adequate control of his/her asthma and reslizumab (Cinqair) is being used as additional maintenance therapy.
 - Current treatment must include high-dose inhaled corticosteroids (ICS) (with or without oral corticosteroids) plus an additional controller (e.g., long-acting beta agonist [LABA], leukotriene inhibitor, theophylline) medication, unless the individual is intolerant of or has a contraindication to these agents.
- Reslizumab (Cinqair) will not be used in combination with other biologics for asthma/allergic conditions (e.g., benralizumab [Fasenra], dupilumab [Dupixent], mepolizumab [Nucala], omalizumab [Xolair])

The dosage, frequency, and route of administration of reslizumab (Cinqair) is 3 mg/kg once every 4 weeks by intravenous infusion.

* Note: 1 microliter is equal to 1 cubic millimeter (mm³)

CONTINUATION THERAPY

Reslizumab (Cinqair) is considered medically necessary and, therefore, covered during continuation therapy for individuals when there is documentation of clinical improvement in respiratory function (e.g., oral corticosteroid elimination or reduction, exacerbation elimination or reduction, reduced absenteeism from school or work) and when reslizumab (Cinqair) will not be used in combination with other biologics for asthma/allergic conditions (e.g., benralizumab [Fasenra], dupilumab [Dupixent], mepolizumab [Nucala], omalizumab [Xolair])

Duration of authorization: 12 months

Version Effective Date: 01/22/2025

Title: Intravenous (IV) Iron Preparations

MEDICALLY NECESSARY:

COMPANY-DESIGNATED PREFERRED PRODUCTS

Although there are many brands of intravenous (IV) iron products on the market for the treatment of iron deficiency (ID) or iron-deficiency anemia (IDA), there is no reliable evidence of the superiority of any one brand of IV iron product compared with other brands. The Company has designated the following as its preferred IV iron products for use in adult individuals aged 18 years and older who are treatment-naïve:

- Ferumoxytol (e.g., Feraheme®)
- Sodium ferric gluconate complex in sucrose (e.g., Ferrlecit®)
- Iron dextran (e.g., INFeD®)
- Iron sucrose (e.g., Venofer®)

Ferumoxytol (e.g., Feraheme), sodium ferric gluconate complex in sucrose (e.g., Ferrlecit), iron dextran (e.g., INFeD), and iron sucrose (e.g., Venofer) are less costly and at least as likely to produce equivalent therapeutic results as the non-preferred IV iron products, which include, but are not limited to, ferric carboxymaltose (Injectafer®), and ferric derisomaltose (Monoferric®).

NON-PREFERRED PRODUCTS

The Company has designated the following as its non-preferred IV iron products for use in adult individuals aged 18 years and older:

- Ferric carboxymaltose (Injectafer)
- Ferric derisomaltose (Monoferric)

For individuals who meet the medically necessary criteria below, use of non-preferred IV iron products (which include, but are not limited to, ferric carboxymaltose [Injectafer], ferric derisomaltose [Monoferric]) is considered medically necessary and, therefore, covered when the individual has a documented intolerance, contraindication, or nonresponse to at least two preferred IV iron preparations (i.e., ferumoxytol [e.g., Feraheme], sodium ferric gluconate complex in sucrose [e.g., Ferrlecit], iron dextran [e.g., INFeD], iron sucrose [e.g., Venofer]).

Management of Heart Failure

The use of ferric carboxymaltose (Injectafer) for the treatment of adult individuals with New York Heart Association class II/III heart failure is considered medically necessary and, therefore, covered without the need to try any preferred IV iron products, to improve exercise capacity.

Management of Iron Deficiency (ID) or Iron Deficiency Anemia (IDA) Without Chronic Kidney Disease (CKD)

The use of a non-preferred IV iron product for the treatment of ID or IDA without CKD is considered medically necessary and, therefore, covered for adult individuals with **ALL** of the following:

- Individual has met the requirements listed in the COMPANY-DESIGNATED PREFERRED PRODUCTS and NON-PREFERRED PRODUCTS sections above
- Diagnosis of anemia based on hemoglobin (hgb) below normal levels for individual's age and sex (if using to treat IDA)
- Ferritin level <30 ng/mL **OR** transferrin saturation (TSAT) <20 percent
- Normal kidney function as demonstrated by laboratory values (e.g., urine albumin, creatinine, glomerular filtration ratio [GFR])
- Documented intolerance, contraindication, or nonresponse to oral iron supplementation for at least 3 months

Management of Iron Deficiency (ID) or Iron Deficiency Anemia (IDA) With Chronic Kidney Disease (CKD)

The use of a non-preferred IV iron product for the treatment of ID or IDA with CKD is considered medically necessary and, therefore, covered for adult individuals with **ALL** of the following:

- Individual has met the requirements listed in the COMPANY-DESIGNATED PREFERRED PRODUCTS and NON-PREFERRED PRODUCTS sections above
- Diagnosis of anemia based on hgb below normal levels for individual's age and sex (if using to treat IDA)
- **ONE** of the following:
 - Ferritin level 100 ng/mL or less **AND** TSAT <20 percent in nondialysis individuals or those receiving peritoneal dialysis
 - Ferritin level 200 ng/mL or less **AND** TSAT <20 percent in individuals on hemodialysis
- CKD as demonstrated by abnormal laboratory values (e.g., urine albumin, creatinine, GFR)
- Documented intolerance, contraindication, or nonresponse to oral iron supplementation for at least 3 months

Management of Cancer- and Chemotherapy-Induced Anemia

The use of a non-preferred IV iron product for the treatment of cancer- and chemotherapy-induced anemia is considered medically necessary and, therefore, covered for adult individuals who have met the requirements listed in the COMPANY-DESIGNATED PREFERRED PRODUCTS and NON-PREFERRED PRODUCTS sections above, and with **EITHER** of the following:

- For the treatment of **EITHER** of the following:
 - Absolute iron deficiency (ferritin <30 ng/mL and transferrin saturation <20 percent)
 - Possible functional iron deficiency (ferritin >500–800 ng/mL and transferrin saturation <50 percent) in selected individuals (with the goal of avoiding allogeneic transfusion)
- In combination with erythropoiesis-stimulating agents (ESAs) for the treatment of **EITHER** of the following:

- Functional iron deficiency (ferritin 30–500 ng/mL and transferrin saturation <50 percent) in individuals receiving myelosuppressive chemotherapy without curative intent and ESAs
- Absolute iron deficiency (ferritin <30 ng/mL and transferrin saturation <20 percent) in individuals who do not experience an increase in hemoglobin after 4 weeks of IV or oral iron supplementation

Duration of authorization: 12 months

Version Effective Date: 01/15/2025

Title: Intravenous Infliximab and Related Biosimilars

MEDICALLY NECESSARY:

Intravenous infliximab (Remicade) and related biosimilars (e.g., unbranded infliximab, infliximab-abda [Renflexis], infliximab-axxq [Avsola], infliximab-dyyb [Inflectra], infliximab-qbtx [Ixifi]) are considered medically necessary and, therefore, covered when the individual meets all of the requirements in the following sections:

- Dosing and frequency requirements listed in Attachment A
- Indications and all the criteria are met

RHEUMATOLOGIC CONDITIONS

- **Ankylosing spondylitis and nonradiographic axial spondyloarthritis**
 - When all of the following criteria are met:
 - Individual is over 18 years of age with evidence of active disease (increasing inflammation, pain, disability, and decreased function)
 - Documentation of an adequate therapeutic trial* of at least two nonsteroidal anti-inflammatory drugs (NSAIDs) that have failed to control symptoms
 - *An adequate therapeutic trial is defined as: Treatment with NSAIDs for at least 3 months at maximum recommended or tolerated anti-inflammatory dose unless treatment is discontinued due to lack of response, intolerance, toxicity or contraindication
 - If the above criteria are not met, there must be documentation both of very severe disease and that the clinician considers infliximab or related biosimilars the best initial drug of choice with appropriate justification (severe pain, disability, and inability to perform activities of daily living [ADLs], or severe impact on quality of life)
- **Autoimmune collagen vascular disease**
 - Consideration may be given for individuals with an autoimmune collagen vascular disease that is refractory to conventional therapies.
- **Behçet syndrome**
 - Documented failure, contraindication or intolerance to conventional therapy, such as: corticosteroids, colchicine, or disease-modifying antirheumatic drugs (DMARDs) (e.g., azathioprine [AZA], cyclosporine, other tumor necrosis factor [TNF] inhibitors)
- **Inflammatory bowel disease arthritis**
 - When all of the following criteria are met:
 - Individual is over 18 years of age with evidence of active disease (increased disease activity evidenced by increasing inflammation, pain, disability, and decreased function)

- Documented failure, contraindication or intolerance to a 3-month trial of any of the DMARDs (e.g., sulfasalazine, AZA, methotrexate, other anti-TNF agents)
 - If the above criteria are not met, there must be documentation of very severe disease and the clinician considers infliximab or related biosimilars the best initial drug of choice with appropriate justification (severe pain, disability, and inability to perform ADLs, or severe impact to quality of life)
- **Polyarticular juvenile idiopathic arthritis (JIA)**
 - When all of the following criteria are met:
 - Individual is 4 years of age and older with moderate-to-severe polyarticular JIA with evidence of active disease (increased disease activity evidenced by increasing inflammation, pain, disability, and decreased function)
 - Documented failure, contraindication, or intolerance to a 3-month trial of any of the nonbiologic DMARDs (e.g., methotrexate, sulfasalazine, leflunomide)
 - Documented failure, contraindication, or intolerance to a 3-month trial of any of the US Food and Drug Administration (FDA)-approved biologic DMARDs for JIA (e.g., anti-TNF, T-cell costimulation modulators)
 - Infliximab or related biosimilars will be used in combination with methotrexate, or as a monotherapy when the individual is intolerant of, or has a contraindication to, methotrexate
 - If the above criteria are not met, there must be documentation of both very severe disease and that the clinician considers infliximab or related biosimilars the best initial drug of choice with appropriate justification (severe pain, disability, and inability to perform ADLs, or severe impact on quality of life)
- **Psoriatic arthritis**
 - When all the following criteria are met:
 - Individual is over 18 years of age with evidence of active disease (increased disease activity evidenced by increasing inflammation, pain, disability, and decreased function)
 - Documented failure, contraindication or intolerance to a 3-month trial of any of the DMARDs (e.g., sulfasalazine, AZA, cyclosporine, methotrexate, other anti-TNF agents)
 - If the above criteria are not met, there must be documentation both of very severe disease and that the clinician considers infliximab or related biosimilars the best initial drug of choice with appropriate justification (severe pain, disability, and inability to perform ADLs, or severe impact to quality of life)
- **Reactive arthritis (Reiter disease)**
 - When all the following criteria are met:
 - Individual is over 18 years of age with evidence of active disease (increased disease activity evidenced by increasing inflammation, pain, disability, and decreased function)

- Documented failure, contraindication, or intolerance to a 3-month trial of any of the DMARDs (e.g., sulfasalazine, methotrexate, other anti-TNF agents)
 - If the above criteria are not met, there must be documentation of very severe disease and the clinician considers infliximab or related biosimilars the best initial drug of choice with appropriate justification (severe pain, disability, and inability to perform ADLs, or severe impact to quality of life)
- **Rheumatoid arthritis (RA)**
 - When all the following criteria are met:
 - Individual is over 18 years of age with moderate-to-severe rheumatoid arthritis with evidence of active disease (increased disease activity evidenced by increasing inflammation, pain, disability, and decreased function)
 - Documented failure, contraindication or intolerance to a 3-month trial of any of the DMARDs (e.g., hydroxychloroquine, leflunomide, sulfasalazine, methotrexate, other anti-TNF agents or non-TNF biologics [abatacept, rituximab, tocilizumab])
 - Infliximab or related biosimilars will be used in combination with methotrexate, or as a monotherapy when the individual is intolerant of, or has a contraindication to, methotrexate
 - If the above criteria are not met, there must be documentation both of very severe disease and that the clinician considers infliximab or related biosimilars the best initial drug of choice with appropriate justification (severe pain, disability, and inability to perform ADLs, or severe impact on quality of life)
- **Sarcoidosis**
 - When both criteria are met:
 - Individual at least 18 years of age
 - Documentation of failure, contraindication or intolerance to a 3-month trial of a standard regimen of corticosteroids and DMARDs (e.g., methotrexate, AZA)
 - If the above criteria are not met, there must be documentation both of very severe disease and that the professional provider considers infliximab or related biosimilars to be the best initial drug of choice with appropriate justification (disability, and inability to perform ADLs, or severe impact on quality of life)
- **Uveitis, noninfectious, due to Behçet syndrome**
 - Documented diagnosis of Behçet disease with vision-threatening uveitis
- **Uveitis, noninfectious, not due to Behçet syndrome**
 - Documented failure, contraindication or intolerance to corticosteroids and at least one DMARD (e.g., AZA, cyclosporine, methotrexate, mycophenolate, tacrolimus, or other TNF inhibitors)

GASTROINTESTINAL INDICATIONS

- **Crohn disease (CD): nonfistulizing**
 - Presence of moderately to severely active CD in adults or pediatric individuals 6 years of age or older when **all** the following criteria are met:
 - The individual has active CD as indicated by any of the following signs or symptoms: gastrointestinal bleeding, weight loss, diarrhea, perianal disease, internal fistula(ae), intestinal obstruction, megacolon or extraintestinal manifestations, such as arthritis or spondylitis
 - The individual has had an inadequate response to conventional therapies (unless intolerant or contraindicated) that include, but are not limited to: antibiotics, 5-aminosalicylates (e.g., mesalamine), DMARDs (e.g., 6-mercaptopurine [6-MP], AZA, corticosteroids)
 - Presence of severe inflammatory disease involving the distal small bowel and/or large bowel in an individual who is having symptoms of gastrointestinal bleeding, diarrhea, profound anemia, and poor nutritional intake associated with weight loss and abdominal pain.
 - **Crohn disease: fistulizing**
 - When both criteria are met:
 - An adult or pediatric individual 6 years of age or older whose presentation of CD involves the formation of a fistula(ae)
 - An adult or pediatric individual 6 years of age or older with diffuse inflammatory disease involving the distal small bowel and/or large bowel who is having symptoms of profound anemia, gastrointestinal bleeding, poor nutritional intake associated with weight loss, and abdominal pain
 - **Ulcerative colitis: adults**
 - When all the following criteria are met:
 - In individuals 18 years of age or older with moderately to severely active ulcerative colitis who have had an inadequate response to conventional therapy, including a documented failure, contraindication, or intolerance to at least two of the following:
 - Aminosaliclates: (e.g., mesalamine [Apriso, Asacol, Canasa, Lialda, Pentasa, Rowasa], sulfasalazine [Azulfidine], olsalazine [Dipentum])
 - Systemic corticosteroids: (e.g., prednisone, prednisolone)
 - DMARDs (e.g., 6-MP, AZA [Imuran], or cyclosporine [e.g., Neoral, Gengraf])
- OR**
- When either of the following criteria are met:
 - In individuals 18 years of age or older, when there is a clinical presentation that requires an intervention with a more immediate effect to resolve the colitis; examples include:
 - Symptoms of profound anemia, poor nutritional intake associated with weight loss, and abdominal pain

- Individuals who have the potential for adverse events to the other, more common treatment regimens or who have contraindication to the use of these treatment regimens (e.g., individuals with underlying diabetes may have worsening control with the addition of prednisone)
 - If the above criteria are not met, there must be documentation of the individual's rapidly worsening disease as indicated by increasing disability, poorly controlled symptoms, and increasing quality of life concerns (cannot perform ADLs without great difficulty) and there is inadequate response to more conventional agents.
- **Ulcerative colitis: children**
 - When all of the following criteria are met:
 - Child is at least 6 years of age
 - Has moderately to severely active ulcerative colitis (see Policy Guidelines section)
 - Has had an inadequate response to conventional therapy, e.g., aminosalicylates, AZA (Imuran), 6-MP, or corticosteroids

DERMATOLOGIC INDICATIONS

- **Hidradenitis suppurativa**
 - When all of the following criteria are met:
 - The individual is 18 years of age or older with documentation of moderate to severe hidradenitis suppurativa with recurrent abscesses/inflammatory nodules and scar formation.
 - Documentation of failure, contraindication, or intolerance to at least 3 months of antibiotics (e.g., doxycycline, clindamycin, rifampin).
 - Documentation of failure, contraindication, or intolerance to a 3-month trial of any of the FDA-approved biologic DMARDs for hidradenitis suppurativa (e.g., anti-TNF agents, T-cell costimulation modulators).
- **Plaque psoriasis**
 - When all the following criteria are met:
 - The individual is 18 years of age or older with chronic, severe psoriasis who is a candidate for systemic therapy but other systemic therapies are less medically appropriate (e.g., presence of other factors such as hypertension, alcohol consumption, the condition of pregnancy, nonmelanoma skin cancers).
 - Individual is affected with plaque psoriasis covering more than 10% of body surface area (BSA) or a lesser percentage if psoriasis affects sensitive body areas, such as hands, feet, face, or genitals.
 - Documentation of failure, contraindication, or intolerance to a trial of at least 3 months with at least one of the following:
 - Phototherapy: either ultraviolet-B or psoralen/ultraviolet A (PUVA)
 - Methotrexate (e.g., Trexall, Rheumatrex)

- Retinoids (e.g., acitretin [Soriatane])
 - Cyclosporine (e.g., Neoral, Gengraf)
- If the above criteria are not met, there must be documentation of severe psoriasis (>10% BSA) or a lesser percentage if psoriasis affects sensitive body areas, such as hands, feet, face, or genitals and is very symptomatic (e.g., pain, pruritus, burning, scaling), the symptoms significantly hinder the quality of life, and the use of other systemic therapy is not appropriate due to other factors (e.g., history of hypertension, alcohol consumption, the condition of pregnancy, nonmelanoma skin cancers).
- **Pyoderma gangrenosum**
 - In individuals 18 years of age or older with documentation of pyoderma gangrenosum that is refractory to a 3-month trial of conventional treatments, such as local steroid injections, topical tacrolimus, systemic corticosteroids, dapsone, DMARDs (e.g., cyclosporine), and conservative wound care, including oral antibiotics
 - If the above criterion is not met, there must be documentation of rapidly worsening disease process as indicated by increasing disability, poorly controlled symptoms, and increasing quality of life concerns (cannot perform ADLs without great difficulty) and who is not adequately responding to more conventional agents.

HEMATOPOIETIC CELL TRANSPLANTATION

- **Acute Graft-Versus Host Disease (aGVHD)**
 - Acute GVHD in those who have undergone hematopoietic cell transplantation, as additional therapy in conjunction with systemic corticosteroids and in combination with original immunosuppressive agent (i.e., tacrolimus, cyclosporine, methotrexate) following no response (steroid-refractory disease) to first-line therapy options

IMMUNOTHERAPY-RELATED TOXICITY INDICATIONS

- Treatment of any of the following immunotherapy-related toxicities as additional immunosuppression
 - Cardiac toxicities
 - In individuals with myocarditis if no improvement within 24 to 48 hours of starting pulse-dose methylprednisolone
 - Esophagitis
 - In individuals with moderate to severe esophagitis, gastritis, or duodenitis if no improvement on corticosteroids or budesonide
 - Diarrhea or colitis
 - In individuals with mild (Grade 1) diarrhea and colitis if persistent or progressive symptoms and positive lactoferrin/calprotectin

- In individuals with moderate (Grade 2) or severe (Grades 3–4) diarrhea or colitis if colonoscopy or flexible sigmoidoscopy shows significant ulceration or extensive nonulcerative inflammation
- Anemia
 - In individuals with G4 hemolytic anemia with hemolysis if no response to corticosteroids and rituximab
- Elevated serum creatinine/acute renal injury
 - In individuals with severe (Stage 3) (creatinine >3 times baseline or >4 mg/dL) elevated serum creatinine/acute kidney injury toxicity remains greater than Stage 2 after 4 to 6 weeks of corticosteroids or if creatinine increases during steroid taper (or once off corticosteroids)
- Inflammatory arthritis
 - In individuals with moderate or severe inflammatory arthritis unable to taper corticosteroids after 1 week
- Pneumonitis
 - In individuals with moderate (G2) pneumonitis if no improvement after 48 to 72 hours of corticosteroids or severe (Grades 3–4) pneumonitis who show no improvement after 48 hours methylprednisolone).
- Uveitis
 - In individuals with G1-4 uveitis that is refractory to high-dose systemic corticosteroids (treatment guided by ophthalmology)

Duration of authorization: 12 months

Version Effective Date: 04/21/2025

Title: Intravenous Infliximab and Related Biosimilars

MEDICALLY NECESSARY:

DOSING AND FREQUENCY REQUIREMENTS

FOR INTRAVENOUS INFlixIMAB (REMICADE) AND RELATED BIOSIMILARS (E.G., UNBRANDED INFlixIMAB, INFlixIMAB-ABDA [RENFLEXIS], INFlixIMAB-AXXQ [AVSOLA], INFlixIMAB-DYYB [INFLECTRA], INFlixIMAB-QBTX [IXIFI])

The Company reserves the right to modify the Dosing and Frequency Requirements listed in this Policy to ensure consistency with the most recently published recommendations for the use of infliximab and related biosimilars. Changes to these guidelines are based on a consensus of information obtained from resources such as, but not limited to: the US Food and Drug Administration (FDA); Company-recognized authoritative pharmacology compendia; or published peer-reviewed clinical research. The professional provider must supply supporting documentation (i.e., published peer-reviewed literature) in order to request coverage for an amount of infliximab or related biosimilars outside of the Dosing and Frequency Requirements listed in this Policy. For a list of Company-recognized pharmacology compendia, view our policy on off-label coverage for prescription drugs and biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of this drug. If the member's dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider **must** submit those changes to the Company for a new approval based on those changes as part of the precertification process. The Company reserves the right to conduct post-payment review and audit procedures for any claims submitted for infliximab or related biosimilars.

Indication	Dosage and Frequency
Acute graft-versus-host disease (aGVHD) ¹⁰	Infliximab 10 mg/kg IV weekly for a maximum of 9 doses
Ankylosing spondylitis and Nonradiographic Axial Spondyloarthritis ¹	Induction: 5 mg/kg IV at weeks 0, 2, and 6 Maintenance: 5 mg/kg IV every 6 weeks (up to a maximum of 10 mg/kg IV every 4 weeks)
Behcet's syndrome ¹³	Induction: 5 mg/kg IV at weeks 0, 2, and 6 Maintenance: 5 mg/kg IV every 6-8 weeks (up to a maximum of 10 mg/kg IV every 8 weeks)
Crohn's disease (moderate to severe) or fistulizing Crohn's disease ^{1, 7}	Adults: Induction: 5 mg/kg IV at weeks 0, 2, and 6 Maintenance: 5 mg/kg IV every 8 weeks. For adults who

	respond and then lose their response, consideration may be given to treatment with 10 mg/kg IV every 8 weeks (up to a maximum of 10 mg/kg IV every 4 weeks) Children: Induction: 5 mg/kg IV at weeks 0, 2, 6. Maintenance: 5 mg/kg IV every 8 weeks (up to a maximum of 10 mg/kg IV every 4 weeks) For children who are steroid-refractory or have severe extensive or fistulizing disease, especially with hypoalbuminemia, consideration may be given for a higher induction dose of 10 mg/kg and/or decreasing the interval between infusions to 4-6 weeks.
Hidradenitis Suppurativa ¹¹	Induction: 5-10 mg/kg IV at weeks 0, 2, and 6 Maintenance: 5-10 mg/kg IV every 4 weeks, and with decreasing dosage as tolerated.
Toxicities Related to Immune Checkpoint Inhibitors ¹²	Infliximab 5 mg/kg IV at weeks 0, 2, and 6
Inflammatory bowel disease arthritis (enteropathic arthritis) ⁵	Induction: 5 mg/kg IV at weeks 0, 2, and 6 Maintenance: 5 mg/kg IV every 8 weeks (up to a maximum of 10 mg/kg IV every 4 weeks)
Plaque Psoriasis, severe ^{1, 8}	Induction: 5 mg/kg IV at weeks 0, 2, and 6 Maintenance: 5 mg/kg IV every 8 weeks (up to a maximum of 10 mg/kg IV every 4 weeks)
Polyarticular Juvenile Idiopathic Arthritis (JIA) ²	Induction: 3 to 6 mg/kg IV at weeks 0, 2, and 6 Maintenance: 3 to 6 mg/kg IV every 8 weeks (up to a maximum of 10 mg/kg IV every 4 weeks)
Psoriatic arthritis ¹	Induction: 5 mg/kg IV at weeks 0, 2, and 6 Maintenance: 5 mg/kg IV every 8 weeks (up to a maximum of 10 mg/kg IV every 4 weeks)
Reactive arthritis (Reiter's disease) ⁶	Induction: 3 to 5 mg/kg IV at weeks 0, 2, and 6 Maintenance: 3 to 5 mg/kg IV every 6-8 weeks (up to a maximum of 10 mg/kg IV every 4 weeks)
Rheumatoid arthritis ¹	Induction: 3 mg/kg IV at weeks 0, 2, and 6 Maintenance: 3 mg/kg IV every 8 weeks (up to a maximum of 10 mg/kg IV every 4 weeks)
Pyoderma gangrenosum ³	Induction: 5 mg/kg IV at week 0. Repeat at week 2 if needed. Maintenance: 5 mg/kg IV every 4-12 weeks (up to a maximum of 10 mg/kg IV every 4 weeks)

Sarcoidosis ⁴	Induction: 3 to 5 mg/kg IV at weeks 0, 2, and 6 Maintenance: 3 to 5 mg/kg IV every 4 to 8 weeks (up to a maximum of 10 mg/kg IV every 4 weeks)
Ulcerative colitis (adult and pediatric) ^{1, 14}	Induction: 5 mg/kg IV at weeks 0, 2, and 6 Maintenance: 5 mg/kg IV every 8 weeks (up to a maximum of 10 mg/kg IV every 4 weeks) For children who are steroid-refractory or have severe extensive or fistulizing disease, especially with hypoalbuminemia, consideration may be given for a higher induction dose of 10mg/kg and/or decreasing the interval between infusions to 4-6 weeks.
Uveitis, non-infectious ⁹	Induction: 3 to 10 mg/kg IV at weeks 0, 2, and 6 Maintenance: 3 to 10 mg/kg IV every 4 to 8 weeks

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Duration of authorization: 12 months

Version Effective Date: 04/21/2025

Title: Intravenous Infliximab and Related Biosimilars

MEDICALLY NECESSARY:

ICD-10-CM Codes and Narratives

This is not an all inclusive list

INFLIXIMAB AND RELATED BIOSIMILARS IS CONSIDERED MEDICALLY NECESSARY WHEN REPORTED WITH ANY OF THE FOLLOWING DIAGNOSIS CODES:

Report the most appropriate diagnosis code for toxicities related to immune checkpoint inhibitors.

D59.0 Drug-induced autoimmune hemolytic anemia

D59.2 Drug-induced nonautoimmune hemolytic anemia

D86.0 Sarcoidosis of lung

D86.2 Sarcoidosis of lung with sarcoidosis of lymph nodes

D86.83 Sarcoid iridocyclitis

D86.86 Sarcoid arthropathy

D86.87 Sarcoid myositis

D86.89 Sarcoidosis of other sites

D86.9 Sarcoidosis, unspecified

D89.810 Acute graft-versus-host disease

H20.041 Secondary noninfectious iridocyclitis, right eye

H20.042 Secondary noninfectious iridocyclitis, left eye

H20.043 Secondary noninfectious iridocyclitis, bilateral

H20.9 Unspecified iridocyclitis

H44.111 Panuveitis, right eye

H44.112 Panuveitis, left eye

H44.113 Panuveitis, bilateral

H44.131 Sympathetic uveitis, right eye

H44.132 Sympathetic uveitis, left eye

H44.133 Sympathetic uveitis, bilateral

I30.0 Acute nonspecific idiopathic pericarditis

I30.8 Other forms of acute pericarditis

I40.8 Other acute myocarditis

I40.9 Acute myocarditis, unspecified

I49.9 Cardiac arrhythmia, unspecified

I77.82 Antineutrophilic cytoplasmic antibody (ANCA) vasculitis

J70.2 Acute drug-induced interstitial lung disorders

J70.4 Drug-induced interstitial lung disorders, unspecified

K20.0 Eosinophilic esophagitis

K20.80 Other esophagitis without bleeding

K20.81 Other esophagitis with bleeding

K20.90 Esophagitis, unspecified without bleeding

K20.91 Esophagitis, unspecified with bleeding

K29.00 Acute gastritis without bleeding

K29.01 Acute gastritis with bleeding

K29.30 Chronic superficial gastritis without bleeding

K29.31 Chronic superficial gastritis with bleeding

K29.40 Chronic atrophic gastritis without bleeding

K29.41 Chronic atrophic gastritis with bleeding

K29.50 Unspecified chronic gastritis without bleeding

K29.51 Unspecified chronic gastritis with bleeding

K29.60 Other gastritis without bleeding

K29.61 Other gastritis with bleeding

K29.70 Gastritis, unspecified, without bleeding

K29.71 Gastritis, unspecified, with bleeding

K29.80 Duodenitis without bleeding

K29.81 Duodenitis with bleeding

K29.90 Gastroduodenitis, unspecified, without bleeding

K29.91 Gastroduodenitis, unspecified, with bleeding

K50.00 Crohn's disease of small intestine without complications

K50.011 Crohn's disease of small intestine with rectal bleeding

K50.012 Crohn's disease of small intestine with intestinal obstruction

K50.013 Crohn's disease of small intestine with fistula

K50.014 Crohn's disease of small intestine with abscess

K50.018 Crohn's disease of small intestine with other complication

K50.019 Crohn's disease of small intestine with unspecified complications

K50.10 Crohn's disease of large intestine without complications

K50.111 Crohn's disease of large intestine with rectal bleeding

K50.112 Crohn's disease of large intestine with intestinal obstruction

K50.113 Crohn's disease of large intestine with fistula

K50.114 Crohn's disease of large intestine with abscess

K50.118 Crohn's disease of large intestine with other complication

K50.119 Crohn's disease of large intestine with unspecified complications

K50.80 Crohn's disease of both small and large intestine without complications

K50.811 Crohn's disease of both small and large intestine with rectal bleeding

K50.812 Crohn's disease of both small and large intestine with intestinal obstruction

K50.813 Crohn's disease of both small and large intestine with fistula

K50.814 Crohn's disease of both small and large intestine with abscess

K50.818 Crohn's disease of both small and large intestine with other complication

K50.819 Crohn's disease of both small and large intestine with unspecified complications

K50.90 Crohn's disease, unspecified, without complications

K50.911 Crohn's disease, unspecified, with rectal bleeding

K50.912 Crohn's disease, unspecified, with intestinal obstruction

K50.913 Crohn's disease, unspecified, with fistula

K50.914 Crohn's disease, unspecified, with abscess

K50.918 Crohn's disease, unspecified, with other complication

K50.919 Crohn's disease, unspecified, with unspecified complications

K51.00 Ulcerative (chronic) pancolitis without complications

K51.011 Ulcerative (chronic) pancolitis with rectal bleeding

K51.012 Ulcerative (chronic) pancolitis with intestinal obstruction

K51.013 Ulcerative (chronic) pancolitis with fistula

K51.014 Ulcerative (chronic) pancolitis with abscess

K51.018 Ulcerative (chronic) pancolitis with other complication

K51.019 Ulcerative (chronic) pancolitis with unspecified complications

K51.20 Ulcerative (chronic) proctitis without complications

K51.211 Ulcerative (chronic) proctitis with rectal bleeding

K51.212 Ulcerative (chronic) proctitis with intestinal obstruction

K51.213 Ulcerative (chronic) proctitis with fistula

K51.214 Ulcerative (chronic) proctitis with abscess

K51.218 Ulcerative (chronic) proctitis with other complication

K51.219 Ulcerative (chronic) proctitis with unspecified complications

K51.30 Ulcerative (chronic) rectosigmoiditis without complications

K51.311 Ulcerative (chronic) rectosigmoiditis with rectal bleeding

K51.312 Ulcerative (chronic) rectosigmoiditis with intestinal obstruction

K51.313 Ulcerative (chronic) rectosigmoiditis with fistula

K51.314 Ulcerative (chronic) rectosigmoiditis with abscess

K51.318 Ulcerative (chronic) rectosigmoiditis with other complication

K51.319 Ulcerative (chronic) rectosigmoiditis with unspecified complications

K51.40 Inflammatory polyps of colon without complications

K51.411 Inflammatory polyps of colon with rectal bleeding

K51.412 Inflammatory polyps of colon with intestinal obstruction

K51.413 Inflammatory polyps of colon with fistula

K51.414 Inflammatory polyps of colon with abscess

K51.418 Inflammatory polyps of colon with other complication

K51.419 Inflammatory polyps of colon with unspecified complications

K51.50 Left sided colitis without complications

K51.511 Left sided colitis with rectal bleeding

K51.512 Left sided colitis with intestinal obstruction

K51.513 Left sided colitis with fistula

K51.514 Left sided colitis with abscess

K51.518 Left sided colitis with other complication

K51.519 Left sided colitis with unspecified complications

K51.80 Other ulcerative colitis without complications

K51.811 Other ulcerative colitis with rectal bleeding

K51.812 Other ulcerative colitis with intestinal obstruction

K51.813 Other ulcerative colitis with fistula

K51.814 Other ulcerative colitis with abscess

K51.818 Other ulcerative colitis with other complication

K51.819 Other ulcerative colitis with unspecified complications

K51.90 Ulcerative colitis, unspecified, without complications

K51.911 Ulcerative colitis, unspecified with rectal bleeding

K51.912 Ulcerative colitis, unspecified with intestinal obstruction

K51.913 Ulcerative colitis, unspecified with fistula

K51.914 Ulcerative colitis, unspecified with abscess

K51.918 Ulcerative colitis, unspecified with other complication

K51.919 Ulcerative colitis, unspecified with unspecified complications

K52.1 Toxic gastroenteritis and colitis

L40.0 Psoriasis vulgaris

L40.50 Arthropathic psoriasis, unspecified

L40.51 Distal interphalangeal psoriatic arthropathy

L40.52 Psoriatic arthritis mutilans

L40.53 Psoriatic spondylitis

L40.54 Psoriatic juvenile arthropathy

L40.59 Other psoriatic arthropathy

L73.2 Hidradenitis suppurativa

L88 Pyoderma gangrenosum

M02.30 Reiter's disease, unspecified site

M02.311 Reiter's disease, right shoulder

M02.312 Reiter's disease, left shoulder

M02.321 Reiter's disease, right elbow

M02.322 Reiter's disease, left elbow

M02.331 Reiter's disease, right wrist

M02.332 Reiter's disease, left wrist

M02.341 Reiter's disease, right hand

M02.342 Reiter's disease, left hand

M02.351 Reiter's disease, right hip

M02.352 Reiter's disease, left hip

M02.361 Reiter's disease, right knee

M02.362 Reiter's disease, left knee

M02.371 Reiter's disease, right ankle and foot

M02.372 Reiter's disease, left ankle and foot

M02.38 Reiter's disease, vertebrae

M02.39 Reiter's disease, multiple sites

M05.7A Rheumatoid arthritis with rheumatoid factor of other specified site without organ or systems involvement

M05.8A Other rheumatoid arthritis with rheumatoid factor of other specified site

M05.00 Felty's syndrome, unspecified site

M05.011 Felty's syndrome, right shoulder

M05.012 Felty's syndrome, left shoulder

M05.021 Felty's syndrome, right elbow

M05.022 Felty's syndrome, left elbow

M05.031 Felty's syndrome, right wrist

M05.032 Felty's syndrome, left wrist

M05.041 Felty's syndrome, right hand

M05.042 Felty's syndrome, left hand

M05.051 Felty's syndrome, right hip

M05.052 Felty's syndrome, left hip

M05.061 Felty's syndrome, right knee

M05.062 Felty's syndrome, left knee

M05.071 Felty's syndrome, right ankle and foot

M05.072 Felty's syndrome, left ankle and foot

M05.09 Felty's syndrome, multiple sites

M05.10 Rheumatoid lung disease with rheumatoid arthritis of unspecified site

M05.111 Rheumatoid lung disease with rheumatoid arthritis of right shoulder

M05.112 Rheumatoid lung disease with rheumatoid arthritis of left shoulder

M05.121 Rheumatoid lung disease with rheumatoid arthritis of right elbow

M05.122 Rheumatoid lung disease with rheumatoid arthritis of left elbow

M05.131 Rheumatoid lung disease with rheumatoid arthritis of right wrist

M05.132 Rheumatoid lung disease with rheumatoid arthritis of left wrist

M05.141 Rheumatoid lung disease with rheumatoid arthritis of right hand

M05.142 Rheumatoid lung disease with rheumatoid arthritis of left hand

M05.151 Rheumatoid lung disease with rheumatoid arthritis of right hip

M05.152 Rheumatoid lung disease with rheumatoid arthritis of left hip

M05.161 Rheumatoid lung disease with rheumatoid arthritis of right knee

M05.162 Rheumatoid lung disease with rheumatoid arthritis of left knee

M05.171 Rheumatoid lung disease with rheumatoid arthritis of right ankle and foot

M05.172 Rheumatoid lung disease with rheumatoid arthritis of left ankle and foot

M05.19 Rheumatoid lung disease with rheumatoid arthritis of multiple sites

M05.20 Rheumatoid vasculitis with rheumatoid arthritis of unspecified site

M05.211 Rheumatoid vasculitis with rheumatoid arthritis of right shoulder

M05.212 Rheumatoid vasculitis with rheumatoid arthritis of left shoulder

M05.221 Rheumatoid vasculitis with rheumatoid arthritis of right elbow

M05.222 Rheumatoid vasculitis with rheumatoid arthritis of left elbow

M05.231 Rheumatoid vasculitis with rheumatoid arthritis of right wrist

M05.232 Rheumatoid vasculitis with rheumatoid arthritis of left wrist

M05.241 Rheumatoid vasculitis with rheumatoid arthritis of right hand

M05.242 Rheumatoid vasculitis with rheumatoid arthritis of left hand

M05.251 Rheumatoid vasculitis with rheumatoid arthritis of right hip

M05.252 Rheumatoid vasculitis with rheumatoid arthritis of left hip

M05.261 Rheumatoid vasculitis with rheumatoid arthritis of right knee

M05.262 Rheumatoid vasculitis with rheumatoid arthritis of left knee

M05.271 Rheumatoid vasculitis with rheumatoid arthritis of right ankle and foot

M05.272 Rheumatoid vasculitis with rheumatoid arthritis of left ankle and foot

M05.29 Rheumatoid vasculitis with rheumatoid arthritis of multiple sites

M05.30 Rheumatoid heart disease with rheumatoid arthritis of unspecified site

M05.311 Rheumatoid heart disease with rheumatoid arthritis of right shoulder

M05.312 Rheumatoid heart disease with rheumatoid arthritis of left shoulder

M05.321 Rheumatoid heart disease with rheumatoid arthritis of right elbow

M05.322 Rheumatoid heart disease with rheumatoid arthritis of left elbow

M05.331 Rheumatoid heart disease with rheumatoid arthritis of right wrist
M05.332 Rheumatoid heart disease with rheumatoid arthritis of left wrist
M05.341 Rheumatoid heart disease with rheumatoid arthritis of right hand
M05.342 Rheumatoid heart disease with rheumatoid arthritis of left hand
M05.351 Rheumatoid heart disease with rheumatoid arthritis of right hip
M05.352 Rheumatoid heart disease with rheumatoid arthritis of left hip
M05.361 Rheumatoid heart disease with rheumatoid arthritis of right knee
M05.362 Rheumatoid heart disease with rheumatoid arthritis of left knee
M05.371 Rheumatoid heart disease with rheumatoid arthritis of right ankle and foot
M05.372 Rheumatoid heart disease with rheumatoid arthritis of left ankle and foot
M05.39 Rheumatoid heart disease with rheumatoid arthritis of multiple sites
M05.40 Rheumatoid myopathy with rheumatoid arthritis of unspecified site
M05.411 Rheumatoid myopathy with rheumatoid arthritis of right shoulder
M05.412 Rheumatoid myopathy with rheumatoid arthritis of left shoulder
M05.421 Rheumatoid myopathy with rheumatoid arthritis of right elbow
M05.422 Rheumatoid myopathy with rheumatoid arthritis of left elbow
M05.431 Rheumatoid myopathy with rheumatoid arthritis of right wrist
M05.432 Rheumatoid myopathy with rheumatoid arthritis of left wrist
M05.441 Rheumatoid myopathy with rheumatoid arthritis of right hand
M05.442 Rheumatoid myopathy with rheumatoid arthritis of left hand
M05.451 Rheumatoid myopathy with rheumatoid arthritis of right hip
M05.452 Rheumatoid myopathy with rheumatoid arthritis of left hip
M05.461 Rheumatoid myopathy with rheumatoid arthritis of right knee
M05.462 Rheumatoid myopathy with rheumatoid arthritis of left knee
M05.471 Rheumatoid myopathy with rheumatoid arthritis of right ankle and foot
M05.472 Rheumatoid myopathy with rheumatoid arthritis of left ankle and foot
M05.49 Rheumatoid myopathy with rheumatoid arthritis of multiple sites

M05.50 Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified site

M05.511 Rheumatoid polyneuropathy with rheumatoid arthritis of right shoulder

M05.512 Rheumatoid polyneuropathy with rheumatoid arthritis of left shoulder

M05.521 Rheumatoid polyneuropathy with rheumatoid arthritis of right elbow

M05.522 Rheumatoid polyneuropathy with rheumatoid arthritis of left elbow

M05.531 Rheumatoid polyneuropathy with rheumatoid arthritis of right wrist

M05.532 Rheumatoid polyneuropathy with rheumatoid arthritis of left wrist

M05.541 Rheumatoid polyneuropathy with rheumatoid arthritis of right hand

M05.542 Rheumatoid polyneuropathy with rheumatoid arthritis of left hand

M05.551 Rheumatoid polyneuropathy with rheumatoid arthritis of right hip

M05.552 Rheumatoid polyneuropathy with rheumatoid arthritis of left hip

M05.561 Rheumatoid polyneuropathy with rheumatoid arthritis of right knee

M05.562 Rheumatoid polyneuropathy with rheumatoid arthritis of left knee

M05.571 Rheumatoid polyneuropathy with rheumatoid arthritis of right ankle and foot

M05.572 Rheumatoid polyneuropathy with rheumatoid arthritis of left ankle and foot

M05.59 Rheumatoid polyneuropathy with rheumatoid arthritis of multiple sites

M05.60 Rheumatoid arthritis of unspecified site with involvement of other organs and systems

M05.611 Rheumatoid arthritis of right shoulder with involvement of other organs and systems

M05.612 Rheumatoid arthritis of left shoulder with involvement of other organs and systems

M05.621 Rheumatoid arthritis of right elbow with involvement of other organs and systems

M05.622 Rheumatoid arthritis of left elbow with involvement of other organs and systems

M05.631 Rheumatoid arthritis of right wrist with involvement of other organs and systems

M05.632 Rheumatoid arthritis of left wrist with involvement of other organs and systems

M05.641 Rheumatoid arthritis of right hand with involvement of other organs and systems

M05.642 Rheumatoid arthritis of left hand with involvement of other organs and systems

M05.651 Rheumatoid arthritis of right hip with involvement of other organs and systems

M05.652 Rheumatoid arthritis of left hip with involvement of other organs and systems

M05.661 Rheumatoid arthritis of right knee with involvement of other organs and systems

M05.662 Rheumatoid arthritis of left knee with involvement of other organs and systems

M05.671 Rheumatoid arthritis of right ankle and foot with involvement of other organs and systems

M05.672 Rheumatoid arthritis of left ankle and foot with involvement of other organs and systems

M05.69 Rheumatoid arthritis of multiple sites with involvement of other organs and systems

M05.70 Rheumatoid arthritis with rheumatoid factor of unspecified site without organ or systems involvement

M05.711 Rheumatoid arthritis with rheumatoid factor of right shoulder without organ or systems involvement

M05.712 Rheumatoid arthritis with rheumatoid factor of left shoulder without organ or systems involvement

M05.721 Rheumatoid arthritis with rheumatoid factor of right elbow without organ or systems involvement

M05.722 Rheumatoid arthritis with rheumatoid factor of left elbow without organ or systems involvement

M05.731 Rheumatoid arthritis with rheumatoid factor of right wrist without organ or systems involvement

M05.732 Rheumatoid arthritis with rheumatoid factor of left wrist without organ or systems involvement

M05.741 Rheumatoid arthritis with rheumatoid factor of right hand without organ or systems involvement

M05.742 Rheumatoid arthritis with rheumatoid factor of left hand without organ or systems involvement

M05.751 Rheumatoid arthritis with rheumatoid factor of right hip without organ or systems involvement

M05.752 Rheumatoid arthritis with rheumatoid factor of left hip without organ or systems involvement

M05.761 Rheumatoid arthritis with rheumatoid factor of right knee without organ or systems involvement

M05.762 Rheumatoid arthritis with rheumatoid factor of left knee without organ or systems involvement

M05.771 Rheumatoid arthritis with rheumatoid factor of right ankle and foot without organ or systems involvement

M05.772 Rheumatoid arthritis with rheumatoid factor of left ankle and foot without organ or systems involvement

M05.79 Rheumatoid arthritis with rheumatoid factor of multiple sites without organ or systems involvement

M05.80 Other rheumatoid arthritis with rheumatoid factor of unspecified site

M05.811 Other rheumatoid arthritis with rheumatoid factor of right shoulder

M05.812 Other rheumatoid arthritis with rheumatoid factor of left shoulder

M05.821 Other rheumatoid arthritis with rheumatoid factor of right elbow

M05.822 Other rheumatoid arthritis with rheumatoid factor of left elbow

M05.831 Other rheumatoid arthritis with rheumatoid factor of right wrist

M05.832 Other rheumatoid arthritis with rheumatoid factor of left wrist

M05.841 Other rheumatoid arthritis with rheumatoid factor of right hand

M05.842 Other rheumatoid arthritis with rheumatoid factor of left hand

M05.851 Other rheumatoid arthritis with rheumatoid factor of right hip

M05.852 Other rheumatoid arthritis with rheumatoid factor of left hip

M05.861 Other rheumatoid arthritis with rheumatoid factor of right knee

M05.862 Other rheumatoid arthritis with rheumatoid factor of left knee

M05.871 Other rheumatoid arthritis with rheumatoid factor of right ankle and foot

M05.872 Other rheumatoid arthritis with rheumatoid factor of left ankle and foot

M05.89 Other rheumatoid arthritis with rheumatoid factor of multiple sites

M05.9 Rheumatoid arthritis with rheumatoid factor, unspecified

M06.0A Rheumatoid arthritis without rheumatoid factor, other specified site

M06.8A Other specified rheumatoid arthritis, other specified site

M06.00 Rheumatoid arthritis without rheumatoid factor, unspecified site

M06.011 Rheumatoid arthritis without rheumatoid factor, right shoulder
M06.012 Rheumatoid arthritis without rheumatoid factor, left shoulder
M06.021 Rheumatoid arthritis without rheumatoid factor, right elbow
M06.022 Rheumatoid arthritis without rheumatoid factor, left elbow
M06.031 Rheumatoid arthritis without rheumatoid factor, right wrist
M06.032 Rheumatoid arthritis without rheumatoid factor, left wrist
M06.041 Rheumatoid arthritis without rheumatoid factor, right hand
M06.042 Rheumatoid arthritis without rheumatoid factor, left hand
M06.051 Rheumatoid arthritis without rheumatoid factor, right hip
M06.052 Rheumatoid arthritis without rheumatoid factor, left hip
M06.061 Rheumatoid arthritis without rheumatoid factor, right knee
M06.062 Rheumatoid arthritis without rheumatoid factor, left knee
M06.071 Rheumatoid arthritis without rheumatoid factor, right ankle and foot
M06.072 Rheumatoid arthritis without rheumatoid factor, left ankle and foot
M06.08 Rheumatoid arthritis without rheumatoid factor, vertebrae
M06.09 Rheumatoid arthritis without rheumatoid factor, multiple sites
M06.4 Inflammatory polyarthropathy
M06.80 Other specified rheumatoid arthritis, unspecified site
M06.811 Other specified rheumatoid arthritis, right shoulder
M06.812 Other specified rheumatoid arthritis, left shoulder
M06.821 Other specified rheumatoid arthritis, right elbow
M06.822 Other specified rheumatoid arthritis, left elbow
M06.831 Other specified rheumatoid arthritis, right wrist
M06.832 Other specified rheumatoid arthritis, left wrist
M06.841 Other specified rheumatoid arthritis, right hand
M06.842 Other specified rheumatoid arthritis, left hand
M06.851 Other specified rheumatoid arthritis, right hip

M06.852 Other specified rheumatoid arthritis, left hip

M06.861 Other specified rheumatoid arthritis, right knee

M06.862 Other specified rheumatoid arthritis, left knee

M06.871 Other specified rheumatoid arthritis, right ankle and foot

M06.872 Other specified rheumatoid arthritis, left ankle and foot

M06.88 Other specified rheumatoid arthritis, vertebrae

M06.89 Other specified rheumatoid arthritis, multiple sites

M06.9 Rheumatoid arthritis, unspecified

M07.60 Enteropathic arthropathies, unspecified site

M07.611 Enteropathic arthropathies, right shoulder

M07.612 Enteropathic arthropathies, left shoulder

M07.621 Enteropathic arthropathies, right elbow

M07.622 Enteropathic arthropathies, left elbow

M07.631 Enteropathic arthropathies, right wrist

M07.632 Enteropathic arthropathies, left wrist

M07.641 Enteropathic arthropathies, right hand

M07.642 Enteropathic arthropathies, left hand

M07.651 Enteropathic arthropathies, right hip

M07.652 Enteropathic arthropathies, left hip

M07.661 Enteropathic arthropathies, right knee

M07.662 Enteropathic arthropathies, left knee

M07.671 Enteropathic arthropathies, right ankle and foot

M07.672 Enteropathic arthropathies, left ankle and foot

M07.68 Enteropathic arthropathies, vertebrae

M07.69 Enteropathic arthropathies, multiple sites

M08.09 Unspecified juvenile rheumatoid arthritis, multiple sites

M08.1 Juvenile ankylosing spondylitis

M08.3 Juvenile rheumatoid polyarthritis (seronegative)

M08.89 Other juvenile arthritis, multiple sites

M08.99 Juvenile arthritis, unspecified, multiple sites

M35.2 Behcet's disease

M35.9 Systemic involvement of connective tissue, unspecified

M45.0 Ankylosing spondylitis of multiple sites in spine

M45.1 Ankylosing spondylitis of occipito-atlanto-axial region

M45.2 Ankylosing spondylitis of cervical region

M45.3 Ankylosing spondylitis of cervicothoracic region

M45.4 Ankylosing spondylitis of thoracic region

M45.5 Ankylosing spondylitis of thoracolumbar region

M45.6 Ankylosing spondylitis lumbar region

M45.7 Ankylosing spondylitis of lumbosacral region

M45.8 Ankylosing spondylitis sacral and sacrococcygeal region

M45.9 Ankylosing spondylitis of unspecified sites in spine

M45.A0 Non-radiographic axial spondyloarthritis of unspecified sites in spine

M45.A1 Non-radiographic axial spondyloarthritis of occipito-atlanto-axial region

M45.A2 Non-radiographic axial spondyloarthritis of cervical region

M45.A3 Non-radiographic axial spondyloarthritis of cervicothoracic region

M45.A4 Non-radiographic axial spondyloarthritis of thoracic region

M45.A5 Non-radiographic axial spondyloarthritis of thoracolumbar region

M45.A6 Non-radiographic axial spondyloarthritis of lumbar region

M45.A7 Non-radiographic axial spondyloarthritis of lumbosacral region

M45.A8 Non-radiographic axial spondyloarthritis of sacral and sacrococcygeal region

M45.AB Non-radiographic axial spondyloarthritis of multiple sites in spine

N17.0 Acute kidney failure with tubular necrosis

N17.1 Acute kidney failure with acute cortical necrosis

N17.2 Acute kidney failure with medullary necrosis

N17.8 Other acute kidney failure

N17.9 Acute kidney failure, unspecified

INFLIXIMAB AND RELATED BIOSIMILARS ARE CONSIDERED EXPERIMENTAL/INVESTIGATIONAL
WHEN REPORTED WITH THE FOLLOWING DIAGNOSIS CODE:

D89.84 IgG4-related disease

Duration of authorization: 12 months

Version Effective Date: 04/21/2025

Title: Intravenous Ketamine (Ketalar®) and Intranasal Esketamine (Spravato®)

MEDICALLY NECESSARY:

KETAMINE (KETALAR)

Ketamine (Ketalar®), administered as an intravenous (IV) infusion, is considered medically necessary and, therefore, covered for individuals aged 16 and older for **any** of the following indications:

- As the sole anesthetic agent for diagnostic and surgical procedures that do not require skeletal muscle relaxation
- For the induction of anesthesia prior to the administration of other general anesthetic agents
- As a supplement to other anesthetic agents
- As an adjuvant to opioids for management of cancer pain resistant to other analgesics in consultation with a pain or palliative care specialist

ESKETAMINE (SPRAVATO)

Initial Therapy for Esketamine (Spravato®)

Esketamine (Spravato), administered as a nasal spray, is considered medically necessary and, therefore, covered for individuals aged 18 and older with major depressive disorder (MDD) when used in conjunction with a newly initiated oral antidepressant (AD) when **all** of the following are met:

- The individual meets **all** of the following:
 - *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition text revision (DSM-5TR) criteria for MDD with either a single episode lasting greater than or equal to 2 years, or a recurrent MDD, without psychotic features
 - Severe depression as determined by a validated rating scale (e.g., Beck Depression Inventory-II [BDI-II], Montgomery-Asberg Depression Rating Scale [MADRS], Patient Health Questionnaire-9 [PHQ-9], Hamilton Rating Scale for Depression [HAM-D])
 - Inadequate response (defined as <25% improvement in the total score on the utilized depression scale) to at least two different US Food and Drug Administration (FDA)-approved drugs indicated for depression (e.g., duloxetine, escitalopram, sertraline, venlafaxine extended release) from at least two different classes (e.g., selective serotonin reuptake inhibitors [SSRIs], serotonin-norepinephrine reuptake inhibitors [SNRIs], tricyclic ADs [TCAs], FDA-approved augmentation agents) prescribed in adequate dosages for an adequate duration (defined as at least 6 weeks) with adherence at least greater than or equal to 80 percent
- The individual has **one** of the following:
 - Treatment-resistant depression (TRD)*
 - Depressive symptoms in individuals with MDD with acute suicidal ideation or behavior* who continue to receive comprehensive standard of care treatment

(e.g., inpatient psychiatric hospitalization, cognitive behavioral therapy, augmentation therapy [the addition of a second drug to an existing AD with the aim of achieving an improved clinical response]) and **without any** of the following:

- Moderate to severe substance or alcohol use disorder within 6 months prior to screening
 - Current or prior diagnosis of psychotic disorder
 - Positive urine test result(s) for phencyclidine, cocaine, or unprescribed amphetamines
- Individual is not receiving concurrent transcranial magnetic stimulation
 - Esketamine (Spravato) is prescribed by, or in consultation with, a licensed behavioral health professional provider (e.g., psychiatrist, psychiatric nurse practitioner)
 - Esketamine (Spravato) is administered under the direct supervision of a licensed healthcare professional provider and each treatment session includes **both** of the following:
 - Nasal administration of esketamine (Spravato)
 - Post-administration observation under supervision, including the monitoring of vital signs for at least 2 hours until the individual is determined to be stable enough to leave the healthcare setting

*The individual prescribed esketamine (Spravato) for TRD or MDD with acute suicidal ideation or behavior must be evaluated by the prescribing licensed behavioral health professional provider after 4 weeks of therapy to determine the need for continued treatment. The use of esketamine (Spravato) beyond 4 weeks has not been systematically evaluated in the treatment of depressive symptoms in individuals with MDD with acute suicidal ideation or behavior.

Reauthorization/Continuation Therapy for Esketamine (Spravato)

Esketamine (Spravato) is considered medically necessary and, therefore, covered for reauthorization/continuation of therapy for TRD, along with an oral AD, after 16 weeks if **one** of the following is met:

- Total scores on the utilized depression scale are improved by at least 50 percent from baseline for at least 3 of the last 4 weeks
- Total scores on the utilized depression scale are indicative of remission

LIMITATIONS OF USE FOR ESKETAMINE (SPRAVATO)

The effectiveness of esketamine (Spravato) in preventing suicide or in reducing suicidal ideation or behavior has not been demonstrated. Use of esketamine (Spravato) does not preclude the need for hospitalization if clinically warranted, even if the individual experiences improvement after an initial dose of esketamine (Spravato).

Duration of authorization: 12 months

Version Effective Date: 07/01/2024

Title: Ipilimumab (Yervoy®)

MEDICALLY NECESSARY:

INITIAL THERAPY

Ipilimumab (Yervoy) is considered medically necessary and, therefore, covered when the Dosing and Frequency Requirements listed in Attachment A and the following indications are met:

BONE CANCER

In combination with nivolumab (Opdivo) for the treatment of unresectable or metastatic chondrosarcoma, osteosarcoma, chordoma, or Ewing sarcoma that has progressed following prior treatment and who have no satisfactory alternative treatment options for tissue tumor mutation burden–high (TMB-H) tumors with 10 or more mutations per megabase.

CENTRAL NERVOUS SYSTEM CANCERS: BRAIN METASTASES

For the treatment of brain metastases in individuals with BRAF nonspecific melanoma (i.e., excluding BRAF V600E mutation), as single-agent therapy or in combination with nivolumab (Opdivo) (National Comprehensive Cancer Network [NCCN]-preferred therapy) in one of the following scenarios:

- Limited metastatic brain lesions*
 - Initial treatment in select individuals (e.g., individuals with small asymptomatic brain metastases)
 - Relapsed metastatic brain lesions and stable systemic disease or having reasonable systemic treatment options
 - Recurrent metastatic brain lesions
- Extensive metastatic brain lesions**
 - Primary treatment in select individuals (e.g., individuals with small asymptomatic brain metastases)
 - Recurrent metastatic brain lesions, and stable systemic disease or having reasonable systemic treatment options

**Limited brain metastases* defines a group of individuals for whom stereotactic radiosurgery is equally effective and offers significant cognitive protection compared with whole brain radiation therapy (RT). The definition of limited brain metastases in terms of number of metastases or total intracranial disease volume is evolving and may depend on the specific clinical situation.

***Extensive brain metastases* defines all cases that do not fit the definition of "limited brain metastases."

HEAD AND NECK CANCERS

First-line therapy for non-nasopharyngeal cancer in individuals with performance status 0-1 for one of the following scenarios:

- metastatic (M1) disease at initial presentation

- recurrent/persistent disease with distant metastases
- unresectable locoregional recurrence, unresectable second primary, or unresectable persistent disease with prior radiation therapy (RT)

HEPATOCELLULAR CARCINOMA

In combination with nivolumab (Opdivo) for the treatment of individuals with HCC who have been previously treated with sorafenib

Subsequent treatment in combination with nivolumab (Opdivo) for progressive disease in individuals who have not been previously treated with a checkpoint inhibitor (unless following atezolizumab plus bevacizumab) and have one of the following:

- Liver-confined disease, unresectable disease and are not a transplant candidate
- Extrahepatic/metastatic disease ineligible for resection, transplant, or locoregional therapy

KAPOSI SARCOMA

For individuals with classic Kaposi sarcoma in combination with nivolumab (Opdivo) as subsequent systemic therapy for relapsed/refractory advanced cutaneous, oral, visceral, or nodal disease that has progressed on or not responded to first-line systemic therapy, and progressed on alternate first-line systemic therapy.

MELANOMA, CUTANEOUS (METASTATIC OR UNRESECTABLE)

For individuals with metastatic or unresectable disease[†] that occurs in one of the following scenarios:

- As a single agent or in combination with nivolumab (Opdivo) for previously untreated or treated individuals ages 12 years and older
- Neoadjuvant systemic therapy in combination with nivolumab (Opdivo) for any of the following scenarios:
 - primary treatment for stage III disease with clinically positive, resectable nodal disease
 - Initial and/or subsequent treatment for limited resectable stage III disease with clinical satellite/in-transit metastases
 - initial and/or subsequent treatment for limited resectable local satellite/in-transit recurrence
 - treatment for resectable disease limited to nodal recurrence
- First-line therapy in combination with nivolumab (Opdivo) as a NCCN-preferred regimen (note: combination checkpoint blockade is NCCN-preferred)
- Second-line or subsequent systemic therapy option after disease progression intolerance, and/or projected risk of progression with BRAF targeted therapy for any of the following scenarios (note: systemic therapy is NCCN-preferred for unresectable or widely disseminated distant metastatic disease):
 - As a single agent (if not previously used alone or in combination with anti-PD-1 therapy)

- In combination with nivolumab (Opdivo) as an NCCN-preferred regimen if anti-PD-1 therapy was not previously used or for disease progression on single-agent anti-PD-1 therapy
- At a low dose in combination with pembrolizumab for individuals who progress on single-agent anti-PD-1 immunotherapy (NCCN-preferred regimen if not previously used alone or in combination with anti-PD-1 immunotherapy)
- Re-induction therapy as a single agent or in combination with anti-PD-1 immunotherapy, if prior use resulted in disease control (complete response, partial response, or stable disease) and no residual toxicity, and disease progression/relapse occurred greater than 3 months after treatment discontinuation.

[†]Metastatic disease includes stage III unresectable/borderline resectable disease with clinically positive nodes or clinical satellite/in-transit metastases, or as well as unresectable local satellite/in-transit recurrence, unresectable nodal recurrence, and widely disseminated distant metastatic disease.

MELANOMA, CUTANEOUS (ADJUVANT TREATMENT)

For individuals with cutaneous melanoma with pathologic involvement of regional lymph nodes of more than 1 mm who have undergone complete resection, including total lymphadenectomy as a high-dose single agent, for adjuvant treatment

As single-agent adjuvant systemic therapy option (if prior exposure to anti-PD-1 therapy)

- For local satellite/in-transit recurrence if no evidence of disease (NED) after complete excision to clear margins
- Following complete therapeutic lymph node dissection and/or complete excision of disease limited to nodal recurrence
- If NED following metastasis-directed therapy (stereotactic ablative therapy, T-VEC/ intralesional therapy or complete resection), or systemic therapy followed by resection for oligometastatic disease

Systemic therapy in combination with nivolumab (Opdivo) as an NCCN-preferred regimen if NED following metastasis-directed therapy (stereotactic ablative therapy, T-VEC/ intralesional therapy or complete resection), or systemic therapy followed by resection for oligometastatic disease

MELANOMA, UVEAL

For individuals with uveal melanoma with metastatic or unresectable disease, as single-agent therapy or in combination with nivolumab (Opdivo) (NCCN-preferred regimen).

MERKEL CELL CARCINOMA

For individuals with Merkel cell carcinoma M1 disseminated disease as single-agent therapy or in combination with nivolumab (Opdivo) if anti-PDL1 or anti-PD-1 therapy is contraindicated or there is disease progression on anti-PDL1 or anti-PD-1 monotherapy therapy.

MESOTHELIOMA: PERITONEAL

Note: includes pericardial mesothelioma and tunica vaginalis testis mesothelioma.

First-line systemic therapy, in combination with nivolumab (Opdivo) (NCCN-preferred for unresectable disease):

- Adjuvant therapy peritoneal mesothelioma (PeM) with unicavitary, epithelioid histology that is medically inoperable and/or complete cytoreduction not achievable (including high-risk features) following cytoreductive surgery (CRS) and Eastern Cooperative Oncology Group (ECOG) performance status (PS) 0–2 (note: high-risk features include Ki-67 >9%, nodal metastasis, high tumor burden [peritoneal cancer index (PCI) >17], completeness of cytoreduction [CC] score >1, biphasic disease, or bicavitary disease)
- PeM with biphasic/sarcomatoid histology or bicavitary disease and ECOG PS 0–2
- Recurrence of PeM with unicavitary, epithelioid histology after prior cytoreductive surgery (CRS) + hyperthermic intraperitoneal chemotherapy (HIPEC), if no previous adjuvant systemic therapy given and ECOG PS 0–2
- Recurrence of PeM with **biphasic/sarcomatoid histology** after prior CRS ± HIPEC for ECOG PS 0–2

Subsequent systemic therapy in combination with nivolumab (Opdivo), if chemotherapy administered first-line and ECOG PS 0–2 (NCCN-preferred).

MESOTHELIOMA: PLEURAL

For individuals with malignant pleural mesothelioma, in combination with nivolumab (Opdivo) for one of the following:

- First-line therapy of unresectable malignant pleural mesothelioma
- First-line systemic therapy (NCCN-preferred regimen):
 - Unresectable clinical stage I–IIIA disease after surgical exploration (if induction chemotherapy was not given) and epithelioid histology
 - Clinical stage I–IIIA disease and epithelioid histology who have not undergone surgical exploration (if induction chemotherapy was not given)
 - Clinical stage IIIB or IV disease, sarcomatoid, or biphasic histology, or medically inoperable tumors in individuals with PS 0–2
 - Pericardial mesothelioma and tunica vaginalis testis mesothelioma
- Subsequent systemic therapy, if chemotherapy administered first-line (as an NCCN-preferred regimen) for malignant pleural mesothelioma, including pericardial mesothelioma and tunica vaginalis testis mesothelioma

MICROSATELLITE INSTABILITY-HIGH CANCER

Ampullary adenocarcinoma

- For individuals with metastatic disease in combination with nivolumab with intestinal type disease if microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) for one of the following as first-line therapy:
 - Unresectable localized disease

- Stage IV resected ampullary cancer
 - Metastatic disease at initial presentation
- Subsequent therapy for disease progression in combination with nivolumab (Opdivo) if no prior immunotherapy and MSI-H or dMMR

Appendiceal adenocarcinoma

- For individuals with advanced or metastatic disease (dMMR/MSI-H or polymerase epsilon/delta [POLE/POLD1] mutation) in combination with nivolumab (Opdivo) if no previous treatment with immunotherapy, in individuals who are candidates for immunotherapy.

Biliary tract cancer (gallbladder cancer, intrahepatic cholangiocarcinoma, extrahepatic cholangiocarcinoma)

For individuals with biliary tract cancer refractory to standard therapy or with no standard treatment options available, in combination with nivolumab (Opdivo) as subsequent therapy for progression on or after systemic treatment for unresectable or resected gross residual (R2) disease, or metastatic disease that is tumor mutational burden-high (TMB-H) in those who have not been previously treated with a checkpoint inhibitor.

For individuals with gallbladder cancer as neoadjuvant systemic therapy in combination with nivolumab (Opdivo) for resectable locoregionally advanced disease that is tumor mutational burden-high (TMB-H) and presents as:

- incidental finding of suspicious mass during surgery where hepatobiliary surgery expertise unavailable
- incidental finding on pathologic review (cystic duct node positive)
- mass on imaging

Colorectal cancer

For individuals ages 12 years and older with metastatic colorectal cancer (mCRC), in combination with nivolumab (Opdivo) as subsequent therapy for metastatic disease (dMMR/MSI-H only) following previous oxaliplatin-, irinotecan-, and/or fluoropyrimidine-based therapy

Colon cancer

For individuals with dMMR/MSI-H only colon cancer in combination with nivolumab (Opdivo) for:

- Neoadjuvant therapy for clinical T4b disease (NCCN-preferred regimen)

For individuals with dMMR/MSI-H or polymerase epsilon/delta [POLE/POLD1] mutation colon cancer in combination with nivolumab (Opdivo) for:

- Locally unresectable or medically inoperable disease (NCCN-preferred regimen)
- Neoadjuvant therapy for resectable synchronous liver and/or lung metastases, if no previous treatment with a checkpoint inhibitor (NCCN-preferred regimen)
- Initial treatment for resectable metachronous metastases if no previous immunotherapy

Therapy in combination with nivolumab (dMMR/MSI-H or polymerase epsilon/delta [POLE/POLD1] mutation) if no prior treatment with an immunotherapy for colon cancer (note: regimens are for use in individuals who are appropriate for intensive therapy)

- Following primary treatment for locally unresectable or medically inoperable disease
- Primary treatment for synchronous abdominal/peritoneal metastases that are nonobstructing, or following local therapy for individuals with existing or imminent obstruction
- Synchronous unresectable metastases
- Treatment for unresectable metachronous metastases

Esophageal and Esophagogastric Junction Cancers

In combination with nivolumab (Opdivo) for the first-line treatment of individuals with unresectable advanced or metastatic esophageal squamous cell carcinoma (ESCC)

For individuals medically fit for surgery in combination with nivolumab (Opdivo) for adenocarcinoma with or without dMMR/MSI-H tumors that are cT2, N0 (high-risk lesions: lymphovascular invasion, ≥ 3 cm, poorly differentiated), cT1b-cT2, N+ or cT3-cT4a, Any N disease as induction systemic treatment, neoadjuvant or perioperative immunotherapy (NCCN-preferred regimen)

Palliative therapy in individuals with good PS 60% or greater [ECOG 0-2] who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease in combination with nivolumab with one of the following scenarios:

- First-line therapy for dMMR/MSI-H tumors regardless of PD-L1 status if no tumor progression while on therapy with a checkpoint inhibitor (NCCN-preferred regimen)
- First-line therapy for squamous cell carcinoma (if no prior tumor progression while on therapy with a checkpoint inhibitor)
- Subsequent therapy for dMMR/MSI-H tumors if no tumor progression while on therapy with a checkpoint inhibitor

Gastric Cancer

For individuals with dMMR/MSI-H tumors in combination with nivolumab as primary treatment with one of the following scenarios:

- Unresectable locoregional disease and are medically fit for surgery (NCCN-preferred regimen)
- Neoadjuvant or perioperative immunotherapy for potentially resectable locoregional disease (cT2 or higher, any N) and are medically fit for surgery

Systemic therapy in combination nivolumab for individuals with early-stage gastric adenocarcinoma with dMMR/MSI-H tumors (independent of PD-L1 status) with endoscopic features suggestive of deep submucosal invasion including converging folds, irregular surface pattern, and ulceration in a large gastric mass with favorable histology and completed an endoscopic resection (NCCN-preferred regimen).

First-line palliative therapy in combination with nivolumab (if no prior tumor progression while on treatment with a checkpoint inhibitor) for dMMR/MSI-H tumors in individuals who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease and good PS 60% or greater [ECOG 0–2].

Subsequent palliative therapy in combination with nivolumab (if no prior tumor progression while on treatment with a checkpoint inhibitor) for dMMR/MSI-H tumors in individuals with locoregional disease who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease and good PS 60% or greater [ECOG 0–2].

Small bowel adenocarcinoma

For individuals with advanced or metastatic disease small bowel adenocarcinoma with dMMR/MSI-H, or POLE/POLD1 mutation in combination with nivolumab (Opdivo) that occurs in either of the following scenarios:

- Initial therapy
- Initial therapy if individual received previous FOLFOX/CAPEOX in the adjuvant setting within past 12 months or contraindication
- Subsequent therapy

Rectal cancer

Therapy in combination with nivolumab (Opdivo) in individuals (dMMR/MSI-H, or POLE/POLD1 only) if candidate for immunotherapy and if no prior immunotherapy received for rectal cancer (note: regimens are for use in individuals who are appropriate for intensive therapy)

- Primary treatment for synchronous abdominal/peritoneal metastases that are nonobstructing, or following local therapy for individuals with existing or imminent obstruction
- Primary treatment for synchronous unresectable metastases
- Primary treatment for potentially resectable or unresectable isolated pelvic/anastomotic recurrence
- Primary treatment for unresectable metachronous metastases

Therapy in combination with nivolumab for individuals dMMR/MSI-H, or POLE/POLD1 only:

- Neoadjuvant treatment for resectable synchronous liver only and/or lung only metastases (NCCN preferred)
- Initial treatment for resectable metachronous metastases and no previous immunotherapy

NON-SMALL CELL LUNG CANCER

For individuals with metastatic or recurrent NSCLC, with no EGFR or ALK genomic tumor aberrations as first-line therapy in combination with nivolumab (Opdivo) and two cycles of platinum-doublet chemotherapy.

For individuals with NSCLC for one of the following conditions:

- First-line treatment for recurrent, advanced, or metastatic disease for PD-L1 expression–positive ($\geq 1\%$) tumors that are negative for actionable molecular markers[§] and no contraindications[¶] to PD-1 or PD-L1 inhibitors and PS 0–2 (regimen does not include disease with locoregional recurrence or symptomatic local disease [with the exception of mediastinal lymph node recurrence with prior RT] with no evidence of disseminated disease)

- In combination with nivolumab (Opdivo) (for PDL1 50% or greater; other recommended for PD-L1, 1%–49%)
- In combination with nivolumab (Opdivo), pemetrexed, and either carboplatin or cisplatin for nonsquamous cell histology
- In combination with nivolumab (Opdivo), paclitaxel, and carboplatin for squamous cell histology
- Treatment for recurrent, advanced, or metastatic disease (for individuals with PS 0–1 and no contraindications[¶] to PD-1 or PD-L1 inhibitors with one of the following regimens for one of the following conditions (regimen does not include disease with locoregional recurrence or symptomatic local disease [with the exception of mediastinal lymph node recurrence with prior RT] with no evidence of disseminated disease):
 - In combination with one of the following regimens:
 - Nivolumab (Opdivo)
 - Nivolumab (Opdivo), pemetrexed, and either carboplatin or cisplatin for nonsquamous cell histology
 - Nivolumab (Opdivo), paclitaxel, and carboplatin for squamous cell histology
 - For one of the following conditions:
 - Initial systemic therapy for PD-L1 <1% and negative for actionable molecular markers[§]
 - First-line therapy for EGFR exon 20 mutation–positive tumors
 - First-line therapy for KRAS G12C mutation–positive tumors
 - First-line or subsequent therapy for BRAF V600E-mutation–positive tumors
 - First-line or subsequent therapy for NTRK1/2/3 gene fusion–positive tumors
 - First-line or subsequent therapy for MET exon 14 skipping mutation–positive tumors
 - First-line or subsequent therapy for RET rearrangement–positive tumors
 - First-line therapy for ERBB2 (HER2) mutation–positive tumors
 - Subsequent therapy for EGFR exon 19 deletion or exon 21 L858R tumors and prior erlotinib ± (ramucirumab or bevacizumab), afatinib, gefitinib, osimertinib, or dacomitinib therapy
 - Subsequent therapy for EGFR S768I, L861Q, and/or G719X mutation–positive tumors and prior afatinib, osimertinib, erlotinib, gefitinib, or dacomitinib therapy
 - Subsequent therapy for ROS1 rearrangement–positive tumors and prior crizotinib, entrectinib, or ceritinib therapy
 - Subsequent therapy for ALK rearrangement positive tumors and prior crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib therapy

- Continuation maintenance therapy in combination with nivolumab (Opdivo) for recurrent, advanced, or metastatic disease for PD-L1 expression–positive ($\geq 1\%$) or PD-L1 expression $< 1\%$ tumors that are negative for actionable molecular markers[§] and no contraindications[¶] to PD-1 or PD-L1 inhibitors in individuals with PS 0–2 who achieve a response or stable disease following first-line therapy if nivolumab (Opdivo) + ipilimumab (Yervoy) $\pm$ chemotherapy given (regimen does not include disease with locoregional recurrence or symptomatic local disease [with the exception of mediastinal lymph node recurrence with prior RT] with no evidence of disseminated disease)

[§]If there is insufficient tissue to allow testing for all of EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET and RET, repeat biopsy and/or plasma testing should be done. If these are not feasible, treatment is guided by available results and, if unknown, these individuals are treated as though they do not have driver oncogenes.

[¶]Contraindications for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or current use of immunosuppressive agents, or presence of an oncogene (e.g., EGFR exon 19 deletion or L858R, ALK rearrangements), which would predict lack of benefit.

RENAL CELL CARCINOMA

For individuals with relapse or stage IV disease with clear cell histology in combination with nivolumab (Opdivo) that occurs in one of the following scenarios:

- First-line therapy and poor/intermediate risk as an NCCN-preferred regimen
- Subsequent therapy if immuno-oncology therapy naïve
- Subsequent therapy if prior history includes immuno-oncology therapy

First-line treatment of individuals with intermediate or poor risk advanced renal cell carcinoma in combination with nivolumab (Opdivo).

SOFT TISSUE SARCOMA

For individuals with advanced/metastatic if atypical lipomatous tumor/well-differentiated liposarcoma (ALT/WDLS) extremity, abdominal wall, trunk disease with disseminated metastases in combination with nivolumab (Opdivo) as subsequent palliative therapy for:

- Myxofibrosarcoma, undifferentiated pleomorphic sarcoma (UPS), dedifferentiated liposarcoma, cutaneous angiosarcoma, and undifferentiated sarcomas

OR

- proved diagnostic test)

Systemic therapy alternative in combination with nivolumab (Opdivo) for unresectable or progressive disease after initial therapy for unresectable or stage IV disease or as subsequent lines of therapy for:

- Myxofibrosarcoma, UPS, dedifferentiated liposarcoma, cutaneous angiosarcoma, and undifferentiated sarcomas

Systemic therapy in combination with nivolumab (Opdivo) for angiosarcoma.

CONTINUATION OF THERAPY

Ipilimumab (Yervoy) is considered medically necessary and, therefore, covered for continuation therapy when treatment guidelines do not specify a limited number of total doses (see Attachment A: Dosing and Frequency Requirements For Ipilimumab (Yervoy®)) and there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

Duration of authorization: 12 months

Version Effective Date: 01/06/2025

Attachment A: [Ipilimumab \(Yervoy®\)](#)

Description: Dosing and Frequency Requirements For Ipilimumab (Yervoy®)

Attachment B: [Ipilimumab \(Yervoy®\)](#)

Description: ICD-10 Diagnosis codes

Policy Attachment

Attachment to Policy # 08.01.01n

Attachment: A

Policy #: 08.01.01n

Description: Dosing and Frequency Requirements For Ipilimumab (Yervoy®)

Title: Ipilimumab (Yervoy®)

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

DOSING AND FREQUENCY REQUIREMENTS FOR IPILIMUMAB (YERVOY)

The Company reserves the right to modify the Dosing and Frequency Requirements listed in this Policy to ensure consistency with the most recently published recommendations for the use of ipilimumab (Yervoy). Changes to these guidelines are based on a consensus of information obtained from resources such as, but not limited to: the US Food and Drug Administration (FDA); Company-recognized authoritative pharmacology compendia; or published peer-reviewed clinical research. The professional provider must supply supporting documentation (i.e., published peer-reviewed literature) in order to request coverage for an amount of ipilimumab (Yervoy) outside of the Dosing and Frequency Requirements listed in this Policy. For a list of Company-recognized pharmacology compendia, view our policy on off-label coverage for prescription drugs and biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of this drug. If the member's dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider must submit those changes to the Company for a new approval based on those changes as part of the precertification process. The Company reserves the right to conduct post-payment review and audit procedures for any claims submitted for ipilimumab (Yervoy).

Indication and References	Dosing and Frequency
BONE CANCER ¹	Combination: Ipilimumab (IPI) + nivolumab (NIVO) IPI 1 mg/kg IV every 6 weeks and NIVO 240 mg IV every 2 weeks until disease progression or unacceptable toxicity or until up to 24 months of therapy has been completed
BRAIN METASTASES ¹	<u>Single:</u> <u>Induction</u> 10 mg/kg IV every 3 weeks for up to 4 doses <u>Maintenance</u> 10 mg/kg IV every 12 weeks until disease progression or unacceptable toxicity (beginning with Week 24)

	<u>Combination:</u> Ipilimumab (IPI) + nivolumab (NIVO) NIVO 1mg/kg IV and IPI 3mg/kg IV every 3 weeks for up to 4 doses; followed by NIVO 240 mg IV every 2 weeks OR NIVO 480 mg IV every 4 weeks until disease progression or unacceptable toxicity
HEAD AND NECK CANCER ¹	Combination: Ipilimumab (IPI) + nivolumab (NIVO) IPI 1 mg/kg IV every 6 weeks and NIVO 3 mg/kg every 2 weeks IV until disease progression, unacceptable toxicity or up to 2 years
ESOPHAGEAL SQUAMOUS CELL CARCINOMA (ESCC) ²	Combination: Ipilimumab (IPI)+ nivolumab (NIVO) IPI 1 mg/kg IV every 6 weeks and NIVO 3 mg/kg every 2 weeks or 360 mg every 3 weeks IV until disease progression, unacceptable toxicity or up to 2 years
GASTRIC CANCER ⁴	Combination: Ipilimumab (IPI)+ nivolumab (NIVO) IPI 1 mg/kg IV every 6 weeks for up to 4 doses administered and NIVO 240 mg IV every 2 weeks; followed by NIVO 240 mg IV every 2 weeks or NIVO 480 mg IV every 4 weeks as a single agent until disease progression or unacceptable toxicity until up to 2 years.
KAPOSI SARCOMA ¹	Combination: Ipilimumab (IPI)+ nivolumab (NIVO) IPI 1 mg/kg IV every 6 weeks and NIVO 240 mg IV every 2 weeks until disease progression or

	unacceptable toxicity for a maximum of 2 years.
HEPATOCELLULAR CARCINOMA (HCC) ^{1,2}	<u>Combination:</u> Ipilimumab (IPI)+ nivolumab (NIVO) IPI 3 mg/kg IV every 3 weeks for up to 4 doses administered on the same day as NIVO; followed by NIVO as a single agent
MALIGNANT PERITONEAL MESOTHELIOMA ¹	Combination: Ipilimumab (IPI)+ nivolumab (NIVO) IPI 1 mg/kg IV every 6 weeks until disease progression or unacceptable toxicity for a maximum of 2 years and NIVO 360 mg IV every 3 weeks or 3 mg/kg every 2 weeks until disease progression, unacceptable toxicity or up to 2 years OR IPI 1 mg/kg IV every 6 weeks for up to 4 doses and NIVO 240 mg IV every 2 weeks until disease progression, unacceptable toxicity or up to 2 years
MALIGNANT PLEURAL MESOTHELIOMA ^{1,2}	<u>Combination:</u> Ipilimumab (IPI)+ nivolumab (NIVO) First-line therapy: IPI 1 mg/kg IV every 6 weeks until disease progression or unacceptable toxicity or up to 2 years and NIVO 360 mg IV every 3 weeks or 3 mg/kg every 2 weeks until disease progression, unacceptable toxicity or up to 2 years Subsequent therapy: IPI 1 mg/kg IV every 6 weeks for up to 4 doses and NIVO 240 mg IV every 2 weeks until disease progression or unacceptable toxicity up to 2 years

MELANOMA (METASTATIC OR UNRESECTABLE)^{1,2,6}	<u>Ipilimumab as a single agent:</u> 3 mg/kg IV every 3 weeks for up to 4 doses. <u>Combination:</u> Ipilimumab (IPI)+ nivolumab (NIVO) NIVO 1 mg/kg IV and IPI 3 mg/kg IV every 3 weeks for up to 4 doses; followed by NIVO as a single agent (see prescribing information for NIVO continued dosing) OR NIVO 3 mg/kg IV and IPI 1 mg/kg IV every 3 weeks for up to 4 doses; followed by NIVO 480mg IV every 4 weeks beginning 6 weeks after last combination dose OR Ipilimumab (IPI) + pembrolizumab IPI 1 mg/kg IV and pembrolizumab 200 mg IV every 3 weeks for up to 4 doses, followed by pembrolizumab as a single agent (see prescribing information for pembrolizumab continued dosing) OR Ipilimumab (IPI) + dacarbazine Induction: IPI 10 mg/kg IV and dacarbazine 850 mg/m² IV every 3 weeks for up to 4 doses; followed by dacarbazine as a single agent through week 22 Maintenance: IPI 10 mg/kg IV every 12 weeks as a single agent until disease progression or unacceptable toxicity (beginning with Week 24)
MELANOMA (ADJUVANT TREATMENT)^{1,2}	Initial treatment for limited resectable local satellite/in-transit recurrence:

	Single: 3 mg/kg IV every 3 weeks for up to 4 doses Adjuvant treatment of cutaneous melanoma with pathologic involvement of regional lymph nodes of more than 1 mm in individuals who have undergone complete resection, including total lymphadenectomy: <u>Induction:</u> 10 mg/kg IV every 3 weeks for 4 doses <u>Maintenance:</u> 10 mg/kg IV every 12 weeks for up to 3 years Adjuvant (all other indications): Single: 3 mg/kg IV every 3 weeks for up to 4 doses, followed by 3 mg/kg every 12 weeks for up to 4 doses. Combination: Ipilimumab (IPI) + nivolumab (NIVO) IPI 3 mg/kg IV and NIVO 1mg/kg every 3 weeks for up to 4 doses, followed by NIVO 240 mg IV every 2 weeks or NIVO 480 mg IV every 4 weeks until up to 12 months.
MERKEL CELL CARCINOMA ¹	Combination: Ipilimumab (IPI)+ nivolumab (NIVO) NIVO 1 mg/kg IV and IPI 3 mg/kg IV every 3 weeks for up to 4 doses; followed by NIVO 3mg/kg IV every 2 weeks until disease progression or unacceptable toxicity OR NIVO 3 mg/kg IV and IPI 1 mg/kg IV every 3 weeks for up to 4 doses; followed by NIVO 3mg/kg IV every 2 weeks until disease progression or unacceptable toxicity OR NIVO 240mg IV every 2 weeks and IPI 1 mg/kg IV

	every 6 weeks until disease progression or unacceptable toxicity
UVEAL MELANOMA ²	<u>Single</u>: 3 mg/kg IV every 3 weeks for up to 4 doses <u>Combination</u>: Ipilimumab (IPI) + nivolumab (NIVO) NIVO 1 mg/kg IV and IPI 3 mg/kg IV every 3 weeks for up to 4 doses; followed by one of the following: NIVO 240 mg IV every 2 weeks until disease progression or unacceptable toxicity, or NIVO 480 mg IV every 4 weeks until disease progression or unacceptable toxicity.
MICROSATELLITE INSTABILITY-HIGH CANCER: ^{1,2} • AMPULLARY ADENOCARCINOMA • APPENDICEAL ADENOCARCINOMA • COLON CANCER • COLORECTAL CANCER • RECTAL CANCER	<u>Combination</u>: Ipilimumab (IPI) + nivolumab (NIVO) NIVO 3 mg/kg IV and IPI 1 mg/kg IV every 3 weeks for up to 4 doses; followed by NIVO as a single agent, until disease progression or unacceptable toxicity: NIVO 240 mg IV every 2 weeks, or NIVO 3 mg/kg IV every 2 weeks, NIVO 480 mg IV every 4 weeks
MICROSATELLITE INSTABILITY-HIGH CANCER: ¹ • BILIARY TRACT CANCER	Combination: Ipilimumab (IPI) + nivolumab (NIVO) NIVO 240 mg IV every 2 weeks followed by IPI 1 mg/kg IV every 6 weeks until disease progression, unacceptable toxicity or up to 2 years
MICROSATELLITE INSTABILITY-HIGH CANCER: ³ • Esophageal and Esophagogastric Junction Cancers	Combination: Ipilimumab (IPI) + nivolumab (NIVO) IPI 1 mg/kg IV every 6 weeks for up to 4 doses and NIVO 240 mg IV every 2 weeks; followed by one of the following: NIVO 240 mg IV every 2 weeks or 480 mg IV every 4 weeks (maximum of 2 years)

MICROSATELLITE INSTABILITY-HIGH CANCER:¹ SMALL BOWEL ADENOCARCINOMA	Combination: Ipilimumab (IPI) + nivolumab (NIVO) NIVO 3 mg/kg IV and IPI 1 mg/kg IV every 3 weeks for up to 4 doses; followed by NIVO 3 mg/kg IV or NIVO 240 mg IV every 2 weeks until disease progression or unacceptable toxicity
NON-SMALL CELL LUNG CANCER (NSCLC) ^{1,2}	<u>Combination:</u> Ipilimumab (IPI) + nivolumab (NIVO) Ipilimumab 1 mg/kg IV every 6 weeks and nivolumab 3 mg/kg IV every 2 weeks or nivolumab 360 mg IV every 3 weeks until disease progression, unacceptable toxicity, or for up to two years in individuals without disease progression. Ipilimumab (IPI) + nivolumab (NIVO) + platinum doublet chemotherapy Ipilimumab 1 mg/kg IV every 6 weeks and nivolumab 360 mg IV every 3 weeks until disease progression, unacceptable toxicity, or for up to two years in individuals without disease progression. Platinum doublet chemotherapy based on tumor histologic type every 3 weeks for two cycles OR Ipilimumab 1 mg/kg IV with nivolumab, pemetrexed, and either carboplatin or cisplatin every 6 weeks for one cycle, followed by ipilimumab 1 mg/kg IV and nivolumab every 6 weeks until disease progression, unacceptable toxicity, or for up to two years in

	individuals without disease progression. OR Ipilimumab 1 mg/kg IV with nivolumab, paclitaxel, and carboplatin every 6 weeks for one cycle, followed by ipilimumab 1 mg/kg IV and nivolumab every 6 weeks until disease progression, unacceptable toxicity, or for up to two years in individuals without disease progression.
RENAL CELL CARINCOMA, ADVANCED ²	<u>Combination:</u> Ipilimumab (IPI)+ nivolumab (NIVO) IPI 1 mg/kg IV every 3 weeks for up to 4 doses administered on the same day as NIVO 3 mg/kg; followed by NIVO 240 mg IV every 2 weeks or NIVO 480 mg IV every 4 weeks as a single agent until disease progression or unacceptable toxicity.
SOFT TISSUE SARCOMA ⁵	<u>Combination:</u> Ipilimumab (IPI)+ nivolumab (NIVO) IPI 1 mg/kg IV every 6 weeks and NIVO 240 mg IV every 2 weeks until disease progression or unacceptable toxicity.

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Version Reissued Date: N/A

Policy Attachment

Attachment to Policy # 08.01.01n

Attachment: B

Policy #: 08.01.01n

Description: ICD-10 Diagnosis codes

Title: Ipilimumab (Yervoy®)

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

Code Numbers & Narratives

C4A.0 Merkel cell carcinoma of lip

C4A.111 Merkel cell carcinoma of right upper eyelid, including canthus

C4A.112 Merkel cell carcinoma of right lower eyelid, including canthus

C4A.121 Merkel cell carcinoma of left upper eyelid, including canthus

C4A.122 Merkel cell carcinoma of left lower eyelid, including canthus

C4A.21 Merkel cell carcinoma of right ear and external auricular canal

C4A.22 Merkel cell carcinoma of left ear and external auricular canal

C4A.30 Merkel cell carcinoma of unspecified part of the face

C4A.31 Merkel cell carcinoma of nose

C4A.39 Merkel cell carcinoma of other parts of face

C4A.4 Merkel cell carcinoma of scalp and neck

C4A.51 Merkel cell carcinoma of anal skin

C4A.52 Merkel cell carcinoma of skin of breast

C4A.59 Merkel cell carcinoma of other part of trunk

C4A.61 Merkel cell carcinoma of right upper limb, including shoulder

C4A.62 Merkel cell carcinoma of left upper limb, including shoulder

C4A.71 Merkel cell carcinoma of right lower limb, including hip

C4A.72 Merkel cell carcinoma of left lower limb, including hip

C4A.8 Merkel cell carcinoma of overlapping sites

C4A.9 Merkel cell carcinoma, unspecified

C7B.1 Secondary Merkel cell carcinoma

C15.3 Malignant neoplasm of upper third of esophagus

C15.4 Malignant neoplasm of middle third of esophagus

C15.5 Malignant neoplasm of lower third of esophagus

C15.8 Malignant neoplasm of overlapping sites of esophagus

C15.9 Malignant neoplasm of esophagus, unspecified

C16.0 Malignant neoplasm of cardia

C16.1 Malignant neoplasm of fundus of stomach

C16.2 Malignant neoplasm of body of stomach

C16.3 Malignant neoplasm of pyloric antrum

C16.4 Malignant neoplasm of pylorus

C16.5 Malignant neoplasm of lesser curvature of stomach, unspecified

C16.6 Malignant neoplasm of greater curvature of stomach, unspecified

C16.8 Malignant neoplasm of overlapping sites of stomach

C16.9 Malignant neoplasm of stomach, unspecified

C17.0 Malignant neoplasm of duodenum

C17.1 Malignant neoplasm of jejunum

C17.2 Malignant neoplasm of ileum

C17.3 Meckel's diverticulum, malignant

C17.8 Malignant neoplasm of overlapping sites of small intestine

C17.9 Malignant neoplasm of small intestine, unspecified

C18.0 Malignant neoplasm of cecum

C18.1 Malignant neoplasm of appendix

C18.2 Malignant neoplasm of ascending colon

C18.3 Malignant neoplasm of hepatic flexure

C18.4 Malignant neoplasm of transverse colon

C18.5 Malignant neoplasm of splenic flexure

C18.6 Malignant neoplasm of descending colon

C18.7 Malignant neoplasm of sigmoid colon

C18.8 Malignant neoplasm of overlapping sites of colon

C18.9 Malignant neoplasm of colon, unspecified

C19 Malignant neoplasm of rectosigmoid junction

C20 Malignant neoplasm of rectum

C21.8 Malignant neoplasm of overlapping sites of rectum, anus and anal canal

C22.0 Liver cell carcinoma

C22.1 Intrahepatic bile duct carcinoma

C22.3 Angiosarcoma of liver

C22.8 Malignant neoplasm of liver, primary, unspecified as to type

C22.9 Malignant neoplasm of liver, not specified as primary or secondary

C23 Malignant neoplasm of gallbladder

C24.0 Malignant neoplasm of extrahepatic bile duct

C24.1 Malignant neoplasm of ampulla of Vater

C24.8 Malignant neoplasm of overlapping sites of biliary tract

C24.9 Malignant neoplasm of biliary tract, unspecified

C33 Malignant neoplasm of trachea

C34.01 Malignant neoplasm of right main bronchus

C34.02 Malignant neoplasm of left main bronchus

C34.11 Malignant neoplasm of upper lobe, right bronchus or lung

C34.12 Malignant neoplasm of upper lobe, left bronchus or lung

C34.2 Malignant neoplasm of middle lobe, bronchus or lung

C34.31 Malignant neoplasm of lower lobe, right bronchus or lung

C34.32 Malignant neoplasm of lower lobe, left bronchus or lung

C34.81 Malignant neoplasm of overlapping sites of right bronchus and lung

C34.82 Malignant neoplasm of overlapping sites of left bronchus and lung

C34.91 Malignant neoplasm of unspecified part of right bronchus or lung

C34.92 Malignant neoplasm of unspecified part of left bronchus or lung

C40.01 Malignant neoplasm of scapula and long bones of right upper limb

C40.02 Malignant neoplasm of scapula and long bones of left upper limb

C40.11 Malignant neoplasm of short bones of right upper limb

C40.12 Malignant neoplasm of short bones of left upper limb

C40.21 Malignant neoplasm of long bones of right lower limb

C40.22 Malignant neoplasm of long bones of left lower limb

C40.31 Malignant neoplasm of short bones of right lower limb

C40.32 Malignant neoplasm of short bones of left lower limb

C40.81 Malignant neoplasm of overlapping sites of bone and articular cartilage of right limb

C40.82 Malignant neoplasm of overlapping sites of bone and articular cartilage of left limb

C40.91 Malignant neoplasm of unspecified bones and articular cartilage of right limb

C40.92 Malignant neoplasm of unspecified bones and articular cartilage of left limb

C41.0 Malignant neoplasm of bones of skull and face

C41.1 Malignant neoplasm of mandible

C41.2 Malignant neoplasm of vertebral column

C41.3 Malignant neoplasm of ribs, sternum and clavicle

C41.4 Malignant neoplasm of pelvic bones, sacrum and coccyx

C41.9 Malignant neoplasm of bone and articular cartilage, unspecified

C43.0 Malignant melanoma of lip

C43.111 Malignant melanoma of right upper eyelid, including canthus

C43.112 Malignant melanoma of right lower eyelid, including canthus

C43.121 Malignant melanoma of left upper eyelid, including canthus

C43.122 Malignant melanoma of left lower eyelid, including canthus

C43.21 Malignant melanoma of right ear and external auricular canal

C43.22 Malignant melanoma of left ear and external auricular canal

C43.30 Malignant melanoma of unspecified part of face

C43.31 Malignant melanoma of nose

C43.39 Malignant melanoma of other parts of face

C43.4 Malignant melanoma of scalp and neck

C43.51 Malignant melanoma of anal skin

C43.52 Malignant melanoma of skin of breast

C43.59 Malignant melanoma of other part of trunk

C43.61 Malignant melanoma of right upper limb, including shoulder

C43.62 Malignant melanoma of left upper limb, including shoulder

C43.71 Malignant melanoma of right lower limb, including hip

C43.72 Malignant melanoma of left lower limb, including hip

C43.8 Malignant melanoma of overlapping sites of skin

C43.9 Malignant melanoma of skin, unspecified

C45.0 Mesothelioma of pleura

C45.1 Mesothelioma of peritoneum

C45.2 Mesothelioma of pericardium

C45.7 Mesothelioma of other sites

C45.9 Mesothelioma, unspecified

C46.0 Kaposi's sarcoma of skin

C46.1 Kaposi's sarcoma of soft tissue

C46.2 Kaposi's sarcoma of palate

C46.3 Kaposi's sarcoma of lymph nodes

C46.4 Kaposi's sarcoma of gastrointestinal sites

C46.51 Kaposi's sarcoma of right lung

C46.52 Kaposi's sarcoma of left lung

C46.7 Kaposi's sarcoma of other sites

C46.9 Kaposi's sarcoma, unspecified

C47.0 Malignant neoplasm of peripheral nerves of head, face and neck

C47.11 Malignant neoplasm of peripheral nerves of right upper limb, including shoulder

C47.12 Malignant neoplasm of peripheral nerves of left upper limb, including shoulder

C47.21 Malignant neoplasm of peripheral nerves of right lower limb, including hip

C47.22 Malignant neoplasm of peripheral nerves of left lower limb, including hip

C47.3 Malignant neoplasm of peripheral nerves of thorax

C47.4 Malignant neoplasm of peripheral nerves of abdomen

C47.5 Malignant neoplasm of peripheral nerves of pelvis

C47.6 Malignant neoplasm of peripheral nerves of trunk, unspecified

C47.8 Malignant neoplasm of overlapping sites of peripheral nerves and autonomic nervous system

C47.9 Malignant neoplasm of peripheral nerves and autonomic nervous system, unspecified

C48.0 Malignant neoplasm of retroperitoneum

C48.1 Malignant neoplasm of specified parts of peritoneum

C48.2 Malignant neoplasm of peritoneum, unspecified

C48.8 Malignant neoplasm of overlapping sites of retroperitoneum and peritoneum

C49.0 Malignant neoplasm of connective and soft tissue of head, face and neck

C49.11 Malignant neoplasm of connective and soft tissue of right upper limb, including shoulder

C49.12 Malignant neoplasm of connective and soft tissue of left upper limb, including shoulder

C49.21 Malignant neoplasm of connective and soft tissue of right lower limb, including hip

C49.22 Malignant neoplasm of connective and soft tissue of left lower limb, including hip

C49.3 Malignant neoplasm of connective and soft tissue of thorax

C49.4 Malignant neoplasm of connective and soft tissue of abdomen

C49.5 Malignant neoplasm of connective and soft tissue of pelvis

C49.6 Malignant neoplasm of connective and soft tissue of trunk, unspecified

C49.8 Malignant neoplasm of overlapping sites of connective and soft tissue

C49.9 Malignant neoplasm of connective and soft tissue, unspecified

C51.0 Malignant neoplasm of labium majus

C51.1 Malignant neoplasm of labium minus

C51.2 Malignant neoplasm of clitoris

C51.8 Malignant neoplasm of overlapping sites of vulva

C51.9 Malignant neoplasm of vulva, unspecified

C57.7 Malignant neoplasm of other specified female genital organs

C57.8 Malignant neoplasm of overlapping sites of female genital organs

C57.9 Malignant neoplasm of female genital organ, unspecified

C60.0 Malignant neoplasm of prepuce

C60.1 Malignant neoplasm of glans penis

C60.2 Malignant neoplasm of body of penis

C60.8 Malignant neoplasm of overlapping sites of penis

C60.9 Malignant neoplasm of penis, unspecified

C62.01 Malignant neoplasm of undescended right testis

C62.02 Malignant neoplasm of undescended left testis

C62.11 Malignant neoplasm of descended right testis

C62.12 Malignant neoplasm of descended left testis

C62.91 Malignant neoplasm of right testis, unspecified whether descended or undescended

C62.92 Malignant neoplasm of left testis, unspecified whether descended or undescended

C63.2 Malignant neoplasm of scrotum

C63.7 Malignant neoplasm of other specified male genital organs

C63.8 Malignant neoplasm of overlapping sites of male genital organs

C63.9 Malignant neoplasm of male genital organ, unspecified

C64.1 Malignant neoplasm of right kidney, except renal pelvis

C64.2 Malignant neoplasm of left kidney, except renal pelvis

C65.1 Malignant neoplasm of right renal pelvis

C65.2 Malignant neoplasm of left renal pelvis

C69.01 Malignant neoplasm of right conjunctiva

C69.02 Malignant neoplasm of left conjunctiva

C69.31 Malignant neoplasm of right choroid

C69.32 Malignant neoplasm of left choroid

C69.41 Malignant neoplasm of right ciliary body

C69.42 Malignant neoplasm of left ciliary body

C69.51 Malignant neoplasm of right lacrimal gland and duct

C69.52 Malignant neoplasm of left lacrimal gland and duct

C69.61 Malignant neoplasm of right orbit

C69.62 Malignant neoplasm of left orbit

C69.81 Malignant neoplasm of overlapping sites of right eye and adnexa

C69.82 Malignant neoplasm of overlapping sites of left eye and adnexa

C72.0 Malignant neoplasm of spinal cord

C72.1 Malignant neoplasm of cauda equina

C76.0 Malignant neoplasm of head, face and neck

C78.01 Secondary malignant neoplasm of right lung

C78.02 Secondary malignant neoplasm of left lung

C78.6 Secondary malignant neoplasm of retroperitoneum and peritoneum

C78.7 Secondary malignant neoplasm of liver and intrahepatic bile duct

C79.31 Secondary malignant neoplasm of brain

D19.1 Benign neoplasm of mesothelial tissue of peritoneum

D37.1 Neoplasm of uncertain behavior of stomach

D37.8 Neoplasm of uncertain behavior of other specified digestive organs

D37.9 Neoplasm of uncertain behavior of digestive organ, unspecified

Version Effective Date: 01/06/2025

Version Issued Date: 12/30/2024

Version Reissued Date: N/A

Title: Ipilimumab (Yervoy®)

MEDICALLY NECESSARY:

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DOSING AND FREQUENCY REQUIREMENTS FOR IPILIMUMAB (YERVOY)

The Company reserves the right to modify the Dosing and Frequency Requirements listed in this Policy to ensure consistency with the most recently published recommendations for the use of ipilimumab (Yervoy). Changes to these guidelines are based on a consensus of information obtained from resources such as, but not limited to: the US Food and Drug Administration (FDA); Company-recognized authoritative pharmacology compendia; or published peer-reviewed clinical research. The professional provider must supply supporting documentation (i.e., published peer-reviewed literature) in order to request coverage for an amount of ipilimumab (Yervoy) outside of the Dosing and Frequency Requirements listed in this Policy. For a list of Company-recognized pharmacology compendia, view our policy on off-label coverage for prescription drugs and biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of this drug. If the member's dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider **must** submit those changes to the Company for a new approval based on those changes as part of the precertification process. The Company reserves the right to conduct post-payment review and audit procedures for any claims submitted for ipilimumab (Yervoy).

Indication and References	Dosing and Frequency
BONE CANCER ¹	Combination: Ipilimumab (IPI) + nivolumab (NIVO) IPI 1 mg/kg IV every 6 weeks and NIVO 240 mg IV every 2 weeks until disease progression or unacceptable toxicity or until up to 24 months of therapy has been completed
BRAIN METASTASES ¹	<u>Single:</u> <u>Induction</u> 10 mg/kg IV every 3 weeks for up to 4 doses <u>Maintenance</u> 10 mg/kg IV every 12 weeks until disease progression or unacceptable toxicity (beginning with Week 24) <u>Combination:</u> Ipilimumab (IPI) + nivolumab (NIVO) NIVO 1mg/kg IV and IPI 3mg/kg IV every 3 weeks for up to 4 doses; followed by NIVO 240 mg IV every 2 weeks OR NIVO 480 mg IV every 4 weeks until disease progression or unacceptable toxicity
HEAD AND NECK CANCER ¹	Combination: Ipilimumab (IPI) + nivolumab (NIVO) IPI 1 mg/kg IV every 6 weeks and NIVO 3 mg/kg every 2 weeks IV until disease progression, unacceptable toxicity or up to 2 years
ESOPHAGEAL SQUAMOUS CELL CARCINOMA (ESCC) ²	Combination: Ipilimumab (IPI)+ nivolumab (NIVO) IPI 1 mg/kg IV every 6 weeks and NIVO 3 mg/kg every 2 weeks or 360 mg every 3 weeks IV until disease progression, unacceptable toxicity or up to 2 years
GASTRIC CANCER ⁴	Combination: Ipilimumab (IPI)+ nivolumab (NIVO) IPI 1 mg/kg IV every 6 weeks for up to 4 doses administered and NIVO 240 mg IV every 2

	weeks; followed by NIVO 240 mg IV every 2 weeks or NIVO 480 mg IV every 4 weeks as a single agent until disease progression or unacceptable toxicity until up to 2 years.
KAPOSI SARCOMA ¹	Combination: Ipilimumab (IPI)+ nivolumab (NIVO) IPI 1 mg/kg IV every 6 weeks and NIVO 240 mg IV every 2 weeks until disease progression or unacceptable toxicity for a maximum of 2 years.
HEPATOCELLULAR CARCINOMA (HCC) ^{1,2}	<u>Combination:</u> Ipilimumab (IPI)+ nivolumab (NIVO) IPI 3 mg/kg IV every 3 weeks for up to 4 doses administered on the same day as NIVO; followed by NIVO as a single agent
MALIGNANT PERITONEAL MESOTHELIOMA ¹	Combination: Ipilimumab (IPI)+ nivolumab (NIVO) IPI 1 mg/kg IV every 6 weeks until disease progression or unacceptable toxicity for a maximum of 2 years and NIVO 360 mg IV every 3 weeks or 3 mg/kg every 2 weeks until disease progression,unacceptable toxicity or up to 2 years OR IPI 1 mg/kg IV every 6 weeks for up to 4 doses and NIVO 240 mg IV every 2 weeks until disease progression,unacceptable toxicity or up to 2 years
MALIGNANT PLEURAL MESOTHELIOMA ^{1,2}	<u>Combination:</u> Ipilimumab (IPI)+ nivolumab (NIVO) First-line therapy: IPI 1 mg/kg IV every 6 weeks until disease progression or unacceptable toxicity or up to 2 years and NIVO 360 mg IV every 3 weeks or 3 mg/kg every 2 weeks until disease progression, unacceptable toxicity or up to 2 years

	Subsequent therapy: IPI 1 mg/kg IV every 6 weeks for up to 4 doses and NIVO 240 mg IV every 2 weeks until disease progression or unacceptable toxicity up to 2 years
MELANOMA (METASTATIC OR UNRESECTABLE) ^{1,2,6}	<u>Ipilimumab as a single agent:</u> 3 mg/kg IV every 3 weeks for up to 4 doses. <u>Combination:</u> Ipilimumab (IPI)+ nivolumab (NIVO) NIVO 1 mg/kg IV and IPI 3 mg/kg IV every 3 weeks for up to 4 doses; followed by NIVO as a single agent (see prescribing information for NIVO continued dosing) OR NIVO 3 mg/kg IV and IPI 1 mg/kg IV every 3 weeks for up to 4 doses; followed by NIVO 480mg IV every 4 weeks beginning 6 weeks after last combination dose OR Ipilimumab (IPI) + pembrolizumab IPI 1 mg/kg IV and pembrolizumab 200 mg IV every 3 weeks for up to 4 doses, followed by pembrolizumab as a single agent (see prescribing information for pembrolizumab continued dosing) OR Ipilimumab (IPI) + dacarbazine Induction: IPI 10 mg/kg IV and dacarbazine 850 mg/m² IV every 3 weeks for up to 4 doses; followed by dacarbazine as a single agent through week 22 Maintenance: IPI 10 mg/kg IV every 12 weeks as a single agent until disease progression or unacceptable toxicity (beginning with Week 24)

MELANOMA (ADJUVANT TREATMENT ^{1,2}	Initial treatment for limited resectable local satellite/in-transit recurrence: Single: 3 mg/kg IV every 3 weeks for up to 4 doses Adjuvant treatment of cutaneous melanoma with pathologic involvement of regional lymph nodes of more than 1 mm in individuals who have undergone complete resection, including total lymphadenectomy: <u>Induction:</u> 10 mg/kg IV every 3 weeks for 4 doses <u>Maintenance:</u> 10 mg/kg IV every 12 weeks for up to 3 years Adjuvant (all other indications): Single: 3 mg/kg IV every 3 weeks for up to 4 doses, followed by 3 mg/kg every 12 weeks for up to 4 doses. Combination: Ipilimumab (IPI) + nivolumab (NIVO) IPI 3 mg/kg IV and NIVO 1mg/kg every 3 weeks for up to 4 doses, followed by NIVO 240 mg IV every 2 weeks or NIVO 480 mg IV every 4 weeks until up to 12 months.
MERKEL CELL CARCINOMA ¹	Combination: Ipilimumab (IPI)+ nivolumab (NIVO) NIVO 1 mg/kg IV and IPI 3 mg/kg IV every 3 weeks for up to 4 doses; followed by NIVO 3mg/kg IV every 2 weeks until disease progression or unacceptable toxicity OR NIVO 3 mg/kg IV and IPI 1 mg/kg IV every 3 weeks for up to 4 doses; followed by NIVO 3mg/kg IV every 2 weeks until disease progression or unacceptable toxicity OR NIVO 240mg IV every 2 weeks and IPI 1 mg/kg IV every 6 weeks until disease progression or unacceptable toxicity

UVEAL MELANOMA ²	<u>Single</u>: 3 mg/kg IV every 3 weeks for up to 4 doses <u>Combination</u>: Ipilimumab (IPI) + nivolumab (NIVO) NIVO 1 mg/kg IV and IPI 3 mg/kg IV every 3 weeks for up to 4 doses; followed by one of the following: NIVO 240 mg IV every 2 weeks until disease progression or unacceptable toxicity, or NIVO 480 mg IV every 4 weeks until disease progression or unacceptable toxicity.
MICROSATELLITE INSTABILITY-HIGH CANCER: ^{1,2} • AMPULLARY ADENOCARCINOMA • APPENDICEAL ADENOCARCINOMA • COLON CANCER • COLORECTAL CANCER • RECTAL CANCER	<u>Combination</u>: Ipilimumab (IPI) + nivolumab (NIVO) NIVO 3 mg/kg IV and IPI 1 mg/kg IV every 3 weeks for up to 4 doses; followed by NIVO as a single agent, until disease progression or unacceptable toxicity: NIVO 240 mg IV every 2 weeks, or NIVO 3 mg/kg IV every 2 weeks, NIVO 480 mg IV every 4 weeks
MICROSATELLITE INSTABILITY-HIGH CANCER: ¹ • BILIARY TRACT CANCER	Combination: Ipilimumab (IPI) + nivolumab (NIVO) NIVO 240 mg IV every 2 weeks followed by IPI 1 mg/kg IV every 6 weeks until disease progression, unacceptable toxicity or up to 2 years
	Combination: Ipilimumab (IPI) + nivolumab (NIVO) IPI 1 mg/kg IV every 6 weeks for up to 4 doses and NIVO 240 mg IV every 2 weeks; followed by one of the following: NIVO 240 mg IV every 2 weeks or 480 mg IV every 4 weeks (maximum of 2 years)
MICROSATELLITE INSTABILITY-HIGH CANCER: ¹ • SMALL BOWEL ADENOCARCINOMA	Combination: Ipilimumab (IPI) + nivolumab (NIVO) NIVO 3 mg/kg IV and IPI 1 mg/kg IV every 3 weeks

	for up to 4 doses; followed by NIVO 3 mg/kg IV or NIVO 240 mg IV every 2 weeks until disease progression or unacceptable toxicity
NON-SMALL CELL LUNG CANCER (NSCLC) ^{1,2}	<u>Combination:</u> Ipilimumab (IPI) + nivolumab (NIVO) Ipilimumab 1 mg/kg IV every 6 weeks and nivolumab 3 mg/kg IV every 2 weeks or nivolumab 360 mg IV every 3 weeks until disease progression, unacceptable toxicity, or for up to two years in individuals without disease progression. Ipilimumab (IPI) + nivolumab (NIVO) + platinum doublet chemotherapy Ipilimumab 1 mg/kg IV every 6 weeks and nivolumab 360 mg IV every 3 weeks until disease progression, unacceptable toxicity, or for up to two years in individuals without disease progression. Platinum doublet chemotherapy based on tumor histologic type every 3 weeks for two cycles OR Ipilimumab 1 mg/kg IV with nivolumab, pemetrexed, and either carboplatin or cisplatin every 6 weeks for one cycle, followed by ipilimumab 1 mg/kg IV and nivolumab every 6 weeks until disease progression, unacceptable toxicity, or for up to two years in individuals without disease progression. OR Ipilimumab 1 mg/kg IV with nivolumab, paclitaxel, and carboplatin every 6 weeks for one cycle, followed by ipilimumab 1 mg/kg IV and nivolumab every 6 weeks until disease progression, unacceptable toxicity, or for up to two years in individuals without disease

	progression.
RENAL CELL CARINCOMA, ADVANCED ²	<u>Combination:</u> Ipilimumab (IPI)+ nivolumab (NIVO) IPI 1 mg/kg IV every 3 weeks for up to 4 doses administered on the same day as NIVO 3 mg/kg; followed by NIVO 240 mg IV every 2 weeks or NIVO 480 mg IV every 4 weeks as a single agent until disease progression or unacceptable toxicity.
SOFT TISSUE SARCOMA ⁵	<u>Combination:</u> Ipilimumab (IPI)+ nivolumab (NIVO) IPI 1 mg/kg IV every 6 weeks and NIVO 240 mg IV every 2 weeks until disease progression or unacceptable toxicity.

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Duration of authorization: 12 months

Version Effective Date: 01/06/2025

Title: Ipilimumab (Yervoy®)

MEDICALLY NECESSARY:

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C4A.122 Merkel cell carcinoma of left lower eyelid, including canthus

C4A.21 Merkel cell carcinoma of right ear and external auricular canal

C4A.22 Merkel cell carcinoma of left ear and external auricular canal

C4A.30 Merkel cell carcinoma of unspecified part of the face

C4A.31 Merkel cell carcinoma of nose

C4A.39 Merkel cell carcinoma of other parts of face

C4A.4 Merkel cell carcinoma of scalp and neck

C4A.51 Merkel cell carcinoma of anal skin

C4A.52 Merkel cell carcinoma of skin of breast

C4A.59 Merkel cell carcinoma of other part of trunk

C4A.61 Merkel cell carcinoma of right upper limb, including shoulder

C4A.62 Merkel cell carcinoma of left upper limb, including shoulder

C4A.71 Merkel cell carcinoma of right lower limb, including hip

C4A.72 Merkel cell carcinoma of left lower limb, including hip

C4A.8 Merkel cell carcinoma of overlapping sites

C4A.9 Merkel cell carcinoma, unspecified

C7B.1 Secondary Merkel cell carcinoma

C15.3 Malignant neoplasm of upper third of esophagus

C15.4 Malignant neoplasm of middle third of esophagus

C15.5 Malignant neoplasm of lower third of esophagus

C15.8 Malignant neoplasm of overlapping sites of esophagus

C15.9 Malignant neoplasm of esophagus, unspecified

C16.0 Malignant neoplasm of cardia

C16.1 Malignant neoplasm of fundus of stomach

C16.2 Malignant neoplasm of body of stomach

C16.3 Malignant neoplasm of pyloric antrum

C16.4 Malignant neoplasm of pylorus

C16.5 Malignant neoplasm of lesser curvature of stomach, unspecified

C16.6 Malignant neoplasm of greater curvature of stomach, unspecified

C16.8 Malignant neoplasm of overlapping sites of stomach

C16.9 Malignant neoplasm of stomach, unspecified

C17.0 Malignant neoplasm of duodenum

C17.1 Malignant neoplasm of jejunum

C17.2 Malignant neoplasm of ileum

C17.3 Meckel's diverticulum, malignant

C17.8 Malignant neoplasm of overlapping sites of small intestine

C17.9 Malignant neoplasm of small intestine, unspecified

C18.0 Malignant neoplasm of cecum

C18.1 Malignant neoplasm of appendix

C18.2 Malignant neoplasm of ascending colon

C18.3 Malignant neoplasm of hepatic flexure

C18.4 Malignant neoplasm of transverse colon

C18.5 Malignant neoplasm of splenic flexure

C18.6 Malignant neoplasm of descending colon

C18.7 Malignant neoplasm of sigmoid colon

C18.8 Malignant neoplasm of overlapping sites of colon

C18.9 Malignant neoplasm of colon, unspecified

C19 Malignant neoplasm of rectosigmoid junction

C20 Malignant neoplasm of rectum

C21.8 Malignant neoplasm of overlapping sites of rectum, anus and anal canal

C22.0 Liver cell carcinoma

C22.1 Intrahepatic bile duct carcinoma

C22.3 Angiosarcoma of liver

C22.8 Malignant neoplasm of liver, primary, unspecified as to type

C22.9 Malignant neoplasm of liver, not specified as primary or secondary

C23 Malignant neoplasm of gallbladder

C24.0 Malignant neoplasm of extrahepatic bile duct

C24.1 Malignant neoplasm of ampulla of Vater

C24.8 Malignant neoplasm of overlapping sites of biliary tract

C24.9 Malignant neoplasm of biliary tract, unspecified

C33 Malignant neoplasm of trachea

C34.01 Malignant neoplasm of right main bronchus

C34.02 Malignant neoplasm of left main bronchus

C34.11 Malignant neoplasm of upper lobe, right bronchus or lung

C34.12 Malignant neoplasm of upper lobe, left bronchus or lung

C34.2 Malignant neoplasm of middle lobe, bronchus or lung

C34.31 Malignant neoplasm of lower lobe, right bronchus or lung

C34.32 Malignant neoplasm of lower lobe, left bronchus or lung

C34.81 Malignant neoplasm of overlapping sites of right bronchus and lung

C34.82 Malignant neoplasm of overlapping sites of left bronchus and lung

C34.91 Malignant neoplasm of unspecified part of right bronchus or lung

C34.92 Malignant neoplasm of unspecified part of left bronchus or lung

C40.01 Malignant neoplasm of scapula and long bones of right upper limb

C40.02 Malignant neoplasm of scapula and long bones of left upper limb

C40.11 Malignant neoplasm of short bones of right upper limb

C40.12 Malignant neoplasm of short bones of left upper limb

C40.21 Malignant neoplasm of long bones of right lower limb

C40.22 Malignant neoplasm of long bones of left lower limb

C40.31 Malignant neoplasm of short bones of right lower limb

C40.32 Malignant neoplasm of short bones of left lower limb

C40.81 Malignant neoplasm of overlapping sites of bone and articular cartilage of right limb

C40.82 Malignant neoplasm of overlapping sites of bone and articular cartilage of left limb

C40.91 Malignant neoplasm of unspecified bones and articular cartilage of right limb

C40.92 Malignant neoplasm of unspecified bones and articular cartilage of left limb

C41.0 Malignant neoplasm of bones of skull and face

C41.1 Malignant neoplasm of mandible

C41.2 Malignant neoplasm of vertebral column

C41.3 Malignant neoplasm of ribs, sternum and clavicle

C41.4 Malignant neoplasm of pelvic bones, sacrum and coccyx

C41.9 Malignant neoplasm of bone and articular cartilage, unspecified

C43.0 Malignant melanoma of lip

C43.111 Malignant melanoma of right upper eyelid, including canthus

C43.112 Malignant melanoma of right lower eyelid, including canthus
C43.121 Malignant melanoma of left upper eyelid, including canthus
C43.122 Malignant melanoma of left lower eyelid, including canthus
C43.21 Malignant melanoma of right ear and external auricular canal
C43.22 Malignant melanoma of left ear and external auricular canal
C43.30 Malignant melanoma of unspecified part of face
C43.31 Malignant melanoma of nose
C43.39 Malignant melanoma of other parts of face
C43.4 Malignant melanoma of scalp and neck
C43.51 Malignant melanoma of anal skin
C43.52 Malignant melanoma of skin of breast
C43.59 Malignant melanoma of other part of trunk
C43.61 Malignant melanoma of right upper limb, including shoulder
C43.62 Malignant melanoma of left upper limb, including shoulder
C43.71 Malignant melanoma of right lower limb, including hip
C43.72 Malignant melanoma of left lower limb, including hip
C43.8 Malignant melanoma of overlapping sites of skin
C43.9 Malignant melanoma of skin, unspecified
C45.0 Mesothelioma of pleura
C45.1 Mesothelioma of peritoneum
C45.2 Mesothelioma of pericardium
C45.7 Mesothelioma of other sites
C45.9 Mesothelioma, unspecified
C46.0 Kaposi's sarcoma of skin
C46.1 Kaposi's sarcoma of soft tissue
C46.2 Kaposi's sarcoma of palate
C46.3 Kaposi's sarcoma of lymph nodes

C46.4 Kaposi's sarcoma of gastrointestinal sites

C46.51 Kaposi's sarcoma of right lung

C46.52 Kaposi's sarcoma of left lung

C46.7 Kaposi's sarcoma of other sites

C46.9 Kaposi's sarcoma, unspecified

C47.0 Malignant neoplasm of peripheral nerves of head, face and neck

C47.11 Malignant neoplasm of peripheral nerves of right upper limb, including shoulder

C47.12 Malignant neoplasm of peripheral nerves of left upper limb, including shoulder

C47.21 Malignant neoplasm of peripheral nerves of right lower limb, including hip

C47.22 Malignant neoplasm of peripheral nerves of left lower limb, including hip

C47.3 Malignant neoplasm of peripheral nerves of thorax

C47.4 Malignant neoplasm of peripheral nerves of abdomen

C47.5 Malignant neoplasm of peripheral nerves of pelvis

C47.6 Malignant neoplasm of peripheral nerves of trunk, unspecified

C47.8 Malignant neoplasm of overlapping sites of peripheral nerves and autonomic nervous system

C47.9 Malignant neoplasm of peripheral nerves and autonomic nervous system, unspecified

C48.0 Malignant neoplasm of retroperitoneum

C48.1 Malignant neoplasm of specified parts of peritoneum

C48.2 Malignant neoplasm of peritoneum, unspecified

C48.8 Malignant neoplasm of overlapping sites of retroperitoneum and peritoneum

C49.0 Malignant neoplasm of connective and soft tissue of head, face and neck

C49.11 Malignant neoplasm of connective and soft tissue of right upper limb, including shoulder

C49.12 Malignant neoplasm of connective and soft tissue of left upper limb, including shoulder

C49.21 Malignant neoplasm of connective and soft tissue of right lower limb, including hip

C49.22 Malignant neoplasm of connective and soft tissue of left lower limb, including hip

C49.3 Malignant neoplasm of connective and soft tissue of thorax

C49.4 Malignant neoplasm of connective and soft tissue of abdomen

C49.5 Malignant neoplasm of connective and soft tissue of pelvis

C49.6 Malignant neoplasm of connective and soft tissue of trunk, unspecified

C49.8 Malignant neoplasm of overlapping sites of connective and soft tissue

C49.9 Malignant neoplasm of connective and soft tissue, unspecified

C51.0 Malignant neoplasm of labium majus

C51.1 Malignant neoplasm of labium minus

C51.2 Malignant neoplasm of clitoris

C51.8 Malignant neoplasm of overlapping sites of vulva

C51.9 Malignant neoplasm of vulva, unspecified

C57.7 Malignant neoplasm of other specified female genital organs

C57.8 Malignant neoplasm of overlapping sites of female genital organs

C57.9 Malignant neoplasm of female genital organ, unspecified

C60.0 Malignant neoplasm of prepuce

C60.1 Malignant neoplasm of glans penis

C60.2 Malignant neoplasm of body of penis

C60.8 Malignant neoplasm of overlapping sites of penis

C60.9 Malignant neoplasm of penis, unspecified

C62.01 Malignant neoplasm of undescended right testis

C62.02 Malignant neoplasm of undescended left testis

C62.11 Malignant neoplasm of descended right testis

C62.12 Malignant neoplasm of descended left testis

C62.91 Malignant neoplasm of right testis, unspecified whether descended or undescended

C62.92 Malignant neoplasm of left testis, unspecified whether descended or undescended

C63.2 Malignant neoplasm of scrotum

C63.7 Malignant neoplasm of other specified male genital organs

C63.8 Malignant neoplasm of overlapping sites of male genital organs

C63.9 Malignant neoplasm of male genital organ, unspecified

C64.1 Malignant neoplasm of right kidney, except renal pelvis

C64.2 Malignant neoplasm of left kidney, except renal pelvis

C65.1 Malignant neoplasm of right renal pelvis

C65.2 Malignant neoplasm of left renal pelvis

C69.01 Malignant neoplasm of right conjunctiva

C69.02 Malignant neoplasm of left conjunctiva

C69.31 Malignant neoplasm of right choroid

C69.32 Malignant neoplasm of left choroid

C69.41 Malignant neoplasm of right ciliary body

C69.42 Malignant neoplasm of left ciliary body

C69.51 Malignant neoplasm of right lacrimal gland and duct

C69.52 Malignant neoplasm of left lacrimal gland and duct

C69.61 Malignant neoplasm of right orbit

C69.62 Malignant neoplasm of left orbit

C69.81 Malignant neoplasm of overlapping sites of right eye and adnexa

C69.82 Malignant neoplasm of overlapping sites of left eye and adnexa

C72.0 Malignant neoplasm of spinal cord

C72.1 Malignant neoplasm of cauda equina

C76.0 Malignant neoplasm of head, face and neck

C78.01 Secondary malignant neoplasm of right lung

C78.02 Secondary malignant neoplasm of left lung

C78.6 Secondary malignant neoplasm of retroperitoneum and peritoneum

C78.7 Secondary malignant neoplasm of liver and intrahepatic bile duct

C79.31 Secondary malignant neoplasm of brain

D19.1 Benign neoplasm of mesothelial tissue of peritoneum

D37.1 Neoplasm of uncertain behavior of stomach

D37.8 Neoplasm of uncertain behavior of other specified digestive organs

D37.9 Neoplasm of uncertain behavior of digestive organ, unspecified

Duration of authorization: 12 months

Version Effective Date: 01/06/2025

Title: Isatuximab-irfc (Sarclisa®)

MEDICALLY NECESSARY:

Isatuximab-irfc (Sarclisa) is considered medically necessary and, therefore, covered for the treatment of multiple myeloma in adult individuals when any of the following criteria are met:

Primary therapy for symptomatic multiple myeloma in combination with bortezomib, lenalidomide, and dexamethasone, when any of the following criteria are met:

- candidates for autologous stem cell transplant (ASCT)
- **non-ASCT candidates** (NOTE: Use in individuals <80 years of age who are not frail is an National Comprehensive Cancer Network [NCCN]-preferred regimen)

Primary therapy for symptomatic multiple myeloma in combination with carfilzomib, lenalidomide, and dexamethasone in transplant candidates

Refractory, relapsed, or progressive multiple myeloma when administered in combination with either of the following regimens:

- In combination with pomalidomide (Pomalyst) and dexamethasone, after receiving at least two prior therapies including lenalidomide (Revlimid) and a proteasome inhibitor (e.g., bortezomib [Velcade], carfilzomib [Kyprolis], ixazomib [Ninlaro]). (NOTE: NCCN-preferred regimen when individual is refractory to lenalidomide or bortezomib.)
- In combination with carfilzomib and dexamethasone, after receiving one to three prior lines of therapy (NOTE: NCCN-preferred regimen when individual is refractory to lenalidomide or bortezomib)

Duration of authorization: 12 months

Version Effective Date: 03/24/2025

Title: Lanreotide (Somatuline® Depot)

MEDICALLY NECESSARY

Lanreotide (Somatuline® Depot) is considered medically necessary and, therefore, covered in individuals with any of the following indications when the corresponding criteria are met:

ACROMEGALY

- For the long-term treatment of individuals with acromegaly who have had an inadequate response to surgery and/or radiotherapy, or for whom surgery and/or radiotherapy is not an option.

NEUROENDOCRINE AND ADRENAL TUMORS

Gastroenteropancreatic Neuroendocrine Tumors (GEP-NETs)

- For the treatment of unresectable, well- or moderately differentiated, locally advanced or metastatic gastroenteropancreatic neuroendocrine tumors (GEP-NETs) to improve progression-free survival.

Neuroendocrine Tumors of the Gastrointestinal Tract (Well-Differentiated Grade 1/2), Lung and Thymus (Carcinoid Tumors)

- For the treatment of adult individuals with carcinoid syndrome to reduce the frequency of short-acting somatostatin analog rescue therapy.
- For the treatment of neuroendocrine tumors of the gastrointestinal tract, lung, and thymus (carcinoid tumors) for any of the following indications:
 - Primary treatment for symptom and/or tumor control of unresected primary gastrinoma
 - As primary therapy for symptom and/or tumor control of multiple lung nodules or tumorlets and evidence of diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH) if chronic cough/dyspnea is not responsive to inhalers or conventional treatment

- For symptom and/or tumor control of recurrent, locoregional advanced disease and/or distant metastases* of the gastrointestinal tract as a single agent for any of the following:
 - For unresectable and a low tumor burden
 - For disease progression (if not already receiving) following resection of primary + metastases
 - For disease progression (if not already receiving) following observation for unresectable low tumor burden
 - Following resection of primary tumor if unresectable and locally symptomatic from primary tumor
 - As a single agent or in combination with alternative front-line therapy if unresectable and clinically significant tumor burden
 - As subsequent therapy at above label dosing after clinical, symptomatic, or radiographic progression (if somatostatin receptor-positive [SSTR-positive]) on standard doses (useful in certain circumstances)
- For symptom and/or tumor control of recurrent and/or locoregional unresectable bronchopulmonary/thymic disease* if SSTR-positive and/or hormonal symptoms for one of the following regimens:
 - As primary therapy
 - As subsequent therapy (as alternate primary therapy) if progression on primary therapy
- For symptom and/or tumor control of recurrent and/or distant metastatic bronchopulmonary/thymic disease* if SSTR-positive and/or hormonal symptoms for one of the following regimens:
 - As primary therapy
 - As subsequent therapy (as alternate primary therapy) if progression on primary therapy
- For symptom and/or tumor control of recurrent and/or distant metastatic bronchopulmonary/thymic disease* if SSTR-positive and/or hormonal symptoms for one of the following regimens:
 - As primary therapy (National Comprehensive Cancer Network [NCCN] preferred if clinically significant tumor burden and low grade [typical carcinoid], evidence of disease progression, intermediate grade [atypical carcinoid], or symptomatic)

- As subsequent therapy (as alternate primary therapy) if progression on primary therapy if clinically significant tumor burden and low grade (typical carcinoid), evidence of disease progression, intermediate grade (atypical carcinoid), or symptomatic (NCCN preferred)
- Treatment of carcinoid syndrome for any of the following regimens:
 - As a single agent
 - In combination with telotristat for persistent diarrhea due to poorly controlled carcinoid syndrome
 - In combination with other systemic therapy options (based on disease site) with or without telotristat for persistent symptoms (i.e., flushing, diarrhea) due to poorly controlled carcinoid syndrome

Neuroendocrine and Adrenal Tumors - Well-Differentiated Grade 3 Neuroendocrine Tumors

- For the treatment and/or tumor control of SSTR-positive (if SSTR-positive and/or hormonal symptoms) for unresectable locally advanced/metastatic disease with favorable biology (e.g., relatively low Ki-67 [$<55\%$], slow growing, positive SSR-based PET imaging) at standard dose

Tumors of the Pancreas (Well-Differentiated Grade 1/2)

- Management of symptoms and/or tumor control of locoregional disease with any of the following indications:
 - Gastrinoma (usually duodenal or head of the pancreas)
 - Glucagonoma (usually tail)
 - VIPoma
- As NCCN-preferred regimen for symptom and/or tumor control* in individuals** with recurrent or locoregional advanced disease and/or distant metastatic disease if SSTR-positive with any of the following indications:
 - As a single agent for asymptomatic, low tumor burden and stable disease
 - As a single agent for symptomatic, clinically significant tumor burden, or clinically significant progression (if not already receiving)

- In combination with alternative front-line therapy for symptomatic, clinically significant tumor burden, or clinically significant progression
- For symptom and/or tumor control as subsequent therapy at above label dosing after clinical, symptomatic or radiographic progression on standard doses (if SSTR-positive)

Pheochromocytoma/Paraganglioma

- As primary treatment for secreting tumors for hormone excess and symptom control of locally unresectable disease or distant metastases (if SSTR-positive)

NCCN note: *If clinically significant disease progression, treatment with lanreotide should be discontinued for nonfunctional tumors and continued in individuals with functional tumors and may be used in combination with any of the subsequent options.

NCCN note: ** For individuals with insulinoma, lanreotide should be used only if SSTR-based imaging is positive.

Duration of authorization: 12 months

Version Effective Date: 10/01/2024

Attachment A: [Lanreotide \(Somatuline® Depot\)](#)

Description: ICD-10 CODES AND NARRATIVES

Policy Attachment

Attachment to Policy # 08.01.40g

Attachment: A

Policy #: 08.01.40g

Description: ICD-10 CODES AND NARRATIVES

Title: Lanreotide (Somatuline® Depot)

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

ICD-10 CODES AND NARRATIVES

C25.0 Malignant neoplasm of head of pancreas
C25.1 Malignant neoplasm of body of pancreas
C25.2 Malignant neoplasm of tail of pancreas
C25.3 Malignant neoplasm of body of pancreatic duct
C25.4 Malignant neoplasm of endocrine pancreas
C25.7 Malignant neoplasm of other parts of pancreas
C25.8 Malignant neoplasm of overlapping sites pancreas
C25.9 Malignant neoplasm of pancreas, unspecified
C26.0 Malignant neoplasm of intestinal tract, part unspecified
C26.9 Malignant neoplasm of ill-defined sites within the digestive system
C7A.00 Malignant carcinoid tumor of unspecified site
C7A.010 Malignant carcinoid tumor of the duodenum
C7A.011 Malignant carcinoid tumor of the jejunum
C7A.012 Malignant carcinoid tumor of the ileum
C7A.019 Malignant carcinoid tumor of the small intestine, unspecified portion
C7A.020 Malignant carcinoid tumor of the appendix
C7A.021 Malignant carcinoid tumor of the cecum
C7A.022 Malignant carcinoid tumor of the ascending colon
C7A.023 Malignant carcinoid tumor of the transverse colon
C7A.024 Malignant carcinoid tumor of the descending colon
C7A.025 Malignant carcinoid tumor of the sigmoid colon
C7A.026 Malignant carcinoid tumor of the rectum
C7A.029 Malignant carcinoid tumor of the large intestine, unspecified portion
C7A.090 Malignant carcinoid tumor of the bronchus and lung
C7A.091 Malignant carcinoid tumor of the thymus
C7A.092 Malignant carcinoid tumor of the stomach
C7A.094 Malignant carcinoid tumor of the foregut, unspecified

C7A.095 Malignant carcinoid tumor of the midgut, unspecified
C7A.096 Malignant carcinoid tumor of the hindgut, unspecified
C7A.098 Malignant carcinoid tumors of other sites
C7A.1 Malignant poorly differentiated neuroendocrine tumors
C7A.8 Other malignant neuroendocrine tumors
C7B.00 Secondary carcinoid tumors, unspecified site
C7B.01 Secondary carcinoid tumors of distant lymph nodes
C7B.02 Secondary carcinoid tumors of liver
C7B.03 Secondary carcinoid tumors of bone
C7B.04 Secondary carcinoid tumors of peritoneum
C7B.09 Secondary carcinoid tumors of other sites
C7B.8 Other secondary neuroendocrine tumors
C74.10 Malignant neoplasm of medulla of unspecified adrenal gland
C74.11 Malignant neoplasm of medulla of right adrenal gland
C74.12 Malignant neoplasm of medulla of left adrenal gland

C74.90 Malignant neoplasm of unspecified part of unspecified adrenal gland
C74.91 Malignant neoplasm of unspecified part of right adrenal gland
C74.92 Malignant neoplasm of unspecified part of left adrenal gland

C75.5 Malignant neoplasm of aortic body and other paraganglia
D13.7 Benign neoplasm of endocrine pancreas

D37.8 Neoplasm of uncertain behavior of other specified digestive organs
D3A.00 Benign carcinoid tumor of unspecified site
D3A.010 Benign carcinoid tumor of the duodenum
D3A.011 Benign carcinoid tumor of the jejunum
D3A.012 Benign carcinoid tumor of the ileum
D3A.019 Benign carcinoid tumor of the small intestine, unspecified portion
D3A.020 Benign carcinoid tumor of the appendix
D3A.021 Benign carcinoid tumor of the cecum
D3A.022 Benign carcinoid tumor of the ascending colon
D3A.023 Benign carcinoid tumor of the transverse colon
D3A.024 Benign carcinoid tumor of the descending colon
D3A.025 Benign carcinoid tumor of the sigmoid colon
D3A.026 Benign carcinoid tumor of the rectum
D3A.029 Benign carcinoid tumor of the large intestine, unspecified portion
D3A.090 Benign carcinoid tumor of the bronchus and lung
D3A.091 Benign carcinoid tumor of the thymus
D3A.092 Benign carcinoid tumor of the stomach
D3A.094 Benign carcinoid tumor of the foregut, unspecified

D3A.095 Benign carcinoid tumor of the midgut, unspecified
D3A.096 Benign carcinoid tumor of the hindgut, unspecified
D3A.098 Benign carcinoid tumors of other sites
D3A.8 Other benign neuroendocrine tumors
D49.0 Neoplasm of unspecified behavior of digestive system

E16.1 Other hypoglycemia
E16.3 Increased secretion of glucagon
E16.4 Increased secretion of gastrin
E16.8 Other specified disorders of pancreatic internal secretion
E22.0 Acromegaly and pituitary gigantism

E22.2 Syndrome of inappropriate secretion of antidiuretic hormone
E34.00 Carcinoid syndrome, unspecified

E34.01 Carcinoid heart syndrome

E34.09 Other carcinoid syndrome

Version Effective Date: 10/01/2024

Version Issued Date: 10/01/2024

Version Reissued Date: N/A

Title: Leuprolide Acetate (Camcevi™, Eligard®, Fensolvi®, Lupron Depot®)

MEDICALLY NECESSARY

COMPANY-DESIGNATED PREFERRED PRODUCTS

Although there are many leuprolide products on the market (e.g., Camcevi, Eligard, Lupron Depot), there is no reliable evidence of the superiority of any one product of leuprolide compared with other products. Although Lupron Depot (leuprolide acetate) and Camcevi (leuprolide mesylate) have been approved by the U.S. Food and Drug Administration (FDA) for prostate cancer, and Company-recognized Drug Compendia support the use of these for certain cancers, leuprolide acetate (Eligard and Lupron Depot 7.5 mg, represented by Healthcare Common Procedure Coding System [HCPCS] J9217) are considered to be the lower cost alternative. The Company has designated leuprolide acetate (Eligard and Lupron Depot 7.5 mg, represented by HCPCS J9217) as its preferred products for the following indications:

- Prostate cancer
- Salivary gland tumors

These products are less costly and at least as likely to produce equivalent therapeutic results as the nonpreferred leuprolide products, which include but are not limited to Camcevi (represented by HCPCS J1952), Lupron Depot (represented by HCPCS J1950), and any other nonpreferred leuprolide products.

The company is managing the following leuprolide acetate products only: Camcevi™, Eligard®, Fensolvi®, Lupron Depot®.

NOTE: All other uses described in this policy as Medically Necessary are eligible for coverage and are not subject to the Company-designated Preferred Product requirement.

NONPREFERRED PRODUCTS

Use of the nonpreferred leuprolide products, which include, but are not limited to, Camcevi (represented by HCPCS J1952), Lupron Depot (represented by HCPCS J1950), and any other nonpreferred leuprolide product is considered medically necessary and, therefore, covered only for individuals who are currently receiving or have previously received a nonpreferred product for the specified leuprolide indication.

If the individual has not previously received leuprolide to treat the specified indication, these nonpreferred products are only eligible for coverage when the individual has contraindication(s) or intolerance(s) to the Company-designated preferred product, leuprolide acetate (Eligard and Lupron Depot 7.5 mg, represented by HCPCS J9217).

MEDICALLY NECESSARY INDICATIONS

Leuprolide acetate/mesylate for injection is considered medically necessary and, therefore, covered when the following criteria are met:

Breast Cancer

Leuprolide acetate for injection is considered medically necessary and, therefore, covered for:

- Invasive or inflammatory breast cancer treatment in premenopausal females* with hormone receptor–positive breast cancer in combination with any of the following:
 - Adjuvant endocrine therapy
 - Endocrine therapy for recurrent unresectable (local or regional) or stage IV (M1) disease

Central Precocious Puberty

Leuprolide acetate for injection is considered medically necessary and, therefore, covered for children with a clinical diagnosis of central precocious puberty confirmed by all of the following criteria:

- An increased pubertal luteinizing hormone response to a GnRH stimulation test
- A bone age greater than at least 1 year compared to chronological age

Endometriosis

Leuprolide acetate for injection is considered medically necessary and, therefore, covered for a maximum of 6 months for initial treatment and a maximum of 6 months for retreatment (total 12 months) for the following:

- Management of endometriosis, including pain relief and reduction of endometriotic lesions
- Initial management of endometriosis and for management of recurrence of symptoms with norethindrone acetate, 5 mg daily

Head and Neck Cancers

Salivary Gland Tumors

Leuprolide acetate for injection is considered medically necessary and, therefore, covered as a single agent for the treatment of androgen receptor–positive recurrent disease with either of the following:

- Distant metastases in individuals with a performance status (PS) of 0–3
- Unresectable locoregional recurrence or second primary with prior radiation therapy

Gender Dysphoria: Male-to-female

Leuprolide acetate for injection is considered medically necessary and, therefore, covered for puberty suppression when all of the following criteria are met:

- The adolescent has meet the definition of gender nonconformity, gender incongruence, gender dysphoria, or is gender diverse.
- If an individual has a diagnosis of gender dysphoria, the gender dysphoria has emerged or worsened with the onset of puberty
- The individual has reached at least Tanner stage 2 of development.

Note: Subject to the terms, conditions, and limitations of the member's contract, oral and self-administered hormones are not covered under the medical benefit.

Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer

Leuprolide acetate for injection is considered medically necessary and, therefore, covered for hormone therapy as a single agent for persistent disease or recurrence of ovarian cancer/fallopian tube cancer/primary peritoneal cancer (endometrioid, serous), carcinosarcoma (malignant mixed Mullerian tumors), clear cell carcinoma of the ovary, grade

1 endometrioid carcinoma, mucinous carcinoma of the ovary when one of the following criteria are met:

- For progression on primary, maintenance, or recurrence therapy (platinum-resistant disease)
- For stable or persistent disease (if not on maintenance therapy) (platinum-resistant disease)
- For complete remission and relapse less than 6 months after completing chemotherapy (platinum-resistant disease)
- For radiographic and/or clinical relapse in individuals with previous complete remission and relapse 6 months or longer after completing prior chemotherapy (platinum-sensitive disease)
- As a single agent for clinical relapse in individuals with stage II–IV granulosa-cell tumors
- Hormone therapy for low-grade serous carcinoma (serous, borderline epithelial), as a single agent for platinum-sensitive or platinum-resistant recurrence (if an aromatase inhibitor was given previously)

Prostate Cancer

Leuprolide acetate/mesylate for injection is considered medically necessary and, therefore, covered for:

- Treatment (including palliative treatment) for individuals with advanced prostate cancer
- Adjuvant ADT as a single agent or in combination with a first-generation antiandrogen, with external beam radiation therapy (EBRT) if adverse features (i.e., positive margins, seminal vesicle invasion, extracapsular extension, or detectable prostate-specific antigen [PSA]) noted after radical prostatectomy (RP) for individuals:
 - In the low-risk group[†] and ≥10 year expected survival
 - With or without pelvic lymph node dissection (PLND) and no lymph node metastases in the favorable or unfavorable intermediate-risk group[†] and >10-year expected survival

- With PLND and no lymph node metastases in the high- or very-high-risk group[†] or regional risk group (any T, N1, M0) and >5-year expected survival or symptomatic
- Adjuvant ADT as a single agent or in combination with a first-generation antiandrogen, without EBRT if lymph node metastasis found during PLND for individuals:
 - In the favorable or unfavorable intermediate-risk group[†] and >10-year expected survival
 - In the high or very-high-risk groups[†] and >5-year expected survival or symptomatic
 - In the regional-risk group (any T, N1, M0) and >5-year expected survival or symptomatic
- ADT as one of the following:
 - A single agent if life expectancy ≤5 years and symptomatic, may be considered in selected patients with very-low-, low-, and intermediate-risk disease
 - A single agent if life expectancy ≤5 years and asymptomatic, may be considered as initial therapy in selected patients with high- or very-high-risk disease where complications such as hydronephrosis or metastasis can be expected within 5 years
 - Initial therapy as a single agent (with or without EBRT), in combination with first-generation antiandrogen (with or without EBRT), or in combination with either abiraterone (preferred with EBRT) (excluding fine-particle formulation) with concurrent steroids (prednisone or methylprednisolone) in patients with regional-risk disease (Any T, N1, M0) and life expectancy > 5 years or symptomatic
 - Initial therapy as a single agent for patients in the regional risk group (Any T, N1, M0) and life expectancy ≤5 years and asymptomatic
- ADT for individuals with life expectancy >5 years or symptomatic and one of the following:
 - In combination with radiation therapy (RT) as a single agent or in combination with a first-generation antiandrogen for 4-6 months for patients in the unfavorable intermediate-risk group

- In combination with RT as a single agent or in combination with a first-generation antiandrogen for patients in the high- or very-high-risk group
- In combination with RT and either abiraterone excluding fine particle formulation with concurrent steroids (prednisone or methylprednisolone) for patients in the very-high-risk group only
- In combination with EBRT as a single agent, in combination with a first generation antiandrogen, or in combination with either abiraterone (preferred) or fine-particle abiraterone with concurrent steroid (prednisone or methylprednisolone) for patients in the regional risk group (Any T, N1, M0)
- ADT as a single agent or in combination with a first-generation antiandrogen for one of the following:
 - M0 PSA persistence/recurrence after radical prostatectomy in combination with EBRT if studies negative for pelvic nodal recurrence and distant metastases ± positive fossa recurrence or imaging not performed and life expectancy >5 years (NCCN preferred)
 - M0 PSA persistence/recurrence after radical prostatectomy in combination with EBRT with or without abiraterone (excluding fine-particle formulation) with concurrent steroids (prednisone or methylprednisolone) if studies are positive for pelvic nodal recurrence and life expectancy >5 years
 - M0 PSA recurrence or positive digital rectal examination (DRE) after RT radiation therapy (RT) if studies negative for regional lymph nodes and distant metastases and life expectancy >5 years
 - Given with or without abiraterone (excluding fine-particle formulation) with concurrent steroids (prednisone or methylprednisolone) for M0 PSA recurrence or positive DRE after RT if studies positive for regional lymph nodes and life expectancy >5 years
- Initial ADT with EBRT as a single agent or in combination with a first-generation antiandrogen if life expectancy greater than 5 years or symptomatic and one of the following:

- For 4–6 months with or without brachytherapy for individuals in the unfavorable intermediate-risk group[†]
- For 1.5–3 years for individuals in the high or very-high-risk group[†]
- For 2 years of ADT in combination with abiraterone for individuals in the very-high-risk group[†] only
- For 1–3 years with brachytherapy for individuals in the high or very-high-risk group[†]
- For individuals in the regional risk group (any T, N1, M0) as a single agent, in combination with a first generation antiandrogen, or in combination with abiraterone with concurrent steroid (prednisone or methylprednisolone) (NCCN-preferred regimen)
- Single-agent treatment for individuals who progressed on observation of localized disease
- For castration-sensitive disease and one of the following:
 - As a single agent as androgen deprivation therapy (ADT) monotherapy if clear contraindications to combination therapy
 - In combination with docetaxel plus either abiraterone (NCCN preferred) (excluding fine-particle formulation) with concurrent steroids (prednisone or methylprednisolone) or darolutamide (NCCN preferred) for high-volume synchronous or metachronous metastases
 - In combination with either apalutamide or enzalutamide (Xtandi) (both NCCN preferred) for high-volume synchronous or metachronous metastases, or low-volume synchronous or metachronous metastases
 - In combination with abiraterone (and prednisone) for high-volume synchronous or metachronous metastases, or low-volume synchronous or metachronous metastases (NCCN preferred)
 - With EBRT to the primary tumor as a single agent or in combination with a first-generation antiandrogen alone

- With EBRT to the primary tumor in combination with either abiraterone or fine particle abiraterone with concurrent steroids (prednisone or methylprednisolone) for low-volume synchronous metastases with low metastatic burden
- For progressive M0 castration-sensitive prostate cancer (CSPC) after maximal pelvic therapy and one of the following:
 - As a single agent
 - In combination with a first-generation antiandrogen
 - In combination with enzalutamide (Xtandi)
- For M0 or M1 castration-resistant disease as ADT to maintain castrate levels of serum testosterone (<50 ng/dL)

** Men with breast cancer should be treated similarly to postmenopausal women, except that use of an aromatase inhibitor is ineffective without concomitant suppression of testicular steroidogenesis.*

[‡]According to NCCN guidelines:

- *Very low risk refers to individuals with clinical stage T1c, Grade Group 1, PSA <10 ng/mL, fewer than three prostate biopsy fragments/cores positive with 50% or less cancer in each fragment/core, and PSA density <0.15 mg/mL/g.*
- *Low risk refers to individuals with clinical stage T1 to T2a, Grade Group 1, and PSA <10 ng/mL.*
- *Intermediate risk refers to individuals*
 - *Who have no high- or very-high-risk features and has one or more intermediate-risk factors (IRF):*
 - *Clinical stage T2b to T2c*
 - *Grade Group 2 or 3*
 - *PSA 10 ng/mL to 20 ng/mL*
 - *Favorable intermediate risk refers to individuals with 1 IRF, Grade Group 1 or 2, and <50% biopsy cores positive.*

- *Unfavorable intermediate risk refers to individuals with two or three IRFs, and/or Grade Group 3, and/or ≥50% biopsy cores positive*
- *High risk refers to individuals who have no very-high-risk features and have at least one high-risk feature:*
 - *Clinical stage T3a, Grade Group 4 or 5, or PSA greater than 20 ng/mL*
- *Very-high-risk refers to individuals with clinical stage T3b to T4 , or primary Gleason pattern 5, or two to three high-risk features, or more than four biopsy cores with grade Group 4 or 5*

Uterine Leiomyomata (Uterine Fibroids)

Leuprolide acetate for injection is considered medically necessary and, therefore, covered for the preoperative hematologic improvement of individuals with anemia caused by uterine leiomyomata concomitantly with iron therapy. According to the FDA-approved label, duration of therapy should be limited to up to 3 months.

Duration of authorization: 12 months

Version Effective Date: 01/06/2025

Attachment A: [Leuprolide Acetate \(Camcevi™, Eligard®, Fensolvi®, Lupron Depot®\)](#)

Description: LEUPROLIDE ACETATE (LUPRON DEPOT - J1950)

Attachment B: [Leuprolide Acetate \(Camcevi™, Eligard®, Fensolvi®, Lupron Depot®\)](#)

Description: LEUPROLIDE ACETATE (FENSOLVI- J1951)

Attachment C: [Leuprolide Acetate \(Camcevi™, Eligard®, Fensolvi®, Lupron Depot®\)](#)

Description: LEUPROLIDE MESYLATE (CAMCEVI- J1952)

Attachment D: [Leuprolide Acetate \(Camcevi™, Eligard®, Fensolvi®, Lupron Depot®\)](#)

Description: LEUPROLIDE ACETATE (ELIGARD and LUPRON DEPOT- J9217)

Policy Attachment

Attachment to Policy # 08.01.33j

Attachment: A

Policy #: 08.01.33j

Description: LEUPROLIDE ACETATE (LUPRON DEPOT - J1950)

Title: Leuprolide Acetate (Camcevi™, Eligard®, Fensolvi®, Lupron Depot®)

ICD-10 Diagnosis Code Numbers and Narratives

MEDICALLY NECESSARY

C48.1 Malignant neoplasm of specified parts of peritoneum
C48.2 Malignant neoplasm of peritoneum, unspecified
C48.8 Malignant neoplasm of overlapping sites of retroperitoneum and peritoneum
C50.011 Malignant neoplasm of nipple and areola, right female breast
C50.012 Malignant neoplasm of nipple and areola, left female breast
C50.021 Malignant neoplasm of nipple and areola, right male breast
C50.022 Malignant neoplasm of nipple and areola, left male breast
C50.111 Malignant neoplasm of central portion of right female breast
C50.112 Malignant neoplasm of central portion of left female breast
C50.121 Malignant neoplasm of central portion of right male breast
C50.122 Malignant neoplasm of central portion of left male breast
C50.211 Malignant neoplasm of upper-inner quadrant of right female breast
C50.212 Malignant neoplasm of upper-inner quadrant of left female breast
C50.221 Malignant neoplasm of upper-inner quadrant of right male breast
C50.222 Malignant neoplasm of upper-inner quadrant of left male breast
C50.311 Malignant neoplasm of lower-inner quadrant of right female breast
C50.312 Malignant neoplasm of lower-inner quadrant of left female breast
C50.321 Malignant neoplasm of lower-inner quadrant of right male breast
C50.322 Malignant neoplasm of lower-inner quadrant of left male breast
C50.411 Malignant neoplasm of upper-outer quadrant of right female breast
C50.412 Malignant neoplasm of upper-outer quadrant of left female breast
C50.421 Malignant neoplasm of upper-outer quadrant of right male breast
C50.422 Malignant neoplasm of upper-outer quadrant of left male breast
C50.511 Malignant neoplasm of lower-outer quadrant of right female breast
C50.512 Malignant neoplasm of lower-outer quadrant of left female breast
C50.521 Malignant neoplasm of lower-outer quadrant of right male breast
C50.522 Malignant neoplasm of lower-outer quadrant of left male breast
C50.611 Malignant neoplasm of axillary tail of right female breast
C50.612 Malignant neoplasm of axillary tail of left female breast
C50.621 Malignant neoplasm of axillary tail of right male breast
C50.622 Malignant neoplasm of axillary tail of left male breast
C50.811 Malignant neoplasm of overlapping sites of right female breast

C50.812 Malignant neoplasm of overlapping sites of left female breast
C50.821 Malignant neoplasm of overlapping sites of right male breast
C50.822 Malignant neoplasm of overlapping sites of left male breast
C50.911 Malignant neoplasm of unspecified site of right female breast
C50.912 Malignant neoplasm of unspecified site of left female breast
C50.921 Malignant neoplasm of unspecified site of right male breast
C50.922 Malignant neoplasm of unspecified site of left male breast
C56.1 Malignant neoplasm of right ovary
C56.2 Malignant neoplasm of left ovary
C56.3 Malignant neoplasm of bilateral ovaries
C57.01 Malignant neoplasm of right fallopian tube
C57.02 Malignant neoplasm of left fallopian tube
C57.11 Malignant neoplasm of right broad ligament
C57.12 Malignant neoplasm of left broad ligament
C57.21 Malignant neoplasm of right round ligament
C57.22 Malignant neoplasm of left round ligament
C57.3 Malignant neoplasm of parametrium
C57.4 Malignant neoplasm of uterine adnexa, unspecified

C79.81 Secondary malignant neoplasm of breast
C79.82 Secondary malignant neoplasm of genital organs
D25.0 Submucous leiomyoma of uterus
D25.1 Intramural leiomyoma of uterus
D25.2 Subserosal leiomyoma of uterus
D25.9 Leiomyoma of uterus, unspecified
E22.8 Other hyperfunction of pituitary gland
E30.1 Precocious puberty
F64.0 Transsexualism
F64.1 Dual role transvestism
F64.2 Gender identity disorder of childhood
F64.8 Other gender identity disorders
F64.9 Gender identity disorder, unspecified
N80.0 Endometriosis of uterus
N80.6 Endometriosis in cutaneous scar
N80.8 Other endometriosis
N80.9 Endometriosis, unspecified
N80.101 Endometriosis of right ovary, unspecified depth
N80.102 Endometriosis of left ovary, unspecified depth
N80.103 Endometriosis of bilateral ovaries, unspecified depth
N80.111 Superficial endometriosis of right ovary
N80.112 Superficial endometriosis of left ovary

N80.113	Superficial endometriosis of bilateral ovaries
N80.121	Deep endometriosis of right ovary
N80.122	Deep endometriosis of left ovary
N80.123	Deep endometriosis of bilateral ovaries
N80.201	Endometriosis of right fallopian tube, unspecified depth
N80.202	Endometriosis of left fallopian tube, unspecified depth
N80.203	Endometriosis of bilateral fallopian tubes, unspecified depth
N80.211	Superficial endometriosis of right fallopian tube
N80.212	Superficial endometriosis of left fallopian tube
N80.213	Superficial endometriosis of bilateral fallopian tubes
N80.221	Deep endometriosis of right fallopian tube
N80.222	Deep endometriosis of left fallopian tube
N80.223	Deep endometriosis of bilateral fallopian tubes
N80.30	Endometriosis of pelvic peritoneum, unspecified
N80.311	Superficial endometriosis of the anterior cul-de-sac
N80.312	Deep endometriosis of the anterior cul-de-sac
N80.319	Endometriosis of the anterior cul-de-sac, unspecified depth
N80.321	Superficial endometriosis of the posterior cul-de-sac
N80.322	Deep endometriosis of the posterior cul-de-sac
N80.329	Endometriosis of the posterior cul-de-sac, unspecified depth
N80.331	Superficial endometriosis of the right pelvic sidewall
N80.332	Superficial endometriosis of the left pelvic sidewall
N80.333	Superficial endometriosis of bilateral pelvic sidewall
N80.341	Deep endometriosis of the right pelvic sidewall
N80.342	Deep endometriosis of the left pelvic sidewall
N80.343	Deep endometriosis of the bilateral pelvic sidewall
N80.351	Endometriosis of the right pelvic sidewall, unspecified depth
N80.352	Endometriosis of the left pelvic sidewall, unspecified depth
N80.353	Endometriosis of bilateral pelvic sidewall, unspecified depth
N80.361	Superficial endometriosis of the right pelvic brim
N80.362	Superficial endometriosis of the left pelvic brim
N80.363	Superficial endometriosis of bilateral pelvic brim
N80.371	Deep endometriosis of the right pelvic brim
N80.372	Deep endometriosis of the left pelvic brim
N80.373	Deep endometriosis of bilateral pelvic brim
N80.381	Endometriosis of the right pelvic brim, unspecified depth
N80.382	Endometriosis of the left pelvic brim, unspecified depth
N80.383	Endometriosis of bilateral pelvic brim, unspecified depth
N80.391	Superficial endometriosis of the pelvic peritoneum, other specified sites
N80.392	Deep endometriosis of the pelvic peritoneum, other specified sites
N80.399	Endometriosis of the pelvic peritoneum, other specified sites, unspecified depth

N80.3A1	Superficial endometriosis of the right uterosacral ligament
N80.3A2	Superficial endometriosis of the left uterosacral ligament
N80.3A3	Superficial endometriosis of the bilateral uterosacral ligament(s)
N80.3B1	Deep endometriosis of the right uterosacral ligament
N80.3B2	Deep endometriosis of the left uterosacral ligament
N80.3B3	Deep endometriosis of bilateral uterosacral ligament(s)
N80.3C1	Endometriosis of the right uterosacral ligament, unspecified depth
N80.3C2	Endometriosis of the left uterosacral ligament, unspecified depth
N80.3C3	Endometriosis of bilateral uterosacral ligament(s), unspecified depth
N80.40	Endometriosis of rectovaginal septum, unspecified involvement of vagina
N80.41	Endometriosis of rectovaginal septum without involvement of vagina
N80.42	Endometriosis of rectovaginal septum with involvement of vagina
N80.50	Endometriosis of intestine, unspecified
N80.511	Superficial endometriosis of the rectum
N80.512	Deep endometriosis of the rectum
N80.519	Endometriosis of the rectum, unspecified depth
N80.521	Superficial endometriosis of the sigmoid colon
N80.522	Deep endometriosis of the sigmoid colon
N80.529	Endometriosis of the sigmoid colon, unspecified depth
N80.531	Superficial endometriosis of the cecum
N80.532	Deep endometriosis of the cecum
N80.539	Endometriosis of the cecum, unspecified depth
N80.541	Superficial endometriosis of the appendix
N80.542	Deep endometriosis of the appendix
N80.549	Endometriosis of the appendix, unspecified depth
N80.551	Superficial endometriosis of other parts of the colon
N80.552	Deep endometriosis of other parts of the colon
N80.559	Endometriosis of other parts of the colon, unspecified depth
N80.561	Superficial endometriosis of the small intestine
N80.562	Deep endometriosis of the small intestine
N80.569	Endometriosis of the small intestine, unspecified depth
N80.A0	Endometriosis of bladder, unspecified depth
N80.A1	Superficial endometriosis of bladder
N80.A2	Deep endometriosis of bladder
N80.A41	Superficial endometriosis of right ureter
N80.A42	Superficial endometriosis of left ureter
N80.A43	Superficial endometriosis of bilateral ureters
N80.A51	Deep endometriosis of right ureter
N80.A52	Deep endometriosis of left ureter
N80.A53	Deep endometriosis of bilateral ureters
N80.A61	Endometriosis of right ureter, unspecified depth

N80.A62 Endometriosis of left ureter, unspecified depth
N80.A63 Endometriosis of bilateral ureters, unspecified depth
N80.B1 Endometriosis of pleura
N80.B2 Endometriosis of lung
N80.B31 Superficial endometriosis of diaphragm
N80.B32 Deep endometriosis of diaphragm
N80.B39 Endometriosis of diaphragm, unspecified depth
N80.B4 Endometriosis of the pericardial space
N80.B5 Endometriosis of the mediastinal space
N80.B6 Endometriosis of cardiothoracic space
N80.C0 Endometriosis of the abdomen, unspecified
N80.C10 Endometriosis of the anterior abdominal wall, subcutaneous tissue
N80.C11 Endometriosis of the anterior abdominal wall, fascia and muscular layers
N80.C19 Endometriosis of the anterior abdominal wall, unspecified depth
N80.C2 Endometriosis of the umbilicus
N80.C3 Endometriosis of the inguinal canal
N80.C4 Endometriosis of extra-pelvic abdominal peritoneum
N80.C9 Endometriosis of other site of abdomen
N80.D0 Endometriosis of the pelvic nerves, unspecified
N80.D1 Endometriosis of the sacral splanchnic nerves
N80.D2 Endometriosis of the sacral nerve roots
N80.D3 Endometriosis of the obturator nerve
N80.D4 Endometriosis of the sciatic nerve
N80.D5 Endometriosis of the pudendal nerve
N80.D6 Endometriosis of the femoral nerve
N80.D9 Endometriosis of other pelvic nerve

NOT MEDICALLY NECESSARY

C07 Malignant neoplasm of parotid gland
C08.0 Malignant neoplasm of submandibular gland
C08.1 Malignant neoplasm of sublingual gland
C08.9 Malignant neoplasm of major salivary gland, unspecified
C61 Malignant neoplasm of prostate

Version Effective Date: 01/06/2025

Version Issued Date: 12/30/2024

Version Reissued Date: N/A

Policy Attachment**Attachment to Policy # 08.01.33j****Attachment: B****Policy #: 08.01.33j****Description:** LEUPROLIDE ACETATE (FENSOLVI- J1951)**Title:** Leuprolide Acetate (Camcevi™, Eligard®, Fensolvi®, Lupron Depot®)

MEDICALLY NECESSARY

E30.1 Precocious puberty

NOT MEDICALLY NECESSARY

C07 Malignant neoplasm of parotid gland
C08.0 Malignant neoplasm of submandibular gland
C08.1 Malignant neoplasm of sublingual gland
C08.9 Malignant neoplasm of major salivary gland, unspecified
C48.1 Malignant neoplasm of specified parts of peritoneum
C48.2 Malignant neoplasm of peritoneum, unspecified
C48.8 Malignant neoplasm of overlapping sites of retroperitoneum and peritoneum
C50.011 Malignant neoplasm of nipple and areola, right female breast
C50.012 Malignant neoplasm of nipple and areola, left female breast
C50.019 Malignant neoplasm of nipple and areola, unspecified female breast
C50.021 Malignant neoplasm of nipple and areola, right male breast
C50.022 Malignant neoplasm of nipple and areola, left male breast
C50.029 Malignant neoplasm of nipple and areola, unspecified male breast
C50.111 Malignant neoplasm of central portion of right female breast
C50.112 Malignant neoplasm of central portion of left female breast
C50.119 Malignant neoplasm of central portion of unspecified female breast
C50.121 Malignant neoplasm of central portion of right male breast
C50.122 Malignant neoplasm of central portion of left male breast
C50.129 Malignant neoplasm of central portion of unspecified male breast
C50.211 Malignant neoplasm of upper-inner quadrant of right female breast
C50.212 Malignant neoplasm of upper-inner quadrant of left female breast
C50.219 Malignant neoplasm of upper-inner quadrant of unspecified female breast
C50.221 Malignant neoplasm of upper-inner quadrant of right male breast
C50.222 Malignant neoplasm of upper-inner quadrant of left male breast
C50.229 Malignant neoplasm of upper-inner quadrant of unspecified male breast

C50.311 Malignant neoplasm of lower-inner quadrant of right female breast
C50.312 Malignant neoplasm of lower-inner quadrant of left female breast
C50.319 Malignant neoplasm of lower-inner quadrant of unspecified female breast
C50.321 Malignant neoplasm of lower-inner quadrant of right male breast
C50.322 Malignant neoplasm of lower-inner quadrant of left male breast
C50.329 Malignant neoplasm of lower-inner quadrant of unspecified male breast
C50.411 Malignant neoplasm of upper-outer quadrant of right female breast
C50.412 Malignant neoplasm of upper-outer quadrant of left female breast
C50.419 Malignant neoplasm of upper-outer quadrant of unspecified female breast
C50.421 Malignant neoplasm of upper-outer quadrant of right male breast
C50.422 Malignant neoplasm of upper-outer quadrant of left male breast
C50.429 Malignant neoplasm of upper-outer quadrant of unspecified male breast
C50.511 Malignant neoplasm of lower-outer quadrant of right female breast
C50.512 Malignant neoplasm of lower-outer quadrant of left female breast
C50.519 Malignant neoplasm of lower-outer quadrant of unspecified female breast
C50.521 Malignant neoplasm of lower-outer quadrant of right male breast
C50.522 Malignant neoplasm of lower-outer quadrant of left male breast
C50.529 Malignant neoplasm of lower-outer quadrant of unspecified male breast
C50.611 Malignant neoplasm of axillary tail of right female breast
C50.612 Malignant neoplasm of axillary tail of left female breast
C50.619 Malignant neoplasm of axillary tail of unspecified female breast
C50.621 Malignant neoplasm of axillary tail of right male breast
C50.622 Malignant neoplasm of axillary tail of left male breast
C50.629 Malignant neoplasm of axillary tail of unspecified male breast
C50.811 Malignant neoplasm of overlapping sites of right female breast
C50.812 Malignant neoplasm of overlapping sites of left female breast
C50.819 Malignant neoplasm of overlapping sites of unspecified female breast
C50.821 Malignant neoplasm of overlapping sites of right male breast
C50.822 Malignant neoplasm of overlapping sites of left male breast
C50.829 Malignant neoplasm of overlapping sites of unspecified male breast
C50.911 Malignant neoplasm of unspecified site of right female breast
C50.912 Malignant neoplasm of unspecified site of left female breast
C50.919 Malignant neoplasm of unspecified site of unspecified female breast
C50.921 Malignant neoplasm of unspecified site of right male breast
C50.922 Malignant neoplasm of unspecified site of left male breast
C50.929 Malignant neoplasm of unspecified site of unspecified male breast
C56.1 Malignant neoplasm of right ovary
C56.2 Malignant neoplasm of left ovary
C56.3 Malignant neoplasm of bilateral ovaries
C56.9 Malignant neoplasm of unspecified ovary
C57.00 Malignant neoplasm of unspecified fallopian tube

C57.01 Malignant neoplasm of right fallopian tube
C57.02 Malignant neoplasm of left fallopian tube
C57.10 Malignant neoplasm of unspecified broad ligament
C57.11 Malignant neoplasm of right broad ligament
C57.12 Malignant neoplasm of left broad ligament
C57.20 Malignant neoplasm of unspecified round ligament
C57.21 Malignant neoplasm of right round ligament
C57.22 Malignant neoplasm of left round ligament
C57.3 Malignant neoplasm of parametrium
C57.4 Malignant neoplasm of uterine adnexa, unspecified
C61 Malignant neoplasm of prostate
C79.81 Secondary malignant neoplasm of breast
C79.82 Secondary malignant neoplasm of genital organs
D25.0 Submucous leiomyoma of uterus
D25.1 Intramural leiomyoma of uterus
D25.2 Subserosal leiomyoma of uterus
D25.9 Leiomyoma of uterus, unspecified
E22.8 Other hyperfunction of pituitary gland
F64.0 Transsexualism
F64.1 Dual role transvestism
F64.2 Gender identity disorder of childhood
F64.8 Other gender identity disorders
F64.9 Gender identity disorder, unspecified
N80.0 Endometriosis of uterus
N80.6 Endometriosis in cutaneous scar
N80.8 Other endometriosis
N80.9 Endometriosis, unspecified
N80.101 Endometriosis of right ovary, unspecified depth
N80.102 Endometriosis of left ovary, unspecified depth
N80.103 Endometriosis of bilateral ovaries, unspecified depth
N80.111 Superficial endometriosis of right ovary
N80.112 Superficial endometriosis of left ovary
N80.113 Superficial endometriosis of bilateral ovaries
N80.121 Deep endometriosis of right ovary
N80.122 Deep endometriosis of left ovary
N80.123 Deep endometriosis of bilateral ovaries
N80.201 Endometriosis of right fallopian tube, unspecified depth
N80.202 Endometriosis of left fallopian tube, unspecified depth
N80.203 Endometriosis of bilateral fallopian tubes, unspecified depth
N80.211 Superficial endometriosis of right fallopian tube
N80.212 Superficial endometriosis of left fallopian tube

N80.213	Superficial endometriosis of bilateral fallopian tubes
N80.221	Deep endometriosis of right fallopian tube
N80.222	Deep endometriosis of left fallopian tube
N80.223	Deep endometriosis of bilateral fallopian tubes
N80.30	Endometriosis of pelvic peritoneum, unspecified
N80.311	Superficial endometriosis of the anterior cul-de-sac
N80.312	Deep endometriosis of the anterior cul-de-sac
N80.319	Endometriosis of the anterior cul-de-sac, unspecified depth
N80.321	Superficial endometriosis of the posterior cul-de-sac
N80.322	Deep endometriosis of the posterior cul-de-sac
N80.329	Endometriosis of the posterior cul-de-sac, unspecified depth
N80.331	Superficial endometriosis of the right pelvic sidewall
N80.332	Superficial endometriosis of the left pelvic sidewall
N80.333	Superficial endometriosis of bilateral pelvic sidewall
N80.341	Deep endometriosis of the right pelvic sidewall
N80.342	Deep endometriosis of the left pelvic sidewall
N80.343	Deep endometriosis of the bilateral pelvic sidewall
N80.351	Endometriosis of the right pelvic sidewall, unspecified depth
N80.352	Endometriosis of the left pelvic sidewall, unspecified depth
N80.353	Endometriosis of bilateral pelvic sidewall, unspecified depth
N80.361	Superficial endometriosis of the right pelvic brim
N80.362	Superficial endometriosis of the left pelvic brim
N80.363	Superficial endometriosis of bilateral pelvic brim
N80.371	Deep endometriosis of the right pelvic brim
N80.372	Deep endometriosis of the left pelvic brim
N80.373	Deep endometriosis of bilateral pelvic brim
N80.381	Endometriosis of the right pelvic brim, unspecified depth
N80.382	Endometriosis of the left pelvic brim, unspecified depth
N80.383	Endometriosis of bilateral pelvic brim, unspecified depth
N80.391	Superficial endometriosis of the pelvic peritoneum, other specified sites
N80.392	Deep endometriosis of the pelvic peritoneum, other specified sites
N80.399	Endometriosis of the pelvic peritoneum, other specified sites, unspecified depth
N80.3A1	Superficial endometriosis of the right uterosacral ligament
N80.3A2	Superficial endometriosis of the left uterosacral ligament
N80.3A3	Superficial endometriosis of the bilateral uterosacral ligament(s)
N80.3B1	Deep endometriosis of the right uterosacral ligament
N80.3B2	Deep endometriosis of the left uterosacral ligament
N80.3B3	Deep endometriosis of bilateral uterosacral ligament(s)
N80.3C1	Endometriosis of the right uterosacral ligament, unspecified depth
N80.3C2	Endometriosis of the left uterosacral ligament, unspecified depth
N80.3C3	Endometriosis of bilateral uterosacral ligament(s), unspecified depth

N80.40	Endometriosis of rectovaginal septum, unspecified involvement of vagina
N80.41	Endometriosis of rectovaginal septum without involvement of vagina
N80.42	Endometriosis of rectovaginal septum with involvement of vagina
N80.50	Endometriosis of intestine, unspecified
N80.511	Superficial endometriosis of the rectum
N80.512	Deep endometriosis of the rectum
N80.519	Endometriosis of the rectum, unspecified depth
N80.521	Superficial endometriosis of the sigmoid colon
N80.522	Deep endometriosis of the sigmoid colon
N80.529	Endometriosis of the sigmoid colon, unspecified depth
N80.531	Superficial endometriosis of the cecum
N80.532	Deep endometriosis of the cecum
N80.539	Endometriosis of the cecum, unspecified depth
N80.541	Superficial endometriosis of the appendix
N80.542	Deep endometriosis of the appendix
N80.549	Endometriosis of the appendix, unspecified depth
N80.551	Superficial endometriosis of other parts of the colon
N80.552	Deep endometriosis of other parts of the colon
N80.559	Endometriosis of other parts of the colon, unspecified depth
N80.561	Superficial endometriosis of the small intestine
N80.562	Deep endometriosis of the small intestine
N80.569	Endometriosis of the small intestine, unspecified depth
N80.A0	Endometriosis of bladder, unspecified depth
N80.A1	Superficial endometriosis of bladder
N80.A2	Deep endometriosis of bladder
N80.A41	Superficial endometriosis of right ureter
N80.A42	Superficial endometriosis of left ureter
N80.A43	Superficial endometriosis of bilateral ureters
N80.A49	Superficial endometriosis of unspecified ureter
N80.A51	Deep endometriosis of right ureter
N80.A52	Deep endometriosis of left ureter
N80.A53	Deep endometriosis of bilateral ureters
N80.A59	Deep endometriosis of unspecified ureter
N80.A61	Endometriosis of right ureter, unspecified depth
N80.A62	Endometriosis of left ureter, unspecified depth
N80.A63	Endometriosis of bilateral ureters, unspecified depth
N80.A69	Endometriosis of unspecified ureter, unspecified depth
N80.B1	Endometriosis of pleura
N80.B2	Endometriosis of lung
N80.B31	Superficial endometriosis of diaphragm
N80.B32	Deep endometriosis of diaphragm

N80.B39	Endometriosis of diaphragm, unspecified depth
N80.B4	Endometriosis of the pericardial space
N80.B5	Endometriosis of the mediastinal space
N80.B6	Endometriosis of cardiothoracic space
N80.C0	Endometriosis of the abdomen, unspecified
N80.C2	Endometriosis of the umbilicus
N80.C3	Endometriosis of the inguinal canal
N80.C4	Endometriosis of extra-pelvic abdominal peritoneum
N80.C9	Endometriosis of other site of abdomen
N80.C10	Endometriosis of the anterior abdominal wall, subcutaneous tissue
N80.C11	Endometriosis of the anterior abdominal wall, fascia and muscular layers
N80.C19	Endometriosis of the anterior abdominal wall, unspecified depth
N80.D0	Endometriosis of the pelvic nerves, unspecified
N80.D1	Endometriosis of the sacral splanchnic nerves
N80.D2	Endometriosis of the sacral nerve roots
N80.D3	Endometriosis of the obturator nerve
N80.D4	Endometriosis of the sciatic nerve
N80.D5	Endometriosis of the pudendal nerve
N80.D6	Endometriosis of the femoral nerve
N80.D9	Endometriosis of other pelvic nerve

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Policy Attachment

Attachment to Policy # 08.01.33j

Attachment: C

Policy #: 08.01.33j

Description: LEUPROLIDE MESYLATE (CAMCEVI- J1952)

Title: Leuprolide Acetate (Camcevi™, Eligard®, Fensolvi®, Lupron Depot®)

NOT MEDICALLY NECESSARY

C07 Malignant neoplasm of parotid gland
C08.0 Malignant neoplasm of submandibular gland
C08.1 Malignant neoplasm of sublingual gland
C08.9 Malignant neoplasm of major salivary gland, unspecified
C48.1 Malignant neoplasm of specified parts of peritoneum
C48.2 Malignant neoplasm of peritoneum, unspecified
C48.8 Malignant neoplasm of overlapping sites of retroperitoneum and peritoneum
C50.011 Malignant neoplasm of nipple and areola, right female breast
C50.012 Malignant neoplasm of nipple and areola, left female breast
C50.019 Malignant neoplasm of nipple and areola, unspecified female breast
C50.021 Malignant neoplasm of nipple and areola, right male breast
C50.022 Malignant neoplasm of nipple and areola, left male breast
C50.029 Malignant neoplasm of nipple and areola, unspecified male breast
C50.111 Malignant neoplasm of central portion of right female breast
C50.112 Malignant neoplasm of central portion of left female breast
C50.119 Malignant neoplasm of central portion of unspecified female breast
C50.121 Malignant neoplasm of central portion of right male breast
C50.122 Malignant neoplasm of central portion of left male breast
C50.129 Malignant neoplasm of central portion of unspecified male breast
C50.211 Malignant neoplasm of upper-inner quadrant of right female breast
C50.212 Malignant neoplasm of upper-inner quadrant of left female breast
C50.219 Malignant neoplasm of upper-inner quadrant of unspecified female breast
C50.221 Malignant neoplasm of upper-inner quadrant of right male breast
C50.222 Malignant neoplasm of upper-inner quadrant of left male breast
C50.229 Malignant neoplasm of upper-inner quadrant of unspecified male breast
C50.311 Malignant neoplasm of lower-inner quadrant of right female breast
C50.312 Malignant neoplasm of lower-inner quadrant of left female breast
C50.319 Malignant neoplasm of lower-inner quadrant of unspecified female breast
C50.321 Malignant neoplasm of lower-inner quadrant of right male breast
C50.322 Malignant neoplasm of lower-inner quadrant of left male breast
C50.329 Malignant neoplasm of lower-inner quadrant of unspecified male breast
C50.411 Malignant neoplasm of upper-outer quadrant of right female breast
C50.412 Malignant neoplasm of upper-outer quadrant of left female breast
C50.419 Malignant neoplasm of upper-outer quadrant of unspecified female breast
C50.421 Malignant neoplasm of upper-outer quadrant of right male breast
C50.422 Malignant neoplasm of upper-outer quadrant of left male breast
C50.429 Malignant neoplasm of upper-outer quadrant of unspecified male breast
C50.511 Malignant neoplasm of lower-outer quadrant of right female breast

C50.512 Malignant neoplasm of lower-outer quadrant of left female breast
C50.519 Malignant neoplasm of lower-outer quadrant of unspecified female breast
C50.521 Malignant neoplasm of lower-outer quadrant of right male breast
C50.522 Malignant neoplasm of lower-outer quadrant of left male breast
C50.529 Malignant neoplasm of lower-outer quadrant of unspecified male breast
C50.611 Malignant neoplasm of axillary tail of right female breast
C50.612 Malignant neoplasm of axillary tail of left female breast
C50.619 Malignant neoplasm of axillary tail of unspecified female breast
C50.621 Malignant neoplasm of axillary tail of right male breast
C50.622 Malignant neoplasm of axillary tail of left male breast
C50.629 Malignant neoplasm of axillary tail of unspecified male breast
C50.811 Malignant neoplasm of overlapping sites of right female breast
C50.812 Malignant neoplasm of overlapping sites of left female breast
C50.819 Malignant neoplasm of overlapping sites of unspecified female breast
C50.821 Malignant neoplasm of overlapping sites of right male breast
C50.822 Malignant neoplasm of overlapping sites of left male breast
C50.829 Malignant neoplasm of overlapping sites of unspecified male breast
C50.911 Malignant neoplasm of unspecified site of right female breast
C50.912 Malignant neoplasm of unspecified site of left female breast
C50.919 Malignant neoplasm of unspecified site of unspecified female breast
C50.921 Malignant neoplasm of unspecified site of right male breast
C50.922 Malignant neoplasm of unspecified site of left male breast
C50.929 Malignant neoplasm of unspecified site of unspecified male breast
C56.1 Malignant neoplasm of right ovary
C56.2 Malignant neoplasm of left ovary
C56.3 Malignant neoplasm of bilateral ovaries
C56.9 Malignant neoplasm of unspecified ovary
C57.00 Malignant neoplasm of unspecified fallopian tube
C57.01 Malignant neoplasm of right fallopian tube
C57.02 Malignant neoplasm of left fallopian tube
C57.10 Malignant neoplasm of unspecified broad ligament
C57.11 Malignant neoplasm of right broad ligament
C57.12 Malignant neoplasm of left broad ligament
C57.20 Malignant neoplasm of unspecified round ligament
C57.21 Malignant neoplasm of right round ligament
C57.22 Malignant neoplasm of left round ligament
C57.3 Malignant neoplasm of parametrium
C57.4 Malignant neoplasm of uterine adnexa, unspecified
C61 Malignant neoplasm of prostate
C79.81 Secondary malignant neoplasm of breast
C79.82 Secondary malignant neoplasm of genital organs

D25.0 Submucous leiomyoma of uterus
D25.1 Intramural leiomyoma of uterus
D25.2 Subserosal leiomyoma of uterus
D25.9 Leiomyoma of uterus, unspecified
E22.8 Other hyperfunction of pituitary gland
E30.1 Precocious puberty
F64.0 Transsexualism
F64.1 Dual role transvestism
F64.2 Gender identity disorder of childhood
F64.8 Other gender identity disorders
F64.9 Gender identity disorder, unspecified
N80.0 Endometriosis of uterus
N80.6 Endometriosis in cutaneous scar
N80.8 Other endometriosis
N80.9 Endometriosis, unspecified
N80.101 Endometriosis of right ovary, unspecified depth
N80.102 Endometriosis of left ovary, unspecified depth
N80.103 Endometriosis of bilateral ovaries, unspecified depth
N80.111 Superficial endometriosis of right ovary
N80.112 Superficial endometriosis of left ovary
N80.113 Superficial endometriosis of bilateral ovaries
N80.121 Deep endometriosis of right ovary
N80.122 Deep endometriosis of left ovary
N80.123 Deep endometriosis of bilateral ovaries
N80.201 Endometriosis of right fallopian tube, unspecified depth
N80.202 Endometriosis of left fallopian tube, unspecified depth
N80.203 Endometriosis of bilateral fallopian tubes, unspecified depth
N80.211 Superficial endometriosis of right fallopian tube
N80.212 Superficial endometriosis of left fallopian tube
N80.213 Superficial endometriosis of bilateral fallopian tubes
N80.221 Deep endometriosis of right fallopian tube
N80.222 Deep endometriosis of left fallopian tube
N80.223 Deep endometriosis of bilateral fallopian tubes
N80.30 Endometriosis of pelvic peritoneum, unspecified
N80.311 Superficial endometriosis of the anterior cul-de-sac
N80.312 Deep endometriosis of the anterior cul-de-sac
N80.319 Endometriosis of the anterior cul-de-sac, unspecified depth
N80.321 Superficial endometriosis of the posterior cul-de-sac
N80.322 Deep endometriosis of the posterior cul-de-sac
N80.329 Endometriosis of the posterior cul-de-sac, unspecified depth
N80.331 Superficial endometriosis of the right pelvic sidewall

N80.332	Superficial endometriosis of the left pelvic sidewall
N80.333	Superficial endometriosis of bilateral pelvic sidewall
N80.341	Deep endometriosis of the right pelvic sidewall
N80.342	Deep endometriosis of the left pelvic sidewall
N80.343	Deep endometriosis of the bilateral pelvic sidewall
N80.351	Endometriosis of the right pelvic sidewall, unspecified depth
N80.352	Endometriosis of the left pelvic sidewall, unspecified depth
N80.353	Endometriosis of bilateral pelvic sidewall, unspecified depth
N80.361	Superficial endometriosis of the right pelvic brim
N80.362	Superficial endometriosis of the left pelvic brim
N80.363	Superficial endometriosis of bilateral pelvic brim
N80.371	Deep endometriosis of the right pelvic brim
N80.372	Deep endometriosis of the left pelvic brim
N80.373	Deep endometriosis of bilateral pelvic brim
N80.381	Endometriosis of the right pelvic brim, unspecified depth
N80.382	Endometriosis of the left pelvic brim, unspecified depth
N80.383	Endometriosis of bilateral pelvic brim, unspecified depth
N80.391	Superficial endometriosis of the pelvic peritoneum, other specified sites
N80.392	Deep endometriosis of the pelvic peritoneum, other specified sites
N80.399	Endometriosis of the pelvic peritoneum, other specified sites, unspecified depth
N80.3A1	Superficial endometriosis of the right uterosacral ligament
N80.3A2	Superficial endometriosis of the left uterosacral ligament
N80.3A3	Superficial endometriosis of the bilateral uterosacral ligament(s)
N80.3B1	Deep endometriosis of the right uterosacral ligament
N80.3B2	Deep endometriosis of the left uterosacral ligament
N80.3B3	Deep endometriosis of bilateral uterosacral ligament(s)
N80.3C1	Endometriosis of the right uterosacral ligament, unspecified depth
N80.3C2	Endometriosis of the left uterosacral ligament, unspecified depth
N80.3C3	Endometriosis of bilateral uterosacral ligament(s), unspecified depth
N80.40	Endometriosis of rectovaginal septum, unspecified involvement of vagina
N80.41	Endometriosis of rectovaginal septum without involvement of vagina
N80.42	Endometriosis of rectovaginal septum with involvement of vagina
N80.50	Endometriosis of intestine, unspecified
N80.511	Superficial endometriosis of the rectum
N80.512	Deep endometriosis of the rectum
N80.519	Endometriosis of the rectum, unspecified depth
N80.521	Superficial endometriosis of the sigmoid colon
N80.522	Deep endometriosis of the sigmoid colon
N80.529	Endometriosis of the sigmoid colon, unspecified depth
N80.531	Superficial endometriosis of the cecum
N80.532	Deep endometriosis of the cecum

N80.539	Endometriosis of the cecum, unspecified depth
N80.541	Superficial endometriosis of the appendix
N80.542	Deep endometriosis of the appendix
N80.549	Endometriosis of the appendix, unspecified depth
N80.551	Superficial endometriosis of other parts of the colon
N80.552	Deep endometriosis of other parts of the colon
N80.559	Endometriosis of other parts of the colon, unspecified depth
N80.561	Superficial endometriosis of the small intestine
N80.562	Deep endometriosis of the small intestine
N80.569	Endometriosis of the small intestine, unspecified depth
N80.A0	Endometriosis of bladder, unspecified depth
N80.A1	Superficial endometriosis of bladder
N80.A2	Deep endometriosis of bladder
N80.A41	Superficial endometriosis of right ureter
N80.A42	Superficial endometriosis of left ureter
N80.A43	Superficial endometriosis of bilateral ureters
N80.A49	Superficial endometriosis of unspecified ureter
N80.A51	Deep endometriosis of right ureter
N80.A52	Deep endometriosis of left ureter
N80.A53	Deep endometriosis of bilateral ureters
N80.A59	Deep endometriosis of unspecified ureter
N80.A61	Endometriosis of right ureter, unspecified depth
N80.A62	Endometriosis of left ureter, unspecified depth
N80.A63	Endometriosis of bilateral ureters, unspecified depth
N80.A69	Endometriosis of unspecified ureter, unspecified depth
N80.B1	Endometriosis of pleura
N80.B2	Endometriosis of lung
N80.B31	Superficial endometriosis of diaphragm
N80.B32	Deep endometriosis of diaphragm
N80.B39	Endometriosis of diaphragm, unspecified depth
N80.B4	Endometriosis of the pericardial space
N80.B5	Endometriosis of the mediastinal space
N80.B6	Endometriosis of cardiothoracic space
N80.C0	Endometriosis of the abdomen, unspecified
N80.C2	Endometriosis of the umbilicus
N80.C3	Endometriosis of the inguinal canal
N80.C4	Endometriosis of extra-pelvic abdominal peritoneum
N80.C9	Endometriosis of other site of abdomen
N80.C10	Endometriosis of the anterior abdominal wall, subcutaneous tissue
N80.C11	Endometriosis of the anterior abdominal wall, fascia and muscular layers

N80.C19	Endometriosis of the anterior abdominal wall, unspecified depth
N80.D0	Endometriosis of the pelvic nerves, unspecified
N80.D1	Endometriosis of the sacral splanchnic nerves
N80.D2	Endometriosis of the sacral nerve roots
N80.D3	Endometriosis of the obturator nerve
N80.D4	Endometriosis of the sciatic nerve
N80.D5	Endometriosis of the pudendal nerve
N80.D6	Endometriosis of the femoral nerve
N80.D9	Endometriosis of other pelvic nerve

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Version Reissued Date: N/A

Policy Attachment

Attachment to Policy # 08.01.33j

Attachment: D

Policy #: 08.01.33j

Description: LEUPROLIDE ACETATE (ELIGARD and LUPRON DEPOT- J9217)

Title: Leuprolide Acetate (Camcevi™, Eligard®, Fensolvi®, Lupron Depot®)

MEDICALLY NECESSARY

C07 Malignant neoplasm of parotid gland
C08.0 Malignant neoplasm of submandibular gland
C08.1 Malignant neoplasm of sublingual gland
C08.9 Malignant neoplasm of major salivary gland, unspecified
C48.1 Malignant neoplasm of specified parts of peritoneum
C48.2 Malignant neoplasm of peritoneum, unspecified
C48.8 Malignant neoplasm of overlapping sites of retroperitoneum and peritoneum
C50.011 Malignant neoplasm of nipple and areola, right female breast
C50.012 Malignant neoplasm of nipple and areola, left female breast
C50.021 Malignant neoplasm of nipple and areola, right male breast
C50.022 Malignant neoplasm of nipple and areola, left male breast

C50.111 Malignant neoplasm of central portion of right female breast
C50.112 Malignant neoplasm of central portion of left female breast
C50.121 Malignant neoplasm of central portion of right male breast
C50.122 Malignant neoplasm of central portion of left male breast
C50.211 Malignant neoplasm of upper-inner quadrant of right female breast
C50.212 Malignant neoplasm of upper-inner quadrant of left female breast
C50.221 Malignant neoplasm of upper-inner quadrant of right male breast
C50.222 Malignant neoplasm of upper-inner quadrant of left male breast
C50.311 Malignant neoplasm of lower-inner quadrant of right female breast
C50.312 Malignant neoplasm of lower-inner quadrant of left female breast
C50.321 Malignant neoplasm of lower-inner quadrant of right male breast
C50.322 Malignant neoplasm of lower-inner quadrant of left male breast
C50.411 Malignant neoplasm of upper-outer quadrant of right female breast
C50.412 Malignant neoplasm of upper-outer quadrant of left female breast
C50.421 Malignant neoplasm of upper-outer quadrant of right male breast
C50.422 Malignant neoplasm of upper-outer quadrant of left male breast
C50.511 Malignant neoplasm of lower-outer quadrant of right female breast
C50.512 Malignant neoplasm of lower-outer quadrant of left female breast
C50.521 Malignant neoplasm of lower-outer quadrant of right male breast
C50.522 Malignant neoplasm of lower-outer quadrant of left male breast
C50.611 Malignant neoplasm of axillary tail of right female breast
C50.612 Malignant neoplasm of axillary tail of left female breast
C50.621 Malignant neoplasm of axillary tail of right male breast
C50.622 Malignant neoplasm of axillary tail of left male breast
C50.811 Malignant neoplasm of overlapping sites of right female breast
C50.812 Malignant neoplasm of overlapping sites of left female breast
C50.821 Malignant neoplasm of overlapping sites of right male breast
C50.822 Malignant neoplasm of overlapping sites of left male breast
C50.911 Malignant neoplasm of unspecified site of right female breast
C50.912 Malignant neoplasm of unspecified site of left female breast
C50.921 Malignant neoplasm of unspecified site of right male breast
C50.922 Malignant neoplasm of unspecified site of left male breast
C56.1 Malignant neoplasm of right ovary
C56.2 Malignant neoplasm of left ovary
C56.3 Malignant neoplasm of bilateral ovaries
C57.01 Malignant neoplasm of right fallopian tube
C57.02 Malignant neoplasm of left fallopian tube
C57.11 Malignant neoplasm of right broad ligament
C57.12 Malignant neoplasm of left broad ligament
C57.21 Malignant neoplasm of right round ligament
C57.22 Malignant neoplasm of left round ligament

C57.3 Malignant neoplasm of parametrium
C57.4 Malignant neoplasm of uterine adnexa, unspecified
C61 Malignant neoplasm of prostate
C79.81 Secondary malignant neoplasm of breast
C79.82 Secondary malignant neoplasm of genital organs
D25.0 Submucous leiomyoma of uterus
D25.1 Intramural leiomyoma of uterus
D25.2 Subserosal leiomyoma of uterus
D25.9 Leiomyoma of uterus, unspecified
E22.8 Other hyperfunction of pituitary gland
E30.1 Precocious puberty
F64.0 Transsexualism
F64.1 Dual role transvestism
F64.2 Gender identity disorder of childhood
F64.8 Other gender identity disorders
F64.9 Gender identity disorder, unspecified
N80.0 Endometriosis of uterus
N80.6 Endometriosis in cutaneous scar
N80.8 Other endometriosis
N80.9 Endometriosis, unspecified
N80.101 Endometriosis of right ovary, unspecified depth
N80.102 Endometriosis of left ovary, unspecified depth
N80.103 Endometriosis of bilateral ovaries, unspecified depth
N80.111 Superficial endometriosis of right ovary
N80.112 Superficial endometriosis of left ovary
N80.113 Superficial endometriosis of bilateral ovaries
N80.121 Deep endometriosis of right ovary
N80.122 Deep endometriosis of left ovary
N80.123 Deep endometriosis of bilateral ovaries
N80.201 Endometriosis of right fallopian tube, unspecified depth
N80.202 Endometriosis of left fallopian tube, unspecified depth
N80.203 Endometriosis of bilateral fallopian tubes, unspecified depth
N80.211 Superficial endometriosis of right fallopian tube
N80.212 Superficial endometriosis of left fallopian tube
N80.213 Superficial endometriosis of bilateral fallopian tubes
N80.221 Deep endometriosis of right fallopian tube
N80.222 Deep endometriosis of left fallopian tube
N80.223 Deep endometriosis of bilateral fallopian tubes
N80.30 Endometriosis of pelvic peritoneum, unspecified
N80.311 Superficial endometriosis of the anterior cul-de-sac
N80.312 Deep endometriosis of the anterior cul-de-sac

N80.319	Endometriosis of the anterior cul-de-sac, unspecified depth
N80.321	Superficial endometriosis of the posterior cul-de-sac
N80.322	Deep endometriosis of the posterior cul-de-sac
N80.329	Endometriosis of the posterior cul-de-sac, unspecified depth
N80.331	Superficial endometriosis of the right pelvic sidewall
N80.332	Superficial endometriosis of the left pelvic sidewall
N80.333	Superficial endometriosis of bilateral pelvic sidewall
N80.341	Deep endometriosis of the right pelvic sidewall
N80.342	Deep endometriosis of the left pelvic sidewall
N80.343	Deep endometriosis of the bilateral pelvic sidewall
N80.351	Endometriosis of the right pelvic sidewall, unspecified depth
N80.352	Endometriosis of the left pelvic sidewall, unspecified depth
N80.353	Endometriosis of bilateral pelvic sidewall, unspecified depth
N80.361	Superficial endometriosis of the right pelvic brim
N80.362	Superficial endometriosis of the left pelvic brim
N80.363	Superficial endometriosis of bilateral pelvic brim
N80.371	Deep endometriosis of the right pelvic brim
N80.372	Deep endometriosis of the left pelvic brim
N80.373	Deep endometriosis of bilateral pelvic brim
N80.381	Endometriosis of the right pelvic brim, unspecified depth
N80.382	Endometriosis of the left pelvic brim, unspecified depth
N80.383	Endometriosis of bilateral pelvic brim, unspecified depth
N80.391	Superficial endometriosis of the pelvic peritoneum, other specified sites
N80.392	Deep endometriosis of the pelvic peritoneum, other specified sites
N80.399	Endometriosis of the pelvic peritoneum, other specified sites, unspecified depth
N80.3A1	Superficial endometriosis of the right uterosacral ligament
N80.3A2	Superficial endometriosis of the left uterosacral ligament
N80.3A3	Superficial endometriosis of the bilateral uterosacral ligament(s)
N80.3B1	Deep endometriosis of the right uterosacral ligament
N80.3B2	Deep endometriosis of the left uterosacral ligament
N80.3B3	Deep endometriosis of bilateral uterosacral ligament(s)
N80.3C1	Endometriosis of the right uterosacral ligament, unspecified depth
N80.3C2	Endometriosis of the left uterosacral ligament, unspecified depth
N80.3C3	Endometriosis of bilateral uterosacral ligament(s), unspecified depth
N80.40	Endometriosis of rectovaginal septum, unspecified involvement of vagina
N80.41	Endometriosis of rectovaginal septum without involvement of vagina
N80.42	Endometriosis of rectovaginal septum with involvement of vagina
N80.50	Endometriosis of intestine, unspecified
N80.511	Superficial endometriosis of the rectum
N80.512	Deep endometriosis of the rectum
N80.519	Endometriosis of the rectum, unspecified depth

N80.521	Superficial endometriosis of the sigmoid colon
N80.522	Deep endometriosis of the sigmoid colon
N80.529	Endometriosis of the sigmoid colon, unspecified depth
N80.531	Superficial endometriosis of the cecum
N80.532	Deep endometriosis of the cecum
N80.539	Endometriosis of the cecum, unspecified depth
N80.541	Superficial endometriosis of the appendix
N80.542	Deep endometriosis of the appendix
N80.549	Endometriosis of the appendix, unspecified depth
N80.551	Superficial endometriosis of other parts of the colon
N80.552	Deep endometriosis of other parts of the colon
N80.559	Endometriosis of other parts of the colon, unspecified depth
N80.561	Superficial endometriosis of the small intestine
N80.562	Deep endometriosis of the small intestine
N80.569	Endometriosis of the small intestine, unspecified depth
N80.A0	Endometriosis of bladder, unspecified depth
N80.A1	Superficial endometriosis of bladder
N80.A2	Deep endometriosis of bladder
N80.A41	Superficial endometriosis of right ureter
N80.A42	Superficial endometriosis of left ureter
N80.A43	Superficial endometriosis of bilateral ureters
N80.A51	Deep endometriosis of right ureter
N80.A52	Deep endometriosis of left ureter
N80.A53	Deep endometriosis of bilateral ureters
N80.A61	Endometriosis of right ureter, unspecified depth
N80.A62	Endometriosis of left ureter, unspecified depth
N80.A63	Endometriosis of bilateral ureters, unspecified depth
N80.B1	Endometriosis of pleura
N80.B2	Endometriosis of lung
N80.B31	Superficial endometriosis of diaphragm
N80.B32	Deep endometriosis of diaphragm
N80.B39	Endometriosis of diaphragm, unspecified depth
N80.B4	Endometriosis of the pericardial space
N80.B5	Endometriosis of the mediastinal space
N80.B6	Endometriosis of cardiothoracic space
N80.C0	Endometriosis of the abdomen, unspecified
N80.C2	Endometriosis of the umbilicus
N80.C3	Endometriosis of the inguinal canal
N80.C4	Endometriosis of extra-pelvic abdominal peritoneum
N80.C9	Endometriosis of other site of abdomen

N80.C10	Endometriosis of the anterior abdominal wall, subcutaneous tissue
N80.C11	Endometriosis of the anterior abdominal wall, fascia and muscular layers
N80.C19	Endometriosis of the anterior abdominal wall, unspecified depth
N80.D0	Endometriosis of the pelvic nerves, unspecified
N80.D1	Endometriosis of the sacral splanchnic nerves
N80.D2	Endometriosis of the sacral nerve roots
N80.D3	Endometriosis of the obturator nerve
N80.D4	Endometriosis of the sciatic nerve
N80.D5	Endometriosis of the pudendal nerve
N80.D6	Endometriosis of the femoral nerve
N80.D9	Endometriosis of other pelvic nerve

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Version Issued Date: 12/30/2024

Version Reissued Date: N/A

Title: Lifileucel (Amtagvi™)

MEDICALLY NECESSARY

Lifileucel (Amtagvi) as a component of tumor-infiltrating lymphocyte (TIL) therapy is considered medically necessary and, therefore, covered in adult individuals with unresectable or metastatic melanoma* and **all** of the following:

- as second-line or subsequent systemic therapy** as National Comprehensive Cancer Network (NCCN)-preferred therapy after progression on **both**
 - PD-1 blocking antibody (e.g., Keytruda, Opdivo) and
 - BRAF inhibitor (e.g., Braftovi, Tafinlar, Zelboraf) with or without a MEK inhibitor (e.g., Cotellic, Mekinist, Mektovi) if BRAF V600 mutation positive.
- Eastern Cooperative Oncology Group (ECOG) performance status score of PS 0 or 1
- The individual has at least one resectable lesion (or aggregate of lesions resected) of a minimum 1.5 cm in diameter, postresection, to generate cell therapy
- The individual has adequate and stable kidney, pulmonary and cardiac function
- The individual does not have clinically significant active systemic infection
- The individual does not have uncontrolled brain metastasis
- The individual does not have uveal or ocular melanoma
- The individual does not have a history of prior cell transfer therapy

Note: one-time lifileucel TIL cell therapy.

*Metastatic disease includes stage III unresectable/borderline resectable disease with clinically positive node(s) or clinical satellite/in-transit metastases, or as well as unresectable/borderline resectable local satellite/in-transit recurrence, unresectable nodal recurrence, and widely disseminated distant metastatic disease.

**Systemic therapy is preferred for unresectable or widely disseminated distant metastatic disease.

MANDATES

PENNSYLVANIA MEMBERS

In accordance with the Commonwealth of Pennsylvania's Act 6 of 2020 or Fair Access to Cancer Treatment Act, for members who are enrolled in Pennsylvania commercial products who have Stage 4, advanced metastatic cancer, refer to the Medical Policy titled "Coverage of Anticancer Prescription Oral and Injectable Drugs and Biologics and Supportive Agents" (08.01.08) for additional information regarding the applicable coverage of drugs and biologics.

EXPERIMENTAL/INVESTIGATIONAL

All other uses for lifileucel (Amtagvi) not identified in this policy are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

NOT ELIGIBLE FOR SEPARATE REIMBURSEMENT

The harvesting and preparation of blood-derived T lymphocytes and the receipt and preparation of T cells are not eligible for separate reimbursement from the TIL administration.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Duration of authorization: 1 month

Version Effective Date: 10/21/2024

Title: Loncastuximab tesirine-lpyl (Zynlonta®)

MEDICALLY NECESSARY

Loncastuximab tesirine (Zynlonta), administered by intravenous (IV) infusion, is considered medically necessary and, therefore, covered for the treatment of adult individuals with relapsed or refractory large B-cell lymphoma (including partial response, no response, or progressive disease but excluding bulky disease [tumor ≥ 10 cm in longest dimension] and active central nervous system lymphoma) after two or more lines of systemic therapy including any of the following types of lymphoma:

- Diffuse large B-cell lymphoma (DLBCL) not otherwise specified (NOS)
- High-grade B-cell lymphoma including NOS, translocations of MYC and BCL2 and/or BCL6 (double/triple hit lymphoma)
- Acquired immunodeficiency syndrome (AIDS)/human immunodeficiency virus (HIV)-related DLBCL, primary effusion lymphoma, human herpesvirus (HHV) 8–positive DLBCL
- Posttransplant lymphoproliferative disorders

Loncastuximab tesirine (Zynlonta), administered by IV infusion, is considered medically necessary and, therefore, covered for the treatment of adult individuals with histologic transformation of a low-grade or indolent lymphoma to DLBCL* in noncandidates for hematopoietic stem cell transplant (HSCT), who have been previously treated with an anthracycline-based regimen, for either of the following:

- As additional therapy for partial response, no response, or progressive disease following chemoimmunotherapy
- For individuals who have received multiple prior therapies for indolent or transformed disease

*Including follicular lymphoma (grade 1–2), extranodal marginal zone lymphoma (MZL) of the stomach (formerly called gastric mucosa-associated lymphoid tissue [MALT] lymphoma), extranodal MZL of nongastric sites (noncutaneous) (formerly called nongastric MALT lymphoma [noncutaneous]), splenic MZL, and nodal MZL.

EXPERIMENTAL/INVESTIGATIONAL

All other uses for loncastuximab tesirine (Zynlonta) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on Off-label Coverage for Prescription Drugs and Biologics.

MANDATES

PENNSYLVANIA MEMBERS

In accordance with the Commonwealth of Pennsylvania's Act 6 of 2020 or Fair Access to Cancer Treatment Act, for members who are enrolled in Pennsylvania commercial products who have Stage 4, advanced metastatic cancer, refer to the Medical Policy titled "Coverage of Anticancer Prescription Oral and Injectable Drugs and Biologics and Supportive agents" (08.01.08) for additional information regarding the applicable coverage of drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Duration of authorization: 12 months

Version Effective Date: 10/02/2024

Title: Lovotibeglogene autotemcel (Lyfgenia®)

MEDICALLY NECESSARY

Lyfgenia® (lovotibeglogene autotemcel) is considered medically necessary and, therefore, covered for the treatment of severe sickle cell disease (SCD) in individuals with age ≥ 12 years when ALL of the associated criteria for them are met:

- Individual has diagnosis of severe SCD with one of the following genotypes as confirmed by genetic testing results [(a or b):
 - a. $\beta S/\beta S$;
 - b. $\beta S/\beta 0$;
- Documentation that the individual is a candidate for an allogeneic HSCT, but ineligible due to absence of an appropriate donor (i.e., individual does not have a Human Leukocyte Antigen (HLA)-matched donor; or individual has an HLA-matched donor, but the potential donor is not able or is not willing to donate);
- Individual has not received a prior allogenic hematopoietic stem cell transplant;
- Individual is eligible to receive an autologous hematopoietic stem cell transplant;
- Individual has had been treated with at least ONE pharmacologic treatment for sickle cell disease (e.g., pharmacologic treatment for sickle cell disease include hydroxyurea, Lglutamine, Adakveo (crizanlizumab-tmca intravenous infusion), and Oxbryta (voxelotor tablets and tablets for oral suspension));
- While receiving appropriate standard treatment for sickle cell disease, individual had at least four severe vaso-occlusive crises or events (VOCs/VOEs) in the previous two years, which can be defined by one or more of the following (i, ii, iii, iv, or v):
 - i. An episode of acute pain that resulted in a visit to a medical facility which required administration of at least ONE of the following (a or b):
 - a) Intravenous opioid; OR
 - b) Intravenous nonsteroidal anti-inflammatory drug;

ii. Acute chest syndrome (acute chest syndrome is defined by the presence of a new pulmonary infiltrate associated with pneumonia-like symptoms (e.g., chest pain, fever [$> 99.5^{\circ}\text{F}$], tachypnea, wheezing or cough, or findings upon lung auscultation);

iii. Acute hepatic sequestration (acute hepatic sequestration is defined by a sudden increase in liver size associated with pain in the right upper quadrant, abnormal results of liver function test not due to biliary tract disease, and the reduction of hemoglobin concentration by ≥ 2 g/dL below the baseline value);

iv. Acute splenic sequestration (acute splenic sequestration is defined by an enlarged spleen, left upper quadrant pain, and an acute decrease in hemoglobin concentration of ≥ 2 g/dL below the baseline value);

v. Acute priapism lasting > 2 hours and requiring a visit to a medical facility;

- The gene therapy is prescribed by a hematologist or a stem cell transplant physician;
AND
- Individual has not received any gene therapy and/or is not under consideration for treatment for another gene therapy for sickle cell disease.

EXPERIMENTAL/INVESTIGATIONAL

All other uses, including when the above criteria are not met, for Lyfgenia® (lovotibeglogene autotemcel) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Duration of authorization: 12 months

Version Effective Date: 01/01/2025

Title: Lumasiran (Oxlumo®)

MEDICALLY NECESSARY

INITIAL APPROVAL

Lumasiran (Oxlumo®) is considered medically necessary and, therefore, covered for the treatment of primary hyperoxaluria type 1 (PH1) to lower urinary oxalate levels in pediatric and adult individuals when ALL of the following criteria are met:

- Diagnosis of PH1 confirmed by identification of biallelic pathogenic variants in alanine:glyoxylate aminotransferase (*AGT* or *AGXT*) gene OR liver biopsy demonstrating AGT deficiency.
- Presence of one of the following, which are associated with clinical presentation of PH1
 - Elevated urine oxalate excretion (body surface area–normalized daily urine oxalate excretion output ≥ 0.7 mmol/1.73 m²)
 - Elevated plasma oxalate concentration >20 μ mol/L or >1.76 mg/L
 - Urine oxalate excretion:creatinine ratio above age-specific upper limit of normal
- Individual has not received a liver transplant.
- Prescribed by or in consultation with a nephrologist, urologist, geneticist, or any healthcare provider with expertise in treating PH1.

CONTINUATION OF TREATMENT

Continuation of lumasiran (Oxlumo®) is considered medically necessary and, therefore, covered when ALL of the following requirements are met:

- Individual continues to meet the initial treatment criteria cited above.
- Documented evidence to support clinically meaningful response to therapy from pretreatment baseline (e.g., decreased urinary oxalate concentrations, decreased urinary oxalate:creatinine ratio, decreased plasma oxalate concentrations, improvement, stabilization or slowed worsening of nephrocalcinosis, renal stone events, renal impairment or systemic calcinosis).
- Does not exceed US Food and Drug Administration–approved maintenance dose.

NOTE: Evio has been selected by the Company to administer clinical outcomes monitoring for patients receiving certain high-cost drug therapies. Lumasiran (Oxlumo®) is included in the portfolio of high-cost drug therapies for which Evio will be tracking clinical outcomes. If a patient meets all medical policy provisions and is approved to receive treatment, the requesting professional provider or member must attest and agree to providing clinical outcomes data and information via Evio's secure web portal as requested.

EXPERIMENTAL/INVESTIGATIONAL

Lumasiran (Oxlumo) is considered experimental/investigational and, therefore, not covered when the above criteria are not met and for all other indications unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Duration of authorization: 12 months

Version Effective Date: 12/02/2024

Title: Lurbinectedin (Zepzelca®)

MEDICALLY NECESSARY

Lurbinectedin (Zepzelca®) is considered medically necessary and, therefore, covered as a single agent for the subsequent treatment of adult individuals with advanced or metastatic small cell lung cancer (SCLC) when all of the following criteria are met:

- Individual has had disease progression on or after platinum-based chemotherapy
- Individual is classified as being in one of the following stages:
 - Relapse following complete or partial response or stable disease with primary treatment
 - Primary progressive disease
- Individual has an Eastern Cooperative Oncology Group (ECOG) performance status of 0–2

MANDATES

PENNSYLVANIA MEMBERS

In accordance with the Commonwealth of Pennsylvania's Act 6 of 2020 or Fair Access to Cancer Treatment Act, for members who are enrolled in Pennsylvania commercial products who have Stage 4, advanced metastatic cancer, refer to the Medical Policy titled "Coverage of Anticancer Prescription Oral and Injectable Drugs and Biologics and Supportive agents" (08.01.08) for additional information regarding the applicable coverage of drugs and biologics.

EXPERIMENTAL/INVESTIGATIONAL

All other uses for lurbinectedin (Zepzelca) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the service.

Duration of authorization: 12 months

Version Effective Date: 05/28/2025

Title: Luspatercept-aamt (Reblozyl®)

MEDICALLY NECESSARY

β-THALASSEMIA

Initial Therapy for β-thalassemia

Luspatercept-aamt (Reblozyl) is considered medically necessary and, therefore, covered for the treatment of anemia in adult individuals with β-thalassemia who require regular red blood cell (RBC) transfusions, when all of the following criteria, including dosing and frequency, are met:

- Documented diagnosis of β-thalassemia, hemoglobin E/β-thalassemia, or β-thalassemia combined with α-thalassemia confirmed by one of the following tests:
 - Molecular genetic testing that reveals pathogenic variation(s) in the *HBB* gene causing β-thalassemia
 - Hemoglobin electrophoresis
- Individual has a baseline hemoglobin (Hgb) level 11 g/dL or less
- There is documentation the individual is transfusion-dependent, requiring regular RBC transfusions (i.e., at least six units of RBC in the previous 24 weeks and no transfusion-free period for ≥35 days during that period).
- Treatment will not be combined with a gene therapy used to treat β-thalassemia.
- Dosing and frequency: 1 mg/kg as a subcutaneous injection every 3 weeks. If a reduction in RBC transfusion burden is not achieved after at least two consecutive doses (6 weeks), luspatercept-aamt (Reblozyl) will be covered up to a maximum dose of 1.25 mg/kg every 3 weeks.

Continuation Therapy for β-thalassemia

Continuation of luspatercept-aamt (Reblozyl) is considered medically necessary and, therefore, covered for individuals who have demonstrated a documented reduction in the number of transfusions compared to baseline.

MYELODYSPLASTIC SYNDROMES (MYELODYSPLASTIC NEOPLASMS) (MDS)

Myelodysplastic Syndromes

(Myelodysplastic Neoplasms) (MDS) and Myelodysplastic/Myeloproliferative Neoplasms (MDS/MPN)

Initial Therapy for MDS

Luspatercept-aamt (Reblozyl) is considered medically necessary and, therefore, covered for the treatment of anemia in adult individuals with myelodysplastic syndromes (myelodysplastic neoplasms) (MDS) and myelodysplastic/myeloproliferative neoplasms (MDS/MPN) when all of the following criteria, including dosing and frequency, are met:

- Individual has presence of the long arm of chromosome 5 (i.e., no del [5q])
- Individual has documented diagnosis of one of the following:
 - Lower risk MDS (defined as International Prognostic Scoring System [IPSS-R] Very Low, Low, Intermediate) with one of the following:
 - Ring sideroblasts (RS) 15% or greater (or RS $\geq 5\%$ with an SF3B1 mutation) with or without prior erythropoiesis-stimulating agent (ESA) therapy
 - RS less than 15% (or RS $< 5\%$ with an SF3B1 mutation) when serum erythropoietin levels are 500 mU/mL or less
 - Following no response to ESAs, despite adequate iron stores (unless contraindication(s) or intolerance(s) to ESAs) (National Comprehensive Cancer Network [NCCN]-preferred regimen)
 - Myelodysplastic/Myeloproliferative Neoplasms (MDS/MPNs) Overlap Neoplasms with SF3B1 mutation and thrombocytosis (i.e., platelets $\geq 450 \times 10^9/L$), and RS 15% or greater
- Individual has a baseline hemoglobin (Hgb) level 11 g/dL or less
- There is documentation that the individual is transfusion-dependent, requiring regular RBC transfusions (i.e., $\geq$ two units every 8 weeks)
 - Exception if there is documentation that the individual can't receive regular blood transfusions (e.g., religious reasons, blood shortages)
- Dosing and frequency: 1 mg/kg as a subcutaneous injection every 3 weeks. If individual is not RBC transfusion-free after at least two consecutive doses, an increased dose of 1.33 mg/kg every 3 weeks will be covered. If individual is still not RBC transfusion-free

after at least two more consecutive doses, an increased maximum dose of 1.75 mg/kg every 3 weeks will be covered.

Continuation Therapy for MDS

Continuation of luspatercept-aamt (Reblozyl) is considered medically necessary and, therefore, covered for individuals who have demonstrated at least one of the following, compared to baseline:

- Increase in RBC transfusion independence (transfusion-free period)
- Increase in hemoglobin levels
- Reduction in transfusion burden (the amount of units required with each red cell transfusion)

Myelofibrosis

Initial Therapy for Myelofibrosis

Luspatercept-aamt (Reblozyl) is considered medically necessary and, therefore, covered for the treatment of myelofibrosis-associated anemia when all of the following criteria, including dosing and frequency, are met:

- The individual has documentation of one of the following features:
 - Presence of symptomatic splenomegaly and/or constitutional symptoms (e.g., fever, night sweats, itching, bone pain, and weight loss) currently controlled on a JAK inhibitor, in combination with ruxolitinib (Jakafi)
 - Presence of symptomatic splenomegaly and/or constitutional symptoms not controlled, in combination with ruxolitinib
 - No symptomatic splenomegaly and/or constitutional symptoms
- Individual has a baseline hemoglobin (Hgb) level 11 g/dL or less
- Dosing and frequency: 1 mg/kg as a subcutaneous injection every 3 weeks. If individual is not RBC transfusion-free after at least two consecutive doses, an increased dose of 1.33 mg/kg every 3 weeks will be covered. If individual is still not RBC transfusion-free after at least two more consecutive doses, an increased maximum dose of 1.75 mg/kg every 3 weeks will be covered.

Continuation Therapy for Myelofibrosis

Continuation of luspatercept-aamt (Reblozyl) is considered medically necessary and, therefore, covered for individuals who have demonstrated at least one of the following, compared to baseline:

- Increase in RBC transfusion independence (transfusion-free period)
- Increase in hemoglobin levels
- Reduction in transfusion burden (the amount of units required with each red cell transfusion)

NOT MEDICALLY NECESSARY

Continuation therapy with luspatercept-aamt (Reblozyl) in individuals with β -thalassemia is considered not medically necessary and, therefore, not covered for individuals who do not experience a decrease in transfusion burden after five doses (two doses at 1 mg/kg and three doses at 1.25 mg/kg). The available published peer-reviewed literature does not support its use in the treatment of this disease.

Continuation therapy with luspatercept-aamt (Reblozyl) in individuals with MDS, MDS/MPN, or myelofibrosis is considered not medically necessary and, therefore, not covered for individuals who do not experience a decrease in transfusion burden after at least three consecutive doses of the maximum dosage of 1.75 mg/kg administered at 3-week intervals. The available published peer-reviewed literature does not support its use in the treatment of this disease.

When molecular genetic testing reveals established benign variation(s) or wild-type genotype in the *HBB* gene, luspatercept-aamt (Reblozyl) is considered not medically necessary and, therefore, not covered because the available published peer-reviewed literature does not support its use in the treatment of this disease.

EXPERIMENTAL/INVESTIGATIONAL

All other uses for luspatercept-aamt (Reblozyl), including those listed below, are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

- Individuals with hemoglobin S/ β -thalassemia or α -thalassemia
- Individuals with non-transfusion-dependent β -thalassemia

- As a substitute for RBC transfusions in those who require immediate correction of anemia

When molecular genetic testing reveals likely pathogenic or variations of unknown significance (VUS) in the *HBB* gene, the use of luspatercept-aamt (Reblozyl) is considered experimental/investigational and, therefore, not covered because the safety and/or effectiveness of this service cannot be established by review of the available published peer-reviewed literature.

DOSING AND FREQUENCY REQUIREMENTS

The Company reserves the right to modify the Dosing and Frequency Requirements listed in this policy to ensure consistency with the most recently published recommendations for the use of luspatercept-aamt (Reblozyl). Changes to these guidelines are based on a consensus of information obtained from resources such as, but not limited to: the US Food and Drug Administration (FDA); Company-recognized authoritative pharmacology compendia; or published peer-reviewed clinical research. The professional provider must supply supporting documentation (i.e., published peer-reviewed literature) in order to request coverage for an amount of luspatercept-aamt (Reblozyl) outside of the Dosing and Frequency Requirements listed in this policy. For a list of Company-recognized pharmacology compendia, view our policy on off-label coverage for prescription drugs and biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of this drug. If the member's dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider must submit those changes to the Company for a new approval based on those changes as part of the utilization management activities. The Company reserves the right to conduct post-payment review and audit procedures for any claims submitted for luspatercept-aamt (Reblozyl).

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the service.

When coverage of luspatercept-aamt (Reblozyl) is requested outside of the Dosing and Frequency Requirements listed in this policy, the prescribing professional provider must supply

documentation (i.e., published peer-reviewed literature) to the Company that supports this request.

Duration of authorization: 12 months

Version Effective Date: 01/17/2025

Title: Lutathera® (Lutetium Lu 177 Dotatate) (Independence Administrators)

MEDICALLY NECESSARY

Lutathera® (Lutetium Lu 177 Dotatate) is considered medically necessary and, therefore, covered in adult and pediatric individuals ages 12 years and older, for the treatment of low- (G1), intermediate- (G2), or high-grade (G3) well-differentiated neuroendocrine tumors (NET) who have progressed on somatostatin analogues (SSAs) when BOTH of the following are met:

- ONE of the following indications:
 - Inoperable or metastatic somatostatin receptor–positive gastroenteropancreatic NETs (GEP-NETs) of the pancreas, foregut, midgut, and hindgut
 - Inoperable or metastatic somatostatin receptor–positive bronchopulmonary or thymic tumors or pheochromocytomas and paragangliomas
- ALL of the following are met:
 - For well-differentiated G1 or G2 NETs with a Ki67 <20 percent OR well-differentiated G3 NETs with a Ki-67 <55 percent
 - Positive somatostatin receptor scintigraphy with correlative magnetic resonance imaging (MRI) or computed tomography (CT) imaging of metastatic measurable disease or 68-Ga-dotatate positron emission tomography (PET) scan positive for metastatic disease
 - In the absence of metastatic disease, a surgical or medical consult documenting the reason for inoperability
 - Progression of disease following treatment with SSA therapy
 - Serum creatine <1.7 mg/dl or creatinine clearance is <50 ml/min
 - Hemoglobin >8 g/dL; white blood cells 2000 mm³ or higher; platelets 75,000 mm³ or higher

EXPERIMENTAL/INVESTIGATIONAL

Lutathera (Lutetium Lu 177 Dotatate) is considered experimental/investigational and, therefore, not covered for poorly differentiated tumors and for G3 well-differentiated tumors with a Ki-67 of 55 percent or greater.

Lutathera (Lutetium Lu 177 Dotatate) is considered experimental/investigational and, therefore, not covered in all other situations in which the above criteria are not met because the safety and/or effectiveness of this service cannot be established by review of the available published peer-reviewed literature.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the health care professional's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the service.

Duration of authorization: 12 months

Version Effective Date: 01/27/2025

Title: Maintenance Treatment of Opioid or Alcohol Use Disorder

MEDICALLY NECESSARY

METHADONE

Methadone maintenance therapy is considered medically necessary and, therefore, covered for individuals with opioid use disorder (OUD)* when all of the following criteria are met:

- The individual is diagnosed with moderate or severe OUD per the *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition text revision (DSM-5-TR).
- The individual is free of an urgent or emergent medical or psychiatric problem(s).
- For individuals less than 18 years of age, both of the following criteria must be met:
 - Documented history of two or more previous unsuccessful withdrawal management attempts in the past 12 months
 - Parental consent
- The individual is able to give informed consent.
- The individual has a documented history of OUD for at least 1 year before admission for treatment unless one of the following is present:
 - The individual was released from a penal institution within 6 months.
 - The individual is confirmed to be pregnant per the program's professional provider and there is documentation that the individual is under the care of an obstetrician.
 - The individual previously participated in documented opioid treatment in the past 2 years.
 - For an individual who is less than 18 years of age, a documented history of two or more previous unsuccessful withdrawal management attempts in the past 12 months
- There is documentation that the professional provider is certified by the Substance Abuse and Mental Health Services Administration (SAMHSA).
- The professional provider attests that the member cannot be treated safely or effectively in a level of care less intensive than an opioid treatment program (OTP).
- The individual will receive counseling or psychotherapy.

*Methadone for OUD must be dispensed in a licensed OTP that adheres to all federal guidelines.

BUPRENORPHINE (PROBUPHINE®) IMPLANTS

Buprenorphine (Probuphine) implants administered subdermally into the inner side of the upper arm as four implants for a period of 6 months are considered medically necessary and, therefore, covered for the maintenance treatment of opioid dependence when **all** of the following criteria are met:

- The individual has a documented diagnosis of an OUD, as per (*DSM-5 TR*).
- The individual has achieved and sustained prolonged clinical stability on low to moderate doses of a transmucosal buprenorphine-containing product (i.e., doses of no more than 8 mg per day of buprenorphine (Subutex) or buprenorphine and naloxone (Suboxone) sublingual tablet or generic equivalent) for 3 months or longer without any need for supplemental dosing or adjustments.
- The individual has not had a positive urine drug screening for illicit opioids within 90 days prior to the administration of implants.
- The individual has shown compliance with scheduled and random urine drug screening.

Continuation of Therapy with Buprenorphine (Probuphine) Implants

If continued therapy is required, another set of implants is considered medically necessary and, therefore, covered when the above criteria have been met and when the implants will be administered in the opposite arm, for a maximum of two sets of implants per lifetime (i.e., one set of implants per arm).

Provider Requirements

Providers must be in compliance with all of the criteria outlined in the Risk Evaluation and Mitigation Strategies (REMS) program, including the completion of the required live training.

Prescribers must have qualifications that include a current, valid state medical license.

BUPRENORPHINE (SUBLOCADE™) INJECTION

Buprenorphine (Sublocade) extended-release subcutaneous injection administered monthly (with a minimum of 26 days between doses) is considered medically necessary and, therefore, covered for the treatment of moderate to severe OUD when **all** of the following criteria are met:

- The individual has a documented diagnosis of an OUD, as per *DSM-5 TR*.
- The individual has initiated treatment with a transmucosal buprenorphine-containing product delivering the equivalent of 8 to 24 mg of buprenorphine daily, followed by dose adjustment for a minimum of 7 days. The individual is clinically stable on this dose.

- The individual is not concurrently receiving supplemental dosing with buprenorphine products.

Continuation of Therapy with Buprenorphine (Sublocade) Injection

If continued therapy is required, buprenorphine (Sublocade) injection is considered medically necessary and, therefore, covered when the above criteria have been met.

Provider Requirements

Providers must be in compliance with all of the criteria outlined in the REMS program.

Prescribers must have qualifications that include a current, valid state medical license.

NALTREXONE (VIVITROL®) INJECTION

Alcohol Use Disorder

Naltrexone (Vivitrol®) intramuscular (IM) injection administered every 4 weeks (or monthly) is considered medically necessary and, therefore, covered for the treatment of alcohol dependence in individuals able to abstain from alcohol when **all** of the following criteria are met:

- The individual has a documented diagnosis of alcohol use disorder, as per (DSM-5-TR)
- The individual has abstained from alcohol prior to naltrexone (Vivitrol®) administration

Continuation of Therapy with Naltrexone (Vivitrol)

If continued therapy is required, naltrexone (Vivitrol) is considered medically necessary and, therefore, covered when the above criteria have been met.

Opioid Use Disorder

Naltrexone (Vivitrol) intramuscular (IM) injection administered every 4 weeks (or monthly) is considered medically necessary and, therefore, covered for the prevention of relapse to opioid dependence (following opioid detoxification) when **all** of the following criteria are met:

- The individual has a documented diagnosis of OUD, as per (DSM-5-TR).
- The individual has abstained from opioids at least 7 to 10 days prior to and on the day of naltrexone (Vivitrol) administration.

Continuation of Therapy with Naltrexone (Vivitrol)

If continued therapy is required, naltrexone (Vivitrol) is considered medically necessary and, therefore, covered when the above criteria have been met.

EXPERIMENTAL/INVESTIGATIONAL

All uses other than those described above for buprenorphine (Probuphine) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics. Examples of uses considered experimental/investigational include, but are not limited to the following:

- The individual is a new entrant to buprenorphine treatment.
- The individual has already had one set of implants administered into each arm.
- The individual has not achieved and sustained prolonged clinical stability while being maintained on buprenorphine 8 mg per day or less of a buprenorphine (Subutex) or buprenorphine and naloxone (Suboxone) sublingual tablet or generic equivalent.
- The individual has been tapered to a lower dose of buprenorphine for the sole purpose of transitioning to buprenorphine (Probuphine).
- The individual is currently receiving other opioids.

All other uses than those described above for buprenorphine (Sublocade) injection are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

All other uses than those described above for naltrexone (Vivitrol) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics. Examples of uses considered experimental/investigational include, but are not limited to the following:

- The individual is receiving opioid analgesics.
- The individual currently has physiologic opioid or alcohol dependence, including the use of partial agonists.
- The individual is in acute opioid or alcohol withdrawal.
- The individual has failed the naloxone challenge or has a positive urine screen for opioids.

Naltrexone implants are considered experimental/investigational and, therefore, not covered because the safety and/or effectiveness of this service cannot be established by review of the available published peer-reviewed literature.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office,

hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Duration of authorization: 12 months

Version Effective Date: 01/01/2025

Attachment A: [Maintenance Treatment of Opioid or Alcohol Use Disorder](#)

Policy Attachment

Attachment to Policy # 08.01.37e

Attachment: A

Policy #: 08.01.37e

Description: ICD10 Codes

Title: Maintenance Treatment of Opioid or Alcohol Use Disorder

F10.20 Alcohol dependence, uncomplicated

F10.21 Alcohol dependence, in remission

F10.220 Alcohol dependence with intoxication, uncomplicated

F10.221 Alcohol dependence with intoxication delirium

F10.229 Alcohol dependence with intoxication, unspecified

F10.230 Alcohol dependence with withdrawal, uncomplicated

F10.231 Alcohol dependence with withdrawal delirium

F10.232 Alcohol dependence with withdrawal with perceptual disturbance

F10.239 Alcohol dependence with withdrawal, unspecified

F10.24 Alcohol dependence with alcohol-induced mood disorder

F10.250 Alcohol dependence with alcohol-induced psychotic disorder with delusions

F10.251 Alcohol dependence with alcohol-induced psychotic disorder with hallucinations

F10.259 Alcohol dependence with alcohol-induced psychotic disorder, unspecified

F10.26 Alcohol dependence with alcohol-induced persisting amnestic disorder

F10.27 Alcohol dependence with alcohol-induced persisting dementia

F10.280 Alcohol dependence with alcohol-induced anxiety disorder

F10.281 Alcohol dependence with alcohol-induced sexual dysfunction

F10.282 Alcohol dependence with alcohol-induced sleep disorder

F10.288 Alcohol dependence with other alcohol-induced disorder

F10.29 Alcohol dependence with unspecified alcohol-induced disorder

F11.10 Opioid abuse, uncomplicated

F11.11 Opioid abuse, in remission
F11.120 Opioid abuse with intoxication, uncomplicated
F11.121 Opioid abuse with intoxication delirium
F11.122 Opioid abuse with intoxication with perceptual disturbance
F11.129 Opioid abuse with intoxication, unspecified
F11.13 Opioid abuse with withdrawal
F11.14 Opioid abuse with opioid-induced mood disorder
F11.150 Opioid abuse with opioid-induced psychotic disorder with delusions
F11.151 Opioid abuse with opioid-induced psychotic disorder with hallucinations
F11.159 Opioid abuse with opioid-induced psychotic disorder, unspecified
F11.181 Opioid abuse with opioid-induced sexual dysfunction
F11.182 Opioid abuse with opioid-induced sleep disorder
F11.188 Opioid abuse with other opioid-induced disorder
F11.19 Opioid abuse with unspecified opioid-induced disorder
F11.20 Opioid dependence, uncomplicated
F11.21 Opioid dependence, in remission
F11.220 Opioid dependence with intoxication, uncomplicated
F11.221 Opioid dependence with intoxication delirium
F11.222 Opioid dependence with intoxication with perceptual disturbance
F11.229 Opioid dependence with intoxication, unspecified
F11.23 Opioid dependence with withdrawal
F11.24 Opioid dependence with opioid-induced mood disorder
F11.250 Opioid dependence with opioid-induced psychotic disorder with delusions
F11.251 Opioid dependence with opioid-induced psychotic disorder with hallucinations
F11.259 Opioid dependence with opioid-induced psychotic disorder, unspecified
F11.281 Opioid dependence with opioid-induced sexual dysfunction
F11.282 Opioid dependence with opioid-induced sleep disorder
F11.288 Opioid dependence with other opioid-induced disorder
F11.29 Opioid dependence with unspecified opioid-induced disorder
F11.90 Opioid use, unspecified, uncomplicated
F11.920 Opioid use, unspecified with intoxication, uncomplicated
F11.921 Opioid use, unspecified with intoxication delirium
F11.922 Opioid use, unspecified with intoxication with perceptual disturbance
F11.929 Opioid use, unspecified with intoxication, unspecified
F11.93 Opioid use, unspecified with withdrawal
F11.94 Opioid use, unspecified with opioid-induced mood disorder
F11.950 Opioid use, unspecified with opioid-induced psychotic disorder with delusions
F11.951 Opioid use, unspecified with opioid-induced psychotic disorder with hallucinations
F11.959 Opioid use, unspecified with opioid-induced psychotic disorder, unspecified
F11.981 Opioid use, unspecified with opioid-induced sexual dysfunction
F11.982 Opioid use, unspecified with opioid-induced sleep disorder
F11.988 Opioid use, unspecified with other opioid-induced disorder
F11.99 Opioid use, unspecified with unspecified opioid-induced disorder
O99.320 Drug use complicating pregnancy, unspecified trimester

O99.321 Drug use complicating pregnancy, first trimester
O99.322 Drug use complicating pregnancy, second trimester
O99.323 Drug use complicating pregnancy, third trimester
O99.324 Drug use complicating childbirth
O99.325 Drug use complicating the puerperium

Version Effective Date: 01/01/2025

Version Issued Date: 01/01/2025

Version Reissued Date: N/A

Title: Margetuximab-cmkb (Margenza)

MEDICALLY NECESSARY

MARGETUXIMAB-CMBK (MARGENZA)

Margetuximab-cmkb (Margenza) injection is considered medically necessary and, therefore, covered in combination with chemotherapy for the treatment of adult individuals with human epidermal growth factor receptor 2 (HER2)-positive breast cancer and left ventricular ejection fraction of 50 percent or greater when any of the following criteria are met, including HER2 protein overexpression testing:

- The individual has received two or more prior anti-HER2-based regimens (e.g., trastuzumab, pertuzumab, ado-trastuzumab emtansine, other anti-HER2 therapies) at least one of which was for metastatic disease
- Fourth-line therapy and beyond for individuals with invasive breast cancer in combination with either capecitabine, eribulin, gemcitabine or vinorelbine for individuals with recurrent unresectable (local or regional) or stage IV (M1) and any of the following:
 - hormone receptor-negative
 - hormone receptor-positive with or without endocrine therapy
- Fourth-line therapy and beyond for individuals with inflammatory breast cancer in combination with either capecitabine, eribulin, gemcitabine or vinorelbine for individuals with no response to preoperative systemic therapy, or recurrent unresectable (local or regional) or stage IV (M1) and any of the following:
 - hormone receptor-negative
 - hormone receptor-positive with or without endocrine therapy

CONTINUATION THERAPY

Margetuximab-cmkb (Margenza) is considered medically necessary and, therefore, covered for continuation therapy until disease progression, drug intolerance, or unacceptable toxicity.

NOT MEDICALLY NECESSARY

When FDA-approved diagnostic tests do not reveal HER2 protein overexpression, margetuximab-cmkb (Margenza) is considered not medically necessary and, therefore, not covered because the available published peer-reviewed literature does not support their use in the treatment of those diseases.

EXPERIMENTAL/INVESTIGATIONAL

All other uses of margetuximab-cmkb (Margenza) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company's medical policy on off-label coverage for prescription drugs and biologics

MANDATES

PENNSYLVANIA MEMBERS

In accordance with the Commonwealth of Pennsylvania's Act 6 of 2020 or Fair Access to Cancer Treatment Act, for members who are enrolled in Pennsylvania commercial products who have Stage 4, advanced metastatic cancer, refer to the Medical Policy titled "Coverage of Anticancer Prescription Oral and Injectable Drugs and Biologics and Supportive agents (08.01.08) for additional information regarding the applicable coverage of drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Duration of authorization: 12 months

Version Effective Date: 05/28/2025

Attachment A: [Margetuximab-cmkb \(Margenza\)](#)

Policy Attachment

Attachment to Policy # 08.01.75d

Attachment: A

Policy #: 08.01.75d

Description: ICD 10 Codes

Title: Margetuximab-cmkb (Margenza)

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

ICD10 Medical Codes & Narratives

C50.011 Malignant neoplasm of nipple and areola, right female breast
C50.012 Malignant neoplasm of nipple and areola, left female breast
C50.021 Malignant neoplasm of nipple and areola, right male breast
C50.022 Malignant neoplasm of nipple and areola, left male breast
C50.111 Malignant neoplasm of central portion of right female breast
C50.112 Malignant neoplasm of central portion of left female breast
C50.121 Malignant neoplasm of central portion of right male breast
C50.122 Malignant neoplasm of central portion of left male breast

C50.211 Malignant neoplasm of upper-inner quadrant of right female breast
C50.212 Malignant neoplasm of upper-inner quadrant of left female breast
C50.221 Malignant neoplasm of upper-inner quadrant of right male breast
C50.222 Malignant neoplasm of upper-inner quadrant of left male breast
C50.311 Malignant neoplasm of lower-inner quadrant of right female breast
C50.312 Malignant neoplasm of lower-inner quadrant of left female breast
C50.321 Malignant neoplasm of lower-inner quadrant of right male breast
C50.322 Malignant neoplasm of lower-inner quadrant of left male breast
C50.411 Malignant neoplasm of upper-outer quadrant of right female breast
C50.412 Malignant neoplasm of upper-outer quadrant of left female breast
C50.421 Malignant neoplasm of upper-outer quadrant of right male breast
C50.422 Malignant neoplasm of upper-outer quadrant of left male breast
C50.511 Malignant neoplasm of lower-outer quadrant of right female breast
C50.512 Malignant neoplasm of lower-outer quadrant of left female breast
C50.521 Malignant neoplasm of lower-outer quadrant of right male breast
C50.522 Malignant neoplasm of lower-outer quadrant of left male breast
C50.611 Malignant neoplasm of axillary tail of right female breast
C50.612 Malignant neoplasm of axillary tail of left female breast
C50.621 Malignant neoplasm of axillary tail of right male breast
C50.622 Malignant neoplasm of axillary tail of left male breast
C50.811 Malignant neoplasm of overlapping sites of right female breast
C50.812 Malignant neoplasm of overlapping sites of left female breast
C50.821 Malignant neoplasm of overlapping sites of right male breast
C50.822 Malignant neoplasm of overlapping sites of left male breast
C50.911 Malignant neoplasm of unspecified site of right female breast
C50.912 Malignant neoplasm of unspecified site of left female breast
C50.921 Malignant neoplasm of unspecified site of right male breast
C50.922 Malignant neoplasm of unspecified site of left male breast
C79.81 Secondary malignant neoplasm of breast

Version Effective Date: 05/28/2025

Title: Mirikizumab-mrkz (Omvo^h[™]) for Intravenous Use

MEDICALLY NECESSARY

Mirikizumab-mrkz (Omvo^h[™]) administered via an intravenous (IV) route, is considered medically necessary and, therefore, covered for the treatment of moderately to severely active ulcerative colitis (UC) in adults when **ALL** the following are met:

- Individual has a diagnosis of moderately to severely active ulcerative colitis, as assessed by a validated rating index/scale (e.g., modified Mayo score [MMS])
- Individual is without a current diagnosis of Crohn's disease or inflammatory bowel disease-unclassified (indeterminate colitis)
- Individual has demonstrated an inadequate response to, loss of response, or intolerance to **BOTH** of the following:
 - One or more conventional therapies (e.g., corticosteroids, aminosalicylates, immunomodulators) for UC*
 - Two advanced therapies (biologic/Janus kinase [JAK] inhibitor therapy) for UC*
- Individual has no prior exposure to anti-interleukin (anti-IL)-12p40 antibodies (e.g., ustekinumab) or anti-IL-23p19 antibodies (e.g., risankizumab, brazikumab, guselkumab, tildrakizumab)
- Three loading doses administered by intravenous infusion at Weeks 0, 4, and 8. (Maintenance doses are administered by subcutaneous injection [may be available through applicable pharmacy benefits] and start at week 12.)
- Mirikizumab-mrkz (Omvo^h) is prescribed by, or in consultation with, a licensed gastroenterology professional provider.

*See Description section for specific examples.

EXPERIMENTAL/INVESTIGATIONAL

All other uses for mirikizumab-mrkz (Omvo^h) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These

medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Duration of authorization: 12 months

Version Effective Date: 08/12/2024

Title: Mirvetuximab soravtansine-gynx (Elahere™)

MEDICALLY NECESSARY

Mirvetuximab soravtansine-gynx (Elahere) is considered medically necessary and, therefore, covered as a single agent or in combination with bevacizumab for the treatment of adult individuals with folate receptor alpha (FR α)-positive*, platinum-resistant (i.e., disease recurring within 6 months of platinum-based chemotherapy) epithelial ovarian, fallopian tube, or primary peritoneal cancer **and** who have received one to three prior systemic treatment regimens with **one** of the following histology types:

- Serous, borderline epithelial histology with recurrent disease (National Comprehensive Cancer Network [NCCN]-preferred therapy)
- Endometrioid (serous), carcinosarcoma (malignant mixed Müllerian tumors), clear cell, mucinous, or endometrioid (grade 1) with persistent or recurrent disease **and one** of the following scenarios (NCCN-preferred):
 - For progression on primary, maintenance, or recurrence therapy (platinum-resistant disease)
 - For stable or persistent disease (if not on maintenance therapy) (platinum-resistant disease)
 - For complete remission and relapse <6 months after completing chemotherapy (platinum-resistant disease)

*Select individuals for therapy based on an US Food and Drug Administration (FDA)-approved test.

Duration of authorization: 12 months

Version Effective Date: 06/16/2025

Title: Mogamulizumab-kpkc (Poteligeo®)

MEDICALLY NECESSARY

ADULT T-CELL LEUKEMIA/LYMPHOMA

Mogamulizumab-kpkc (Poteligeo®) injection is considered medically necessary and, therefore, covered for individuals with a diagnosis of adult T-cell leukemia/lymphoma (ATTL), as a second-line or subsequent therapy as a single agent for nonresponders to first-line therapy for acute or lymphoma* subtypes (National Comprehensive Cancer Network [NCCN]-preferred treatment)

MYCOSIS FUNGOIDES OR SÉZARY SYNDROME

Mogamulizumab-kpkc (Poteligeo®) injection is considered medically necessary and, therefore, covered as monotherapy for individuals 18 years of age or older with diagnosis of relapsed or refractory mycosis fungoides (MF) or Sézary syndrome (SS) after at least one prior systemic therapy, when any of the following criteria are met:

- The individual is receiving primary systemic therapy for one of the following stages of the disease:
 - Stage IB-IIA MF, in combination with skin-directed therapy in select cases** (NCCN-preferred treatment)
 - Stage IIB MF with limited tumor lesions, with or without local radiation therapy and with or without skin-directed therapy (NCCN-preferred treatment)
 - Stage IIB MF with generalized tumor lesions, in combination with skin-directed therapy (NCCN-preferred treatment)
 - Stage III MF in combination with skin-directed therapy (NCCN-preferred treatment)
 - Stage IVA1 or IVA2 SS, in combination with skin-directed therapy (NCCN-preferred treatment)
 - Stage IVA2 non-SS or stage IVB visceral disease (solid organ), with or without radiation therapy for local control
- The individual is receiving subsequent systemic therapy for one of the following stages of the disease:

- Stage IA MF that is refractory to multiple previous therapies, in combination with skin-directed therapy** (NCCN-preferred treatment)
- Stage IB-IIA MF that is relapsed with a lower skin disease burden (e.g., predominantly patch disease), in combination with skin-directed therapy in selected cases** (NCCN-preferred treatment)
- Stage IB-IIA MF with a higher skin disease burden (e.g., predominantly plaque disease) that is relapsed or persistent with T1-T2 disease, in combination with skin-directed therapy in selected cases** (NCCN-preferred treatment)
- Stage IB-IIA MF that is refractory to multiple previous therapies, in combination with skin-directed therapy (NCCN-preferred treatment)
- Stage IIB MF that is relapsed with T1-2 limited tumor lesions, in combination with skin-directed therapy in selected cases** (NCCN-preferred treatment)
- Stage IIB MF with T3 limited tumor lesions that is relapsed with or without local radiation therapy and with or without skin-directed therapy (NCCN-preferred treatment)
- Stage IIB MF that is persistent with T1-3 limited tumor lesions with or without local radiation therapy and with or without skin-directed therapy (NCCN-preferred treatment)
- Stage IIB MF with limited tumor lesions that is refractory to multiple previous therapies, in combination with skin-directed therapy (NCCN-preferred treatment)
- Stage IIB MF that is relapsed with T1-2 generalized tumor lesions, in combination with skin-directed therapy in selected cases** (NCCN-preferred treatment)
- Stage IIB MF that is persistent with T1-3 generalized tumor lesions, in combination with skin-directed therapy (NCCN-preferred treatment)
- Stage IIB MF with generalized tumor lesions refractory to multiple previous therapies
- Stage IIB MF with T3 generalized tumor lesions that is relapsed in combination with or without skin-directed therapy (NCCN-preferred treatment)
- Stage III MF that is relapsed or persistent in combination with skin-directed therapy (NCCN-preferred treatment)

- Stage III MF that is refractory to multiple previous therapies in combination with skin-directed therapies
- Stage IVA1 or IVA2 SS that is relapsed or persistent in combination with skin-directed therapy ([NCCN]-preferred treatment)
- Stage IVA2 that is relapsed or persistent non-SS or stage IVB visceral disease (solid organ), with or without radiation therapy for local control

NCCN note: *The Lymphoma Study Group of the Japan Clinical Oncology Group (JCOG) has classified ATLL into four subtypes (smoldering, chronic, acute, or lymphoma based on laboratory evaluations [e.g., serum LDH, calcemia, lymphocytosis] and clinical features [e.g., lymphadenopathy, hepatosplenomegaly, skin involvement]).

NCCN note: **Systemic therapies should be considered for individuals with extensive skin involvement, higher skin disease burden, predominantly plaque disease, blood involvement, and/or inadequate response to skin-directed therapy.

CONTINUATION THERAPY

Mogamulizumab-kpkc (Poteligeo) is considered medically necessary and, therefore, covered for continuation therapy until disease progression, drug intolerance, unacceptable toxicity, or any other criteria for discontinuation of the therapy.

EXPERIMENTAL/INVESTIGATIONAL

There may be additional indications contained in the Policy section of this document due to evaluation of criteria highlighted in the Company's off-label policy, and/or review of clinical guidelines issued by leading professional organizations and government entities.

MANDATES

PENNSYLVANIA MEMBERS

In accordance with the Commonwealth of Pennsylvania's Act 6 of 2020 or Fair Access to Cancer Treatment Act, for members who are enrolled in Pennsylvania commercial products who have Stage 4, advanced metastatic cancer, refer to the Medical Policy titled "Coverage of Anticancer Prescription Oral and Injectable Drugs and Biologics and Supportive Agents" (08.01.08) for additional information regarding the applicable coverage of drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Duration of authorization: 12 months

Version Effective Date: 05/20/2024

Title: Monoclonal Antibodies Directed Against Amyloid for the Treatment of Alzheimer Disease

Policy

Coverage is subject to the terms, conditions, and limitations of the member's contract.

BENEFIT EXCLUSION

Monoclonal antibodies directed against amyloid for the treatment of Alzheimer disease (e.g., aducanumab [Aduhelm], Leqembi (lecanemab-irmb), and/or KISUNLA (donanemab-azbt)) are a benefit contract exclusion for most plans, and, therefore, not eligible for reimbursement consideration. Individual benefits must be verified.

EXPERIMENTAL/INVESTIGATIONAL

For plans that do not have a monoclonal antibodies directed against amyloid for the treatment of Alzheimer disease (e.g., Aducanumab (Aduhelm), Leqembi (lecanemab-irmb), and/or KISUNLA (donanemab-azbt)) benefit contract exclusion, Aducanumab (Aduhelm), Leqembi (lecanemab-irmb), and/or KISUNLA (donanemab-azbt) are considered experimental/investigational and, therefore, not covered for all indications, including treatment of Alzheimer disease, because the safety and effectiveness of these services cannot be established by review of the available published peer-reviewed literature.

Guidelines

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, aducanumab (Aduhelm), lecanemab-irmb (Leqembi), and donanemab-azbt (Kisunla), which are monoclonal antibodies directed against amyloid for the treatment of Alzheimer disease (AD), are not eligible for payment under the medical benefits of the Company's commercial products because the services are considered experimental/investigational and, therefore, not covered.

Services that are experimental/investigational are a benefit contract exclusion for all products of the Company. Therefore, they are not eligible for reimbursement consideration.

US FOOD AND DRUG ADMINISTRATION (FDA) STATUS

In June 2021, aducanumab (Aduhelm) was approved by the FDA for treatment of AD. This indication was approved under accelerated approval based on reduction in amyloid beta plaques observed in patients treated with aducanumab. Continued approval for this indication may be contingent upon verification of clinical benefit in confirmatory trial(s).

In July 2021, the FDA amended the approved label to emphasize the disease stages studied in the clinical

trials. The amended label states that "Treatment with aducanumab should be initiated in patients with MCI or mild dementia stage of disease, the population in which treatment was initiated in clinical trials. There are no safety or effectiveness data on initiating treatment at earlier or later stages of the disease than were studied."

The FDA, under the accelerated approval regulations (21 CFR 601.41), requires that Biogen conduct a randomized controlled trial to evaluate the efficacy of aducanumab-avwa (Aduhelm) compared to an appropriate control for the treatment of AD. The trial should be of sufficient duration to observe changes on an acceptable endpoint in the patient population enrolled in the trial. The expected date of trial completion is August 2029 and final report submission to the FDA by February 2030.

In January 2023, the FDA approved lecanemab-irmb (Leqembi) as the second humanized IgG1 monoclonal antibody directed against amyloid beta for the treatment of AD. Like aducanumab (Aduhelm), lecanemab-irmb (Leqembi) was approved via the accelerated approval pathway based on amyloid plaque reduction in a Phase 2 clinical trial, and continued approval will be contingent upon verification of a clinical benefit in a confirmatory trial. Lecanemab-irmb (Leqembi) is limited to treating patients with MCI due to Alzheimer or mild Alzheimer dementia, as this was the population evaluated in clinical trials, and no safety or effectiveness data are available on initiating treatment earlier or later in the disease course.

In July 2023, the FDA converted lecanemab-irmb (Leqembi), indicated to treat adult patients with AD, to traditional approval. Lecanemab-irmb (Leqembi) is the first amyloid beta–directed antibody to be converted from an accelerated approval to a traditional approval for the treatment of AD.

In July 2024, the FDA approved donanemab-azbt (Kisunla), which is an amyloid beta–directed antibody, as indicated for the treatment of AD. Per the FDA: "Treatment with KISUNLA should be initiated in patients with mild cognitive impairment or mild dementia stage of disease, the population in which treatment was initiated in the clinical trials."

Duration of authorization: 12 months

Version Effective Date: 03/05/2025

Title: Mosunetuzumab-axgb (Lunsumio™)

MEDICALLY NECESSARY

INITIAL THERAPY

Mosunetuzumab-axgb (Lunsumio) is considered medically necessary and, therefore, covered for adult individuals for any of the following conditions for a maximum of eight cycles, when all of the following criteria are met:

Diffuse Large B-Cell Lymphoma

- Second-line and subsequent therapy in combination with polatuzumab vedotin-piiq (Polivy) as National Comprehensive Cancer Network (NCCN)-preferred regimen, for one of the following:
 - relapsed disease <12 months after completion of first-line therapy or primary refractory disease in noncandidates for chimeric antigen receptor (CAR) T-cell therapy (includes individuals who do not have access to CAR T-cell therapy)
 - relapsed disease >12 months after completion of first-line therapy if no intention to proceed to transplant

Follicular Lymphoma, Classic

- Relapsed or refractory follicular lymphoma (grade 1–3a) after two or more lines of systemic therapy*
- Third-line and subsequent therapy (if not previously given) for partial response, no response, relapsed, or progressive disease in individuals with indications for treatment**, as NCCN-preferred regimen.
 - *Prior systemic therapy includes an anti-CD20 monoclonal antibody (e.g., rituximab, obinutuzumab) and an alkylating agent (e.g., bendamustine, cyclophosphamide)

**Indications for treatment: symptoms attributable to follicular lymphoma (not limited to B symptoms; defined as fever, drenching night sweats, and loss of >10% body weight over 6 months), threatened end-organ function, clinically significant or progressive cytopenia secondary to lymphoma, clinically significant bulky disease (any nodal or extranodal tumor mass with a diameter of ≥ 7 cm) and steady or rapid progression.

High-Grade B-Cell Lymphomas

- Second-line and subsequent therapy in combination with polatuzumab vedotin-piiq (Polivy) for one of the following:
 - relapsed disease <12 months after completion of first-line therapy or primary refractory disease in noncandidates for CAR T-cell therapy (includes individuals who do not have access to CAR T-cell therapy)
 - relapsed disease >12 months after completion of first-line therapy if no intention to proceed to transplant

- as alternative systemic therapy (if not previously used) for relapsed or refractory disease

Human Immunodeficiency Virus (HIV)-Related B-Cell Lymphomas

- In combination with polatuzumab vedotin-piiq (Polivy) as second-line and subsequent therapy when all of the following criteria are met:
 - one of the following subtypes:
 - HIV-related diffuse large B-cell lymphoma
 - primary effusion lymphoma
 - HHV8-positive diffuse large B-cell lymphoma, not otherwise specified
 - HIV-related plasmablastic lymphoma
 - one of the following disease states:
 - relapsed disease <12 months after completion of first-line therapy or primary refractory disease in noncandidates for CAR T-cell therapy (includes individuals who do not have access to CAR T-cell therapy)
 - relapsed disease >12 months after completion of first-line therapy if no intention to proceed to transplant
 - as alternative systemic therapy (if not previously used) for relapsed or refractory disease

Posttransplant Lymphoproliferative Disorders (PTLD)

- Second-line and subsequent therapy in combination with polatuzumab vedotin-piiq (Polivy) for monomorphic PTLD (B-cell type) for one of the following:
 - relapsed disease <12 months after completion of initial treatment with chemoimmunotherapy or primary refractory disease in noncandidates for CAR T-cell therapy (includes individuals who do not have access to CAR T-cell therapy)
 - relapsed disease >12 months after completion of initial treatment with chemoimmunotherapy if no intention to proceed to transplant
 - as alternative systemic therapy (if not previously used) for relapsed or refractory disease

CONTINUATION THERAPY (BEYOND INITIAL EIGHT CYCLES)

Mosunetuzumab-axgb (Lunsumio) is considered medically necessary and, therefore, covered for continuation therapy of up to nine additional cycles (17 total cycles of treatment) for adult individuals who achieve partial response or have stable disease in response to eight cycles of treatment with mosunetuzumab-axgb (Lunsumio). (For individuals who achieve a complete response, no further treatment beyond eight cycles is required.)

EXPERIMENTAL/INVESTIGATIONAL

All other uses for mosunetuzumab-axgb (Lunsumio) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

MANDATES

PENNSYLVANIA MEMBERS

In accordance with the Commonwealth of Pennsylvania's Act 6 of 2020 or Fair Access to Cancer Treatment Act, for members who are enrolled in Pennsylvania commercial products who have Stage 4, advanced metastatic cancer, refer to the Medical Policy titled "Coverage of Anticancer Prescription Oral and Injectable Drugs and Biologics and Supportive agents" (08.01.08) for additional information regarding the applicable coverage of drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the service.

Duration of authorization: 12 months

Version Effective Date: 06/16/2025

Title: Nadofaragene Firadenovec-vncg (Adstiladrin®)

MEDICALLY NECESSARY

INITIATION THERAPY

Nadofaragene firadenovec-vncg (Adstiladrin) is considered medically necessary and, therefore, covered in individuals 18 years and older for the treatment of high-risk non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors for the first two doses when ALL of the following criteria are met:

- Individual has Bacillus Calmette-Guérin (BCG)-unresponsive* disease, defined as persistent or recurrent disease following adequate BCG therapy:**
 - As initial management
 - As recurrent or persistent disease that is cytology-positive, imaging- and cystoscopy-negative, and bladder positive
- All visible papillary tumors for the individual have been resected and those with persistent T1 disease on transurethral resection of bladder tumor (TURBT) have undergone an additional re-TURBT within 14 to 60 days prior to beginning nadofaragene firadenovec-vncg (Adstiladrin).
- Individual's Eastern Cooperative Oncology Group (ECOG) performance score is less than or equal to 2.
- Individual does not have concomitant upper tract urothelial carcinoma or urothelial carcinoma within the prostatic urethra.
- Individual is not currently receiving systemic therapy for bladder cancer.
- Individual has not received any prior treatment with adenovirus-based therapies.

*High-grade T1 at the first evaluation following induction BCG (3 months); recurrent high-grade Ta/T1 within 6 months of adequate BCG treatment; or recurrent CIS within 12 months of the last adequate BCG treatment.

**Adequate BCG therapy defined as having received at least two previous courses of BCG within a 12-month period defined as either:

- At least five of six induction BCG instillations AND at least two of three instillations of maintenance BCG; or

- At least two of six instillations of a second induction course where maintenance BCG is not given.

CONTINUATION THERAPY

Continued therapy with nadofaragene firadenovec-vncg (Adstiladrin) is considered medically necessary and, therefore, covered when ALL of the following criteria are met while on the current regimen:

- There is no unacceptable toxicity.
- Clinical documentations demonstrate that the individual continues to show a positive clinical response to therapy (i.e., absence of recurrent high-grade NMIBC).
 - Positive clinical response can be reported through any of the following methods:
- Urine cytology reports as normal, atypical, degenerative, reactive, inflammatory, or nonspecific AND cystoscopy reports as normal or with findings that did not include evidence of low-grade or high-grade recurrence' OR
- Bladder biopsy, if performed, demonstrates an absence of low-grade or high-grade recurrence.

MANDATES

PENNSYLVANIA MEMBERS

In accordance with the Commonwealth of Pennsylvania's Act 6 of 2020 or Fair Access to Cancer Treatment Act, for members who are enrolled in Pennsylvania commercial products who have stage 4, advanced metastatic cancer, refer to the Medical Policy titled "Coverage of Anticancer Prescription Oral and Injectable Drugs and Biologics and Supportive Agents" (08.01.08) for additional information regarding the applicable coverage of drugs and biologics.

EXPERIMENTAL/INVESTIGATIONAL

All other uses for nadofaragene firadenovec-vncg (Adstiladrin) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Duration of authorization: 12 months

Version Effective Date: 10/21/2024

Title: Natalizumab (Tysabri®) and Related Biosimilars

MEDICALLY NECESSARY

MULTIPLE SCLEROSIS

Natalizumab (Tysabri®) and related biosimilars are considered medically necessary and, therefore, covered as monotherapy for the treatment of adults with relapsing forms of multiple sclerosis (MS) (to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease) when **ONE** of the following criteria is met:

- The individual has documentation of highly active (aggressive) relapsing MS defined as, but not limited to, accumulating disability, multiple new or enlarging of lesions of brain and/or spinal cord that developed in the first year of illness
- The individual has had an inadequate response to, or is unable to tolerate, alternate MS therapies (e.g., interferon beta-1a [Avonex®, Rebif®], interferon beta-1b [Betaseron®], glatiramer acetate [Copaxone®])

CROHN'S DISEASE

Natalizumab (Tysabri) and related biosimilars are considered medically necessary and, therefore, covered for the treatment of adults with moderately to severely active Crohn's disease (CD), who have evidence of inflammation, to induce and maintain clinical response and remission when **ALL** of the following criteria are met:

- The individual has had an inadequate response to, or is unable to tolerate, conventional CD therapies and inhibitors of tumor necrosis factor-alpha (TNF- α)
- Natalizumab (Tysabri) and related biosimilars will not be used in combination with immunosuppressants (e.g., 6-mercaptopurine, azathioprine, cyclosporine, methotrexate) or TNF- α inhibitors (e.g., adalimumab, infliximab)

ANTI-JCV ANTIBODY

Measurement of anti-JCV antibodies (John Cunningham Virus) with ELISA (enzyme-linked immunosorbent assay) is considered medically necessary and, therefore, covered when tested prior to initiation of natalizumab (Tysabri) and related biosimilars treatment and every 6 months thereafter, to assess the risk of developing progressive multifocal leukoencephalopathy (PML).

ANTI-NATALIZUMAB ANTIBODIES

Measurement of anti-natalizumab antibodies is considered medically necessary and, therefore, covered in an individual receiving treatment with natalizumab (Tysabri) and related biosimilars when persistent anti-natalizumab antibodies are suspected to have caused a documented hypersensitivity or when there has been an extended dose interruption of

natalizumab (Tysabri) and related biosimilars therapy. This test should be repeated 3 months after an initial positive result is detected to confirm that the antibodies are persistent.

EXPERIMENTAL/INVESTIGATIONAL

All other uses of natalizumab (Tysabri) and related biosimilars, including nonrelapsing secondary progressive MS, are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Duration of authorization: 12 months

Version Effective Date: 04/01/2024

Title: Nivolumab (Opdivo®), Nivolumab and Hyaluronidase-nvhy (Opdivo Qvantig™)

MEDICALLY NECESSARY

INITIAL THERAPY

ANAL CARCINOMA

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered as a single agent for metastatic squamous cell anal carcinoma as a National Comprehensive Cancer Network (NCCN)-preferred second-line or subsequent therapy, if no prior immunotherapy received.

BONE CANCER

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered for the treatment of chondrosarcoma, osteosarcoma, chordoma, or Ewing sarcoma in combination with ipilimumab for unresectable or metastatic disease that has progressed following prior treatment and who have no satisfactory alternative treatment options for tissue tumor mutation burden–high (TMB-H) tumors with 10 or more mutations per megabase.

CENTRAL NERVOUS SYSTEM CANCERS

Limited brain metastases in adults

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered for the following:

- Single agent for limited brain metastases in individuals with PD-L1–positive NSCLC, in one of the following scenarios:
 - Initial treatment in select individuals (e.g., individuals with small asymptomatic brain metastases)
 - For recurrent brain metastases
 - Treatment for relapsed disease with either stable systemic disease or reasonable systemic treatment options
- In combination with ipilimumab (NCCN-preferred) or as a single agent for limited brain metastases in individuals with BRAF nonspecific melanoma, in one of the following scenarios:
 - Initial treatment in select individuals (e.g., individuals with small asymptomatic brain metastases)
 - For recurrent brain metastases
 - Treatment for relapsed disease with either stable systemic disease or reasonable systemic treatment options

Extensive brain metastases in adults

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered for the following:

- Single-agent treatment for extensive brain metastases in individuals with PD-L1–positive NSCLC
 - Primary treatment in select individuals (e.g., individuals with small asymptomatic brain metastases)
 - Treatment for recurrent disease with stable systemic disease or reasonable systemic treatment options
- In combination with ipilimumab (NCCN-preferred) or as a single agent for extensive brain metastases in individuals with BRAF nonspecific melanoma, in one of the following scenarios:
 - Primary treatment in select individuals (e.g., individuals with small asymptomatic brain metastases)
 - Treatment for recurrent disease with stable systemic disease or reasonable systemic treatment options

Diffuse high-grade gliomas in pediatrics

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered in one of the following scenarios:

- Adjuvant treatment in individuals less than 3 years old for hypermutant tumor (excluding diffuse midline glioma, H3 K27-altered or pontine location)
- Adjuvant treatment in individuals 3 years or older following standard brain radiation therapy (RT) with or without concurrent temozolomide
- Systemic treatment (NCCN preferred) in individuals with recurrent or progressive disease for hypermutant tumor (excluding oligodendroglioma, IDH-mutant and 1p/19q co-deleted or astrocytoma IDH-mutant)

CERVICAL CANCER

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered for cervical cancer as NCCN-preferred second-line or subsequent therapy as a single agent if PD-L1 positive (combined positive score [CPS] ≥ 1) as determined by a US Food and Drug Administration (FDA)-approved assay or a validated test performed in a CLIA-certified lab for one of the following:

- Local/regional recurrence
- Stage IVB or recurrence with distant metastases

CHRONIC LYMPHOCYTIC LEUKEMIA/SMALL LYMPHOCYTIC LYMPHOMA

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered as a single agent or in combination with ibrutinib (Imbruvica) for histologic (Richter) transformation to diffuse large B-cell lymphoma in individuals with del(17p)/TP53 mutation or who are chemotherapy refractory or unable to receive chemoimmunotherapy.

GASTRIC CANCER

HER2 overexpression negative disease

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered for HER2 overexpression negative disease for any of the following:

- Systemic treatment in combination with oxaliplatin and fluorouracil or capecitabine for individuals with early-stage gastric adenocarcinoma with endoscopic features suggestive of deep submucosal invasion including converging folds, irregular surface pattern, and ulceration in a large gastric mass with favorable histology and completed an endoscopic resection (PD-L1 CPS ≥ 5) (NCCN-preferred)
- Primary treatment for medically fit individuals with surgically unresectable locoregional disease, in combination with oxaliplatin and fluorouracil or capecitabine (PD-L1 CPS ≥ 5) (NCCN-preferred)
- Palliative therapy for individuals who are not surgical candidates or have unresectable, locally advanced, recurrent, or metastatic disease (including peritoneal-only metastatic disease, including positive cytology) and Karnofsky performance score 60% or greater or Eastern Cooperative Oncology Group (ECOG) performance score 2 or less as first-line therapy in combination with oxaliplatin and fluorouracil or capecitabine (PD-L1 CPS ≥ 5) (if no prior tumor progression while on therapy with a checkpoint inhibitor) (NCCN-preferred)

Microsatellite instability–high (MSI-H)/deficient mismatch repair (dMMR) cancer

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered for dMMR/MSI-H tumors for any of the following:

- Primary treatment for dMMR/MSI-H tumors with one of the following scenarios
 - Unresectable locoregional disease and are medically fit for surgery in combination with ipilimumab or oxaliplatin and fluorouracil or capecitabine (NCCN-preferred regimen)
 - Neoadjuvant or perioperative immunotherapy in combination with ipilimumab for potentially resectable locoregional disease (cT2 or higher, any N) and if medically fit for surgery
- Perioperative treatment as a single agent as postoperative management following R0 resection in individuals who received preoperative treatment with nivolumab and ipilimumab
- First-line palliative therapy in combination with ipilimumab (if no prior tumor progression while on treatment with a checkpoint inhibitor) in individuals who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease (including peritoneal-only metastatic disease, including positive cytology) and good PS 60% or greater [ECOG 0-2]
- First-line palliative therapy in combination with oxaliplatin and fluorouracil or capecitabine (if no prior tumor progression while on treatment with a checkpoint inhibitor) in individuals who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease (including peritoneal only metastatic disease, including positive cytology) and good PS 60% or greater [ECOG 0-2]
- Systemic treatment in combination with ipilimumab or oxaliplatin and fluorouracil or capecitabine for individuals with early-stage gastric adenocarcinoma with endoscopic features suggestive of deep submucosal invasion including converging folds, irregular surface pattern, and ulceration in a large gastric mass with favorable histology and completed an endoscopic resection (NCCN-preferred)
- Subsequent or second-line palliative therapy in combination with ipilimumab (if no prior tumor progression while on treatment with a checkpoint inhibitor) for individuals with locoregional disease who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease (including peritoneal only metastatic disease, including positive cytology) and good PS 60% or greater [ECOG 0-2]

GASTROESOPHAGEAL JUNCTION CANCER, ESOPHAGEAL ADENOCARCINOMA/SQUAMOUS CELL

Non-microsatellite instability-high cancer

Nivolumab and hyaluronidase-nvhy (Opdivo Qvantig) is considered medically necessary and, therefore, covered for any of the following:

- Adjuvant treatment of completely resected esophageal or gastroesophageal junction cancer with residual pathologic disease in individuals who have received neoadjuvant chemoradiotherapy (CRT)
- First-line treatment of unresectable advanced or metastatic ESCC, in combination with fluoropyrimidine- and platinum-based chemotherapy
- Unresectable advanced, recurrent, or metastatic ESCC after prior fluoropyrimidine- and platinum-based chemotherapy
- Advanced or metastatic gastric cancer, gastroesophageal junction cancer or esophageal adenocarcinoma, in combination with fluoropyrimidine- and platinum-containing chemotherapy

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered for any of the following:

- First-line treatment of unresectable advanced or metastatic esophageal squamous cell carcinoma (ESCC), in combination with ipilimumab (Yervoy)
- First-line treatment of unresectable advanced or metastatic ESCC, in combination with fluoropyrimidine- and platinum-based chemotherapy
- Induction systemic therapy in combination with oxaliplatin and capecitabine or fluorouracil for relieving dysphagia in individuals who are medically fit and planned for esophagectomy with cT2, N0 (high-risk lesions: lymphovascular invasion, ≥ 3 cm, poorly differentiated), cT1b-cT2, N+ or cT3-cT4a, Any N disease (NCCN-preferred)
- Induction systemic therapy in combination with cisplatin or oxaliplatin and capecitabine or fluorouracil for relieving dysphagia in individuals who are medically fit and planned for esophagectomy with cT2, N0 (high-risk lesions: lymphovascular invasion, ≥ 3 cm, poorly differentiated), cT1b-cT2, N+ or cT3-cT4a, Any N disease (NCCN-preferred)
- Induction systemic therapy in combination with ipilimumab for relieving dysphagia in individuals who are medically fit and planned for esophagectomy with cT2, N0 (high-risk

lesions: lymphovascular invasion, ≥ 3 cm, poorly differentiated), cT1b-cT2, N+ or cT3-cT4a, Any N disease (NCCN-preferred)

- Unresectable advanced, recurrent, or metastatic ESCC after prior fluoropyrimidine- and platinum-based chemotherapy
- Adjuvant treatment of completely resected esophageal or gastroesophageal junction cancer with residual pathologic disease in individuals who have received neoadjuvant chemoradiotherapy (CRT)
- Advanced or metastatic gastric cancer, gastroesophageal junction cancer or esophageal adenocarcinoma, in combination with fluoropyrimidine- and platinum-containing chemotherapy
- Postoperative therapy (NCCN-preferred) for individuals who have received preoperative chemoradiation and R0 resection and residual disease (yp T positive and/or N positive)
- Palliative therapy for HER2 overexpression–negative individuals who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease and Karnofsky performance score 60% or greater [ECOG 0-2] as preferred first-line therapy in combination with oxaliplatin and fluorouracil or capecitabine (PD-L1 CPS ≥ 5) for adenocarcinoma only (if no prior tumor progression while on therapy with a checkpoint inhibitor)
- Palliative therapy in individuals with esophageal squamous cell carcinoma (SCC) if no prior tumor progression while on therapy with a checkpoint inhibitor and are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease and Karnofsky performance score 60% or greater [ECOG 0-2] as either:
 - Second-line or subsequent therapy (NCCN-preferred) as a single agent
 - First-line therapy (NCCN-preferred) in combination with fluorouracil or capecitabine and cisplatin or oxaliplatin
 - First-line therapy (NCCN-preferred) in combination with ipilimumab

Microsatellite instability-high cancer (MSI-H)

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered for dMMR/MSI-H tumors for any of the following:

- Primary treatment as neoadjuvant or perioperative immunotherapy in individuals medically fit for surgery in combination with ipilimumab for adenocarcinoma tumors

that is cT2, N0 (high-risk lesions: lymphovascular invasion, ≥ 3 cm, poorly differentiated), cT1b-cT2, N+ or cT3-cT4a, Any N disease

- Palliative treatment in individuals with good PS 60% or greater [ECOG 0-2] who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease in one of the following scenarios:
 - First-line treatment with ipilimumab regardless of PD-L1 status if no tumor progression while on therapy with a checkpoint inhibitor (NCCN-preferred regimen)
 - First-line treatment with oxaliplatin and fluorouracil or capecitabine regardless of PD-L1 status if no tumor progression while on therapy with a checkpoint inhibitor (NCCN-preferred regimen)
 - Second-line or subsequent therapy with ipilimumab if no tumor progression while on therapy with a checkpoint inhibitor
- Induction systemic therapy for relieving dysphagia in individuals who are medically fit and planned for esophagectomy with cT2, N0 (high-risk lesions: lymphovascular invasion, ≥ 3 cm, poorly differentiated), cT1b-cT2, N+ or cT3-cT4a, Any N disease in combination with either of the following:
 - Ipilimumab (NCCN-preferred)
 - Oxaliplatin and capecitabine or fluorouracil (NCCN-preferred)
- Perioperative treatment as a single agent for adenocarcinoma tumors as postoperative management following R0 resection in individuals who received preoperative treatment with nivolumab and ipilimumab

GESTATIONAL TROPHOBLASTIC NEOPLASIA

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered as single-agent therapy for gestational trophoblastic neoplasia that is resistant to multiagent chemotherapy in those with one of the following conditions:

- High-risk disease (NCCN-preferred regimen)
- Recurrent or progressive intermediate trophoblastic tumor (placental site trophoblastic tumor or epithelioid trophoblastic tumor)

HEPATOCELLULAR CARCINOMA

Nivolumab and hyaluronidase-nvhy (Opdivo Qvantig) is considered medically necessary and, therefore, covered as a single agent for the treatment of individuals with hepatocellular

carcinoma (HCC) who have been previously treated with sorafenib following combination treatment with intravenous nivolumab (Opdivo) and ipilimumab (Yervoy)

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered in combination with ipilimumab (Yervoy) for the treatment of individuals with HCC who have been previously treated with sorafenib.

Subsequent treatment as a single agent (Child-Pugh Class A or B only) who have not been previously treated with a checkpoint inhibitor, or in combination with ipilimumab (Child-Pugh Class A only) for progressive disease in individuals who have one of the following:

- Liver-confined disease, inoperable and are not a transplant candidate
- Metastatic disease and are deemed ineligible for resection, transplant, or locoregional therapy

HEAD AND NECK CANCERS

Squamous cell carcinoma of the head and neck

Nivolumab (Opdivo) and nivolumab and hyaluronidase-nvhy (Opdivo Qvantig) is considered medically necessary and, therefore, covered as single-agent therapy for the treatment of recurrent or metastatic SCC of the head and neck with disease progression on or after a platinum-based therapy.

Cancer of the nasopharynx (squamous cell carcinoma with mixed subtypes)

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered in the following regimens:

First-line systemic therapy, in combination with cisplatin and gemcitabine for T1-4, N0-3, M1 disease for (NCCN-preferred regimen):

- Oligometastatic disease and PS 0-2

- Widely metastatic disease and good PS (0-2)

Subsequent-line systemic therapy, if not previously used, in combination with cisplatin and gemcitabine for T1-4, N0-3, M1 disease for:

- Oligometastatic disease and PS 0-2
- Widely metastatic disease and good PS (0-2)

Subsequent-line systemic therapy as a single agent if previously treated, recurrent or metastatic non-keratinizing T1-4, N0-3, M1 disease for:

- Oligometastatic disease and PS 0-2
- Widely metastatic disease and good PS (0-2)

Very advanced head and neck cancer (squamous cell carcinoma with mixed subtypes)

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered in the following regimens:

- Systemic therapy as a first-line or subsequent-line (note: if not previously used, may be considered in subsequent lines) option for nasopharyngeal cancer in combination with cisplatin and gemcitabine in individuals with performance status 0-1 for: unresectable locoregional recurrence with prior radiation therapy (RT), unresectable second primary with prior RT, unresectable persistent disease with prior RT, or recurrent/persistent disease with distant metastases
- Systemic therapy as a first-line or subsequent-line (note: if not previously used, may be considered in subsequent lines) option for non-nasopharyngeal cancer as a single agent in individuals with performance status 0-1 for: metastatic (M1) disease as presentation, unresectable locoregional recurrence with prior radiation therapy (RT), unresectable second primary with prior RT, unresectable persistent disease with prior RT, or recurrent/persistent disease with distant metastases
- Systemic therapy as a subsequent-line if previously treated, recurrent or metastatic non-keratinizing nasopharyngeal cancer as a single agent in individuals with performance status 0-3 for: unresectable locoregional recurrence with prior radiation therapy (RT), unresectable second primary with prior RT, unresectable persistent disease with prior RT, or recurrent/persistent disease with distant metastases

- Systemic therapy as a preferred alternate single agent subsequent-line option, if immunotherapy not previously used, for non-nasopharyngeal cancer if disease progression on or after platinum therapy in:
 - PS 0-3 and persistent or progressive metastatic disease (M1) at initial presentation following first-line therapy
 - Recurrent/persistent disease with distant metastases and PS 0-3
 - Unresectable locoregional recurrence, unresectable second primary, or unresectable persistent disease with prior RT and PS 0-3
 - Unresectable locoregional recurrence or persistent disease without prior RT and PS 3
- Systemic therapy as a first-line or subsequent-line option for non-nasopharyngeal cancer in combination with cetuximab in individuals with performance status 0-1 for:
 - Metastatic (M1) disease at initial presentation
 - Recurrent/persistent disease with distant metastases
 - Unresectable locoregional recurrence, unresectable second primary, or unresectable persistent disease with prior radiation therapy (RT)
- Systemic therapy for non-nasopharyngeal cancer in combination with cetuximab in individuals with resectable locoregional recurrence or persistent disease without prior radiation therapy (RT)

HODGKIN LYMPHOMA

Classical Hodgkin lymphoma in adults

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered for the treatment of adult individuals with classical Hodgkin lymphoma (cHL) as primary treatment in combination with AVD (doxorubicin, vinblastine, dacarbazine) for stage III-IV disease

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered for the treatment of adult individuals with classical Hodgkin lymphoma (cHL) who have relapsed, refractory, or refractory disease after any of the following:

- Autologous hematopoietic stem cell transplantation (HSCT) and brentuximab vedotin (Adcetris)

- Second-line in combination with brentuximab vedotin or ICE (ifosfamide, carboplatin, etoposide)
- Subsequent therapy (if not previously used) for Deauville 4 or 5 following restaging with FDG-PET/CT in combination with brentuximab vedotin or ICE
- Therapy as a single agent for refractory disease to at least 3 or more lines of therapy
- Three or more lines of systemic therapy that includes autologous HSCT
- Palliative therapy as a single agent, in adults ages 60 years and older with poor performance status or substantial comorbidities

Classical Hodgkin lymphoma in pediatric individuals

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered for the treatment of relapsed or refractory cHL in pediatric individuals who are heavily pretreated (with platinum or anthracycline-based chemotherapy) or if a decrease in cardiac function observed as:

- Re-induction therapy or subsequent therapy (if not previously used) in combination with brentuximab vedotin
- Re-induction therapy in combination with brentuximab vedotin and Involved-Site RT (ISRT), in highly favorable individuals (i.e., those who may avoid autologous stem cell rescue [ASCR]: initial stage other than IIIB or IVB, no prior exposure to RT, duration of CR1 >1 year, absence of extranodal disease or B symptoms at relapse)
- Subsequent therapy (if not previously used) as a single agent

KAPOSI SARCOMA

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered for the treatment of classic Kaposi sarcoma in individuals with relapsed/refractory advanced cutaneous, oral, visceral, or nodal disease

- Subsequent therapy as a single agent or in combination with ipilimumab (Yervoy) if progressed on or not responded to first-line systemic therapy, and progressed on alternate first-line systemic therapy

PERITONEAL MESOTHELIOMA

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered for the treatment of peritoneal mesothelioma (including mesothelioma and tunica vaginalis testis mesothelioma), in combination with ipilimumab (Yervoy) (NCCN-preferred for biphasic or sarcomatoid histology; NCCN-other recommended regimen for epithelioid histology) as first-line systemic therapy for unresectable disease:

- Diffuse peritoneal mesothelioma (PeM) with unicavitary, epithelioid histology that is medically inoperable and/or complete cytoreduction not achievable (including high-risk features, e.g., Ki-67 >9%, nodal metastasis, high tumor burden [Peritoneal Cancer Index (PCI) >17], completeness of cytoreduction [CC] score >1, biphasic disease, or bicavitary disease) and ECOG PS 0-2
- Diffuse PeM with biphasic/sarcomatoid histology or bicavitary disease and ECOG PS 0-2
- Recurrence of diffuse PeM with unicavitary, epithelioid histology after prior cytoreductive surgery (CRS) + hyperthermic intraperitoneal chemotherapy (HIPEC), if no previous adjuvant systemic therapy given and ECOG PS 0-2
- Recurrence of benign multicystic or well-differentiated papillary peritoneal mesothelioma after prior CRS ± HIPEC for ECOG PS 0-2

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered for the treatment of PeM (including pericardial mesothelioma and tunica vaginalis testis mesothelioma), as a single agent or in combination with ipilimumab (Yervoy) as NCCN-preferred subsequent systemic therapy, if chemotherapy administered first-line

PLEURAL MESOTHELIOMA

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered for the treatment of PeM (including mesothelioma and tunica vaginalis testis mesothelioma):

- Induction systemic therapy, in combination with ipilimumab (NCCN-preferred prior to surgical exploration for clinical stage I disease and epithelioid histology
- First-line therapy in combination with ipilimumab (Yervoy) for:
 - Clinical stage I disease and epithelioid histology as initial treatment
 - Clinical stage II-IV disease and epithelioid histology, sarcomatoid or biphasic histology (any stage), or if medically inoperable as initial treatment

- Clinical stage I disease and epithelioid histology following surgical exploration (if induction systemic therapy not given)
- Subsequent systemic therapy (NCCN-preferred), as a single agent or in combination with ipilimumab (Yervoy), if chemotherapy administered first-line

MELANOMA

Cutaneous melanoma

Nivolumab and hyaluronidase-nvhy (Opdivo Qvantig) is considered medically necessary and, therefore, covered as single-agent therapy in adult individuals with one of the following:

- Unresectable or metastatic melanoma**
- Unresectable or metastatic melanoma** following combination treatment with intravenous nivolumab (Opdivo) and ipilimumab (Yervoy)
- Adjuvant treatment for Stage IIB, Stage IIC, Stage III, or Stage IV melanoma who have undergone complete resection

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered as single-agent therapy or in combination with ipilimumab (Yervoy) for the treatment in individuals ages 12 years and older with unresectable or metastatic melanoma** in one of the following regimen:

- First-line systemic* therapy (NCCN-preferred) combination checkpoint blockade preferred

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered as single-agent therapy for the following regimens:

- Adjuvant treatment in individuals ages 12 years and older with Stage IIB, Stage IIC, Stage III, or Stage IV melanoma who have undergone complete resection
- Adjuvant treatment option for one of the following:
 - Pathologically staged IIB/IIC disease following wide excision alone or wide excision with negative sentinel lymph node (SLN) biopsy
 - Clinical stage IIIB/C/D disease following wide excision alone or wide excision with negative sentinel lymph node (SLN) biopsy after microscopic satellites found in biopsy specimen from primary lesion

- Clinical stage IIIB/C/D disease that is SLN negative or SLN biopsy not performed after microscopic satellites found in wide excision specimen
- NCCN-preferred adjuvant systemic therapy option for one of the following:
 - Resected stage III sentinel node–positive disease during observation without additional nodal surgery and with mandatory radiographic nodal surveillance (NCCN-preferred) or after completion of lymph node dissection (CLND), based on risk of recurrence
 - Stage III disease with clinically positive node(s) following wide excision of primary tumor and therapeutic lymph node dissection (TLND) or neoadjuvant therapy
 - Stage III disease with clinical satellite/in-transit metastases if no evidence of disease (NED) after complete excision to clear margins
 - Local satellite/in-transit recurrence if NED after complete excision to clear margins
 - Resectable disease following complete TLND, neoadjuvant therapy and/or complete excision of disease limited to nodal recurrence
 - If NED following metastasis-directed therapy (stereotactic ablative therapy or complete resection), or systemic therapy followed by resection for oligometastatic disease
- NCCN-preferred neoadjuvant systemic therapy in combination with ipilimumab (Yervoy) or as a single agent as:
 - Primary treatment for stage III disease with clinically positive, resectable nodal disease
 - Treatment for resectable disease limited to nodal recurrence
 - Initial and/or subsequent treatment for limited resectable for one of the following:
 - Stage III disease with clinical satellite/in-transit metastases
 - Local satellite/in-transit recurrence

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered in combination with ipilimumab (Yervoy) as NCCN-preferred second-line or subsequent systemic therapy* option for metastatic or unresectable disease** after progression, intolerance, and/or projected risk of progression with BRAF targeted therapy:

- As a single agent (if not previously used) or in combination with ipilimumab (Yervoy) if anti-PD-1 therapy was not previously used
- In combination with ipilimumab (Yervoy) for disease progression on single-agent anti-PD-1 therapy
- May be considered as re-induction therapy (as a single agent or in combination with ipilimumab [Yervoy]) if prior anti-PD-1 immunotherapy resulted in disease control (complete response, partial response, or stable disease) with no residual toxicity, and disease progression/relapse occurred >3 months after treatment discontinuation

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered as adjuvant systemic therapy in combination with ipilimumab (Yervoy) (NCCN-preferred) if NED following metastasis-directed therapy (stereotactic ablative therapy, T-VEC/intralesional therapy or complete resection), or systemic therapy followed by resection for oligometastatic disease

*Systemic therapy is preferred by NCCN for unresectable or widely disseminated distant metastatic disease.

**Metastatic disease includes stage III unresectable/borderline resectable disease with clinically positive node(s) or clinical satellite/in-transit metastases, or as well as unresectable local satellite/in-transit recurrence, unresectable nodal recurrence, and widely disseminated distant metastatic disease.

Uveal melanoma

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered as single-agent therapy or in combination with ipilimumab (Yervoy) (NCCN-preferred) for the treatment of individuals with uveal melanoma who have metastatic or unresectable disease.

MERKEL CELL CARCINOMA

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered as a single agent for the treatment of individuals with Merkel cell carcinoma as neoadjuvant treatment for either of the following:

- Surgical candidates after multidisciplinary consultation if diagnosed with primary clinical N0 locally advanced disease where curative surgery and curative radiation therapy were originally deemed not feasible
- Primary clinical N+, M0 regional disease with biopsy-positive draining nodal basin

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered as systemic therapy for individuals with Merkel cell carcinoma M1 disseminated disease as single-agent therapy (NCCN-preferred) or in combination with ipilimumab (Yervoy) if anti-PDL1 or anti-PD-1 therapy is contraindicated or there is disease progression on anti-PDL1 or anti-PD-1 monotherapy.

MICROSATELLITE INSTABILITY-HIGH AND Tumor mutational burden CANCER

Ampullary adenocarcinoma

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered as first-line therapy in combination with ipilimumab (Yervoy)[‡] in individuals with intestinal-type disease if dMMR/MSI-H for:

- Unresectable localized disease
- Stage IV resected ampullary cancer
- Metastatic disease at initial presentation

[‡]May be followed by chemoradiation for palliative indications in those with good performance status (ECOG 0-1, with good biliary drainage and adequate nutritional intake).

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered in combination with ipilimumab as subsequent therapy for disease progression if no prior immunotherapy.

Appendiceal adenocarcinoma

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered as a single agent or in combination with ipilimumab (Yervoy), if no previous treatment with a checkpoint inhibitor, for one of the following appendiceal adenocarcinoma regimens:

- Systemic therapy for advanced or metastatic disease (dMMR/MSI-H or polymerase epsilon/delta [POLE/POLD1]) if candidate for immunotherapy and no prior immunotherapy received

Colorectal

Nivolumab and hyaluronidase-nvhy (Opdivo Qvantig) is considered medically necessary and, therefore, covered as a single agent for treatment of adult individuals with MSI-H or dMMR metastatic colorectal cancer that has progressed following previous oxaliplatin-, irinotecan-, and fluoropyrimidine-based therapy or following combination treatment with intravenous nivolumab (Opdivo) and ipilimumab (Yervoy).

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered as a single agent or in combination with ipilimumab (Yervoy) for treatment for individuals ages 12 years and older with MSI-H or mismatch repair–deficient (dMMR) metastatic colorectal cancer that has progressed following previous oxaliplatin-, irinotecan-, and fluoropyrimidine-based therapy

Colon

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered as a single agent or in combination with ipilimumab (dMMR/MSI-H or polymerase epsilon/delta [POLE/POLD1])

- As neoadjuvant therapy for clinical T4b dMMR/MSI-H only disease (NCCN-preferred regimen)
- As neoadjuvant therapy for resectable synchronous liver and/or lung metastases, if no previous treatment with a checkpoint inhibitor (NCCN-preferred regimen)

- As Initial treatment for resectable metachronous metastases if no previous immunotherapy
- For locally unresectable or medically inoperable disease (NCCN-preferred regimen)

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered as a single agent or in combination with ipilimumab (dMMR/MSI-H or polymerase epsilon/delta [POLE/POLD1]) if candidate for immunotherapy and no prior immunotherapy received)

- Locally unresectable or medically inoperable disease
- As primary treatment for synchronous abdominal/peritoneal metastases that are nonobstructing, or following local therapy for individuals with existing or imminent obstruction
- For synchronous unresectable metastases
- Treatment for unresectable metachronous metastases

Biliary tract cancer (gallbladder cancer, intrahepatic cholangiocarcinoma, extrahepatic cholangiocarcinoma)

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered as in combination with ipilimumab (Yervoy) in individuals with tumor mutational burden-high (TMB-H) as subsequent therapy (refractory to standard therapy or with no standard treatment options available) for progression on or after systemic treatment for unresectable or resected gross residual (R2) disease, or metastatic disease in those who have not been previously treated with a checkpoint inhibitor.

Gallbladder cancer

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered as in combination with ipilimumab (Yervoy) in individuals with TMB-H as neoadjuvant therapy for resectable locoregionally advanced disease and presents as:

- Incidental finding of suspicious mass during surgery where hepatobiliary surgery expertise unavailable

- Incidental finding on pathologic review (cystic duct node positive)
- Mass on imaging

Rectal

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered as a single agent or in combination with ipilimumab (Yervoy) in individuals (dMMR/MSI-H or polymerase epsilon/delta [POLE/POLD1]) if candidate for immunotherapy and if no prior immunotherapy received (note: regimens are excluded when used in combination with ipilimumab in individuals who are not appropriate for intensive therapy):

- As primary treatment as a single only for T3, N Any; T1-2, N1-2; T4, N Any; or locally unresectable or medically inoperable dMMR/MSI-H only disease if resection is contraindicated following neoadjuvant/definitive immunotherapy (NCCN preferred) or total neoadjuvant therapy
- As primary treatment for synchronous abdominal/peritoneal metastases that are nonobstructing, or following local therapy for individuals with existing or imminent obstruction
- As primary treatment for synchronous unresectable metastases of other sites
- As primary treatment for unresectable isolated pelvic/anastomotic recurrence
- As primary treatment for unresectable metachronous metastases

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered for as a single agent or in combination with ipilimumab for individuals (dMMR/MSI-H or polymerase epsilon/delta [POLE/POLD1]) with no previous treatment with a checkpoint inhibitor:

- As neoadjuvant treatment for resectable synchronous liver only and/or lung only metastases (NCCN preferred)
- As initial treatment for resectable metachronous metastases and no previous immunotherapy

Small bowel adenocarcinoma

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered as a single agent or in combination with ipilimumab (Yervoy) for one of the following small bowel adenocarcinoma regimens:

- Primary treatment for locally unresectable or medically inoperable disease (deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] or polymerase epsilon/delta [POLE/POLD1] mutation with ultra-hypermutated phenotype [e.g., tumor mutational burden (TMB) >50 mut/Mb])
- Subsequent therapy for advanced or metastatic disease (dMMR/MSI-H dMMR/MSI-H] or polymerase epsilon/delta [POLE/POLD1] mutation with ultrahypermutated phenotype [e.g., tumor mutational burden (TMB) >50 mut/Mb])), if no previous treatment with a checkpoint inhibitor for any line of therapy

NON-SMALL CELL LUNG CANCER

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered in combination with platinum-doublet chemotherapy as neoadjuvant treatment of adults with resectable (tumors 4 cm or larger or node positive) NSCLC.

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered in combination with platinum-doublet chemotherapy as neoadjuvant treatment of adults with resectable (tumors 4 cm or larger or node positive) NSCLC and no known EGFR mutations or ALK rearrangements followed by single-agent Nivolumab (Opdivo) as adjuvant treatment after surgery.

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered for the following:

- Adjuvant therapy as a single agent for individuals with completely resected stage II-IIIb NSCLC who received previous neoadjuvant nivolumab plus chemotherapy (and no known EGFR mutations or ALK rearrangements)
- Induction systemic therapy as an alternative for individuals likely to receive adjuvant chemotherapy (for resectable disease, i.e., tumors 4 cm or larger or node positive), when both of the following criteria are met:
 - In combination with one of the following regimens:

- Paclitaxel and carboplatin
- Paclitaxel and cisplatin
- Pemetrexed and cisplatin or carboplatin for those not candidates for cisplatin-based therapy (nonsquamous cell histology)
- Gemcitabine and cisplatin or carboplatin for those not candidates for cisplatin-based therapy (squamous cell histology)
- For one of the following conditions:
 - Operable stage IB (peripheral T2a, N0), stage I (central T2a, N0), stage II (T1abc-2ab, N1 or T2b, N0), stage IIB (T3, N0), or stage IIIA (T3, N1)
 - T3 invasion or resectable T4 extension, N0-1 disease in the chest wall, proximal airway, or mediastinum
 - Stage IIIA (T4, N0-1)
 - T1, N1 or T2-3, N0-1 (including T3 with multiple nodules in the same lobe)
 - Separate pulmonary nodule(s), same lobe (T3, N0-1), or ipsilateral nonprimary lobe (T4, N0-1)

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered in combination with ipilimumab (Yervoy) for the following conditions:

- First-line treatment of adults with recurrent, advanced, or metastatic NSCLC whose tumors express PD-L1 ($\geq 1\%$) as determined by an FDA-approved test, that are negative for actionable molecular biomarkers[†] and no contraindications^{††} to PD-1 or PD-L1 inhibitors and PS 0-2 (not including locoregional recurrence or symptomatic local disease [except mediastinal lymph node recurrence with prior RT] with no evidence of disseminated disease)
 - In combination with ipilimumab
 - In combination with ipilimumab, pemetrexed and either carboplatin or cisplatin for nonsquamous cell histology
 - In combination with ipilimumab, paclitaxel and carboplatin for squamous cell histology
- First-line treatment of adults with metastatic or recurrent NSCLC, with no EGFR or ALK genomic tumor aberrations, in combination with ipilimumab and two cycles of platinum-doublet chemotherapy

- First-line treatment of adults with metastatic NSCLC, with no EGFR or ALK genomic tumor aberrations, whose tumors express PD-L1 ($\geq 1\%$) as determined by an FDA-approved test in combination with ipilimumab
- Recurrent, advanced or metastatic disease (not including locoregional recurrence or symptomatic local disease [except mediastinal lymph node recurrence with prior RT] with no evidence of disseminated disease) in individuals with PS 0-1 and no contraindications^{††} to PD-1 or PD-L1 inhibitors, when both of the following criteria are met:
 - In combination with one of the following regimens:
 - Ipilimumab
 - Ipilimumab, pemetrexed, and either carboplatin or cisplatin for nonsquamous cell histology
 - Ipilimumab, paclitaxel and carboplatin for squamous cell histology
 - For one of the following conditions:
 - Initial systemic therapy for PD-L1 $< 1\%$ and negative for actionable molecular biomarkers[†]
 - First-line therapy for
 - EGFR exon 20 mutation–positive tumors
 - KRAS G12C mutation–positive tumors
 - ERBB2 (HER2) mutation positive tumors
 - First-line or subsequent therapy for:
 - BRAF V600E-mutation–positive tumors
 - NTRK1/2/3 gene fusion–positive tumors
 - MET exon 14 skipping mutation–positive tumors
 - RET rearrangement–positive tumors

- Subsequent therapy for EGFR S768I, L861Q, and/or G719X mutation–positive tumors and prior afatinib, osimertinib, erlotinib, gefitinib, or dacomitinib therapy
 - Subsequent therapy for ROS1 rearrangement–positive tumors and prior crizotinib, entrectinib, or ceritinib therapy
 - Subsequent therapy for EGFR exon 19 deletion or exon 21 L858R tumors and prior erlotinib +/- (ramucirumab or bevacizumab), afatinib, gefitinib, osimertinib, or dacomitinib therapy
 - Subsequent therapy for ALK rearrangement positive tumors and prior crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib therapy
- Continuation maintenance therapy in combination with ipilimumab for recurrent, advanced, or metastatic disease for PD-L1 expression–positive ($\geq 1\%$) or PD-L1 expression $< 1\%$ tumors that are negative for actionable molecular markers[†] and no contraindications^{††} to PD-1 or PD-L1 inhibitors in individuals with PS 0-2 who achieve a response or stable disease following first-line therapy if nivolumab + ipilimumab $\pm$ chemotherapy given (not including locoregional recurrence or symptomatic local disease [except mediastinal lymph node recurrence with prior RT] with no evidence of disseminated disease)

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered as single-agent therapy for the following conditions:

- Metastatic NSCLC with progression on or after platinum-based chemotherapy
 - Prior to receiving nivolumab (Opdivo), individuals with EGFR or ALK genomic tumor aberrations should have disease progression on an FDA-approved therapy (e.g., afatinib [Gilotrif], alectinib [Alecensa], brigatinib [Alunbrig], ceritinib [Zykadia], crizotinib [Xalkori], dacomitinib [Vizimpro], entrectinib [Rozlytrek], erlotinib [Tarceva], gefitinib [Iressa], lorlatinib [Lorbrena], osimertinib [Tagrisso])
- NCCN-preferred subsequent therapy for recurrent, advanced, or metastatic disease in individuals with PS 0-2 and no prior progression on a PD-1/PD-L1 inhibitor (not including locoregional recurrence or symptomatic local disease [except mediastinal lymph node recurrence with prior RT] with no evidence of disseminated disease)

[†]If there is insufficient tissue to allow testing for all of EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET and RET, repeat biopsy and/or plasma testing should be done. If these are not feasible, treatment is guided by available results and, if unknown, these individuals are treated as though they do not have driver oncogenes.

^{††}Contraindications for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or current use of immunosuppressive agents, or presence of an oncogene (i.e., EGFR exon 19 deletion or L858R, ALK rearrangements), which would predict lack of benefit.

Pediatric aggressive mature B-cell lymphomas

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered as a single agent (NCCN-preferred) for primary mediastinal large B-cell lymphoma (PMBL) for individuals with relapsed or refractory disease.

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered in combination with brentuximab vedotin (Adcentris) (NCCN-preferred) for PMBL as consolidation/additional therapy for individuals with partial response after therapy for relapsed or refractory disease.

RENAL CELL CARCINOMA (RCC)/KIDNEY CANCER

Nivolumab and hyaluronidase-nvhy (Opdivo Qvantig) is considered medically necessary and, therefore, covered in adult individuals with advanced RCC in one of the following:

- As single-agent first-line therapy in individuals with intermediate or poor risk following combination treatment with intravenous nivolumab (Opdivo) and ipilimumab (Yervoy)
- First-line therapy in combination with cabozantinib
- As single-agent therapy in individuals who have received prior antiangiogenic therapy (e.g., sorafenib [Nexavar], sunitinib [Sutent], bevacizumab [Avastin], pazopanib [Votrient], axitinib [Inlyta])

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered for the treatment of individuals with RCC, for the following regimens:

- As single-agent therapy in individuals with advanced disease who have received prior antiangiogenic therapy (e.g., sorafenib [Nexavar], sunitinib [Sutent], bevacizumab [Avastin], pazopanib [Votrient], axitinib [Inlyta])
- As single-agent therapy for relapse or stage IV disease
 - As subsequent therapy for clear cell histology if immune-oncology therapy naïve
 - As systemic therapy for non-clear cell histology
- In combination with ipilimumab, for the first-line treatment of individuals with intermediate or poor risk
- In combination with ipilimumab for four cycles, followed by single-agent nivolumab (Opdivo) for relapse or stage IV disease with clear cell histology as:
 - NCCN-preferred first-line therapy for poor/intermediate risk
 - Subsequent therapy if immune-oncology therapy naïve or prior history immune-oncology therapy
- In combination with cabozantinib for relapse or stage IV disease with clear cell histology as:
 - NCCN-preferred first-line therapy
 - Subsequent therapy if immune-oncology therapy naïve or prior history immune-oncology therapy
 - Subsequent therapy if prior history includes immuno-oncology therapy
- In combination with cabozantinib for relapse or stage IV disease as systemic therapy for non-clear cell histology (NCCN-preferred)
- In combination with cabozantinib as systemic therapy for non-clear cell histology including hereditary leiomyomatosis and renal cell carcinoma (HLRCC)-associated RCC

SMALL CELL LUNG CANCER (SCLC)

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered as a single agent for small cell lung cancer with no previous treatment with a checkpoint inhibitor with a chemotherapy-free interval of 6 months or less, as subsequent systemic therapy for individuals with PS 0-2 for one of the following:

- Relapse following complete or partial response or stable disease with primary treatment
- Primary progressive disease

SOFT TISSUE SARCOMA

Extremity/body wall, head/neck

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered as a single agent or in combination with ipilimumab (Yervoy) as palliative therapy for advanced/metastatic disease with disseminated metastases for either of the following:

- Myxofibrosarcoma, undifferentiated pleomorphic sarcoma (UPS), dedifferentiated liposarcoma, cutaneous angiosarcoma, and undifferentiated sarcomas
- Unresectable or metastatic tumor mutational burden-high (TMB-H) [10 mutations/megabase (mut/Mb) or greater] tumors that have progressed following prior treatment and have no satisfactory alternative treatment options regardless of soft tissue sarcoma subtype

Retroperitoneal/Intra-abdominal

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered as a single agent or in combination with ipilimumab (Yervoy) for unresectable or progressive disease as alternative systemic therapy after initial therapy for unresectable or stage IV disease or as subsequent lines of therapy for recurrent unresectable or recurrent stage IV disease for either of the following:

- Myxofibrosarcoma, undifferentiated pleomorphic sarcoma (UPS), dedifferentiated liposarcoma, cutaneous angiosarcoma, and undifferentiated sarcomas
- Unresectable or metastatic TMB-H tumors that have progressed following prior treatment and have no satisfactory alternative treatment options regardless of soft tissue sarcoma subtype

Pleomorphic rhabdomyosarcoma

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered as a single agent or in combination with ipilimumab (Yervoy) for advanced/metastatic disease as subsequent line of therapy, including for unresectable or metastatic TMB-H tumors that have progressed following prior treatment and have no satisfactory alternative treatment options

Angiosarcoma

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered in combination with ipilimumab (Yervoy) for advanced/metastatic or unresectable disease

T-CELL LYMPHOMAS - EXTRANODAL NK/T-CELL LYMPHOMA

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered as NCCN-preferred therapy for relapsed/refractory disease following additional therapy with an alternate combination chemotherapy regimen (asparaginase-based) not previously used, if a clinical trial is unavailable.

THYROID CARCINOMA

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered as a single agent for anaplastic carcinoma in one of the following scenarios:

- First-line therapy (aggressive) for stage IVC (metastatic) disease
- Second-line therapy for stage IVC (metastatic) disease

UROTHELIAL CARCINOMA (UC)

Nivolumab (Opdivo) and Nivolumab and Hyaluronidase-nvhy (Opdivo Qvantig) is considered medically necessary and, therefore, covered in combination with cisplatin and gemcitabine as first-line therapy for individuals with unresectable or metastatic UC

Nivolumab (Opdivo) and nivolumab and hyaluronidase-nvhy (Opdivo Qvantig) is considered medically necessary and, therefore, covered as single-agent therapy for the treatment of one of the following indications:

- Adjuvant therapy for UC in individuals who are at high risk of recurrence after undergoing radical resection of UC
- Locally advanced or metastatic UC in individuals with disease progression, in one of the following scenarios:
 - During or following platinum-containing chemotherapy

- Within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy

Bladder cancer

- Adjuvant therapy for bladder cancer, in one of the following scenarios:
 - Stage II (cT2, N0) disease following cystectomy based on pathologic risk if no cisplatin neoadjuvant treatment was given and pT3, pT4a, or pN+
 - Stage II (cT2, N0) disease following cystectomy based on pathologic risk if cisplatin neoadjuvant treatment was given and ypT2-ypT4a or ypN+
 - Stage IIIA (cT3, N0; cT4a, N0; cT1-4a, N1) disease following cystectomy based on pathologic risk if no cisplatin neoadjuvant treatment was given and pT3, pT4a, or pN+
 - Stage IIIA (cT3, N0; cT4a, N0; cT1-4a, N1) disease following cystectomy based on pathologic risk if cisplatin neoadjuvant treatment was given ypT2-ypT4a or ypN+
- First-line systemic therapy in combination with cisplatin and gemcitabine followed by nivolumab maintenance therapy in cisplatin eligible individuals in one of the following scenarios:
 - Stage II (cT2, N0) disease or stage IIIA (cT3, N0; cT4a, N0; cT1-T4a, N1) disease if tumor is present following reassessment of tumor status 2-3 months after primary treatment with bladder preserving concurrent chemoradiotherapy and maximal TURBT
 - Stage II (cT2, N0) disease or stage IIIA (cT3, N0; cT4a, N0; cT1-T4a, N1) disease if tumor is present following reassessment of tumor status 2-3 months after primary treatment with radiotherapy alone or TURBT
 - Stage IIIB (cT1-T4a, N2,3) disease as downstaging systemic therapy
 - Stage IIIB (cT1-T4a, N2,3) disease following partial response or progression after primary treatment with concurrent chemoradiotherapy
 - Stage IVA (cT4b, any N, M0; any T, any N, M1a) disease
 - Stage IVA (cT4b, any N, M0) disease as consolidation systemic therapy if no tumor present following reassessment of tumor status 2-3 months after primary treatment with concurrent chemoradiotherapy

- Stage IVA (cT4b, any N, M0) disease if tumor present following reassessment of tumor status 2-3 months after primary treatment with concurrent chemoradiotherapy
 - Metastatic stage IVB (any T, any N, M1b) disease
 - Muscle invasive local recurrence or persistent disease in a preserved bladder treated with curative intent
 - Metastatic or local recurrence post cystectomy treated with curative intent
- Second-line systemic therapy postplatinum or other chemotherapy for bladder cancer, as a single agent (NCCN-alternative preferred) in one of the following scenarios:
 - Stage II (cT2, N0) disease or stage IIIA (cT3, N0; cT4a, N0; cT1-T4a, N1) disease if tumor is present following reassessment of tumor status 2-3 months after primary treatment with concurrent bladder preserving chemoradiotherapy and maximal TURBT
 - Stage IIIB (cT1-T4a, N2,3) disease following partial response or progression after primary treatment with downstaging systemic therapy or concurrent chemoradiotherapy
 - Stage IVA (cT4b, any N, M0) disease if tumor is present following reassessment of tumor status after primary treatment with first-line systemic therapy or concurrent chemoradiotherapy
 - Stage IVA (any T, any N, M1a) disease if stable disease or progression following reassessment of tumor status after primary treatment with first-line systemic therapy
 - Metastatic stage IVB (any T, any N, M1b) disease
 - Muscle invasive local recurrence or persistent disease in a preserved bladder treated with curative intent
 - Metastatic or local recurrence postcystectomy treated with curative intent

Primary carcinoma of the urethra

- Primary treatment for clinical stage T3-4, cN1-2 disease or cN1-2 palpable inguinal lymph nodes as first-line systemic therapy in combination with cisplatin and gemcitabine

in cisplatin eligible patients followed by nivolumab maintenance therapy

- Adjuvant treatment may be considered for pathologic stage T3-4 or N1-2 disease in the male bulbar urethra:
 - If platinum-based neoadjuvant chemotherapy not given and pT3, pT4a, pN+
 - If platinum-based neoadjuvant chemotherapy given and ypT2-ypT4a or ypN+
- First-line therapy in combination with cisplatin and gemcitabine in cisplatin eligible patients followed by nivolumab maintenance therapy or as single agent for recurrent or metastatic disease as second-line systemic therapy post-platinum or other chemotherapy (NCCN-alternative preferred) (regimen excludes coverage for the recurrence of clinical stage T3-4 disease or palpable inguinal lymph nodes)

Upper genitourinary tract tumors

- Adjuvant therapy for pathologic stage T2-4 or nodal disease (N+) of the renal pelvis or UC of the ureter, if platinum-based neoadjuvant chemotherapy given or not given and ypT2-ypT4 or ypN+
- Therapy for metastatic disease as first-line therapy in combination with cisplatin and gemcitabine in cisplatin eligible patients followed by nivolumab maintenance therapy or as a single agent for second-line systemic therapy postplatinum or other chemotherapy (NCCN-alternative preferred)

Urothelial carcinoma of the prostate

- Primary treatment for tumors with stromal invasion as adjuvant therapy if platinum-based neoadjuvant chemotherapy not given and pT3, pT4a, pN+
- Therapy for metastatic disease first-line therapy in combination with cisplatin and gemcitabine in cisplatin-eligible patients followed by nivolumab maintenance therapy or as a single agent for second-line systemic therapy postplatinum or other chemotherapy (NCCN-alternative preferred)

UTERINE NEOPLASMS - ENDOMETRIAL CARCINOMA

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered as single-agent therapy for second-line or subsequent treatment for recurrent MSI-H or dMMR tumors in one of the following scenarios:

- For isolated metastases

- For disseminated metastases with or without sequential palliative external beam radiation therapy (EBRT)
- With sequential EBRT and with or without brachytherapy for locoregional recurrence in individuals with no prior RT to site of recurrence, or previous vaginal brachytherapy only
- After surgical exploration, with sequential EBRT for locoregional recurrence in individuals with disease confined to the vagina or paravaginal soft tissue, or in pelvic or para-aortic lymph nodes
- After surgical exploration, with or without sequential EBRT for locoregional recurrence in individuals with upper abdominal or peritoneal disease
- With or without sequential palliative EBRT or brachytherapy for locoregional recurrence in individuals who have received prior EBRT to site of recurrence

VAGINAL CANCER

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered as single-agent therapy for second-line or subsequent treatment if PD-L1 positive (CPS ≥ 1) in one of the following scenarios:

- Locoregional recurrence
- Stage IVB or recurrent distant metastases

VULVAR CANCER

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered as single-agent therapy for second-line or subsequent treatment of human papillomavirus (HPV)-related advanced, recurrent, or metastatic disease

CONTINUATION OF THERAPY

Nivolumab (Opdivo) is considered medically necessary and, therefore, covered for continuation therapy when treatment guidelines do not specify a limited number of total doses (see NCCN and/or current version MA08.059 Ipilimumab (Yervoy®) Attachment A - Dosing and Frequency Requirements For Ipilimumab [Yervoy®]) and there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

MANDATES

PENNSYLVANIA MEMBERS

In accordance with the Commonwealth of Pennsylvania's Act 6 of 2020 or Fair Access to Cancer Treatment Act, for members who are enrolled in Pennsylvania commercial products who have stage 4, advanced metastatic cancer, refer to the Medical Policy titled "Coverage of Anticancer Prescription Oral and Injectable Drugs and Biologics and Supportive Agents" (08.01.08) for additional information regarding the applicable coverage of drugs and biologics.

EXPERIMENTAL/INVESTIGATIONAL

All other uses for nivolumab (Opdivo) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Duration of authorization: 12 months

Version Effective Date: 03/24/2025

Title: Nivolumab and Relatlimab-rmbw (Opdualag™)

MEDICALLY NECESSARY

MELANOMA: CUTANEOUS

Nivolumab and relatlimab-rmbw (Opdualag), administered as an intravenous (IV) infusion, is considered medically necessary and, therefore, covered for adult and pediatric individuals 12 years of age or older with unresectable or metastatic* melanoma, as National Comprehensive Cancer Network (NCCN)-preferred systemic therapy** for any of the following therapies:

- First-line therapy (NCCN-preferred combination checkpoint blockade therapy)
- Second-line or subsequent therapy for disease progression, intolerance and/or projected risk of progression with b-rapidly accelerated fibrosarcoma (BRAF)-targeted therapy
- Re-induction therapy if prior combination anti-PD-1/LAG-3 therapy (e.g., nivolumab and relatlimab-rmbw [Opdualag]) resulted in disease control (complete response, partial response, or stable disease) with no residual toxicity, and disease progression/relapse more than 3 months after treatment discontinuation

*Metastatic disease includes stage III unresectable/borderline resectable disease with clinically positive node(s) or clinical satellite/in-transit metastases, or as well as unresectable/borderline resectable local satellite/in-transit recurrence, unresectable nodal recurrence, and widely disseminated distant metastatic disease.

**Systemic therapy is NCCN-preferred for unresectable or widely disseminated distant metastatic disease.

Nivolumab and relatlimab-rmbw (Opdualag) is considered medically necessary and, therefore, covered for adult individuals with resectable melanoma as neoadjuvant therapy for any of the following therapies:

- Primary treatment for stage III clinically positive, resectable nodal disease
- Initial and/or subsequent treatment for:
 - Limited resectable stage III disease with clinical satellite/in-transit metastases
 - Limited resectable local satellite/in-transit recurrence
- Treatment for resectable disease limited to nodal recurrence

MANDATES

PENNSYLVANIA MEMBERS

In accordance with the Commonwealth of Pennsylvania's Act 6 of 2020 or Fair Access to Cancer Treatment Act, for members who are enrolled in Pennsylvania commercial products who have Stage 4, advanced metastatic cancer, refer to the medical policy titled "Coverage of Anticancer Prescription Oral and Injectable Drugs and Biologics and Supportive Agents" (08.01.08) for additional information regarding the applicable coverage of drugs and biologics.

EXPERIMENTAL/INVESTIGATIONAL

All other uses for nivolumab and relatlimab-rmbw (Opdualag) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the service.

Duration of authorization: 12 months

Version Effective Date: 06/16/2025

Title: Nogapendekin alfa inbakicept-pmIn (Anktiva®)

MEDICALLY NECESSARY

NOGAPENDEKIN ALFA INBAKICEPT-PMLN (ANKTIVA)

Initial therapy

Nogapendekin alfa inbakicept-pmIn (Anktiva) injection for intravesical instillation is considered medically necessary and, therefore, covered in individuals 18 years and older for the treatment of high-risk non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors when ALL of the following criteria are met:

- The individual has Bacillus Calmette-Guérin (BCG)-unresponsive* disease, defined as persistent or recurrent disease following adequate BCG therapy:**
 - As initial management
 - As recurrent or persistent disease that is cytology-positive, imaging- and cystoscopy-negative, and bladder-positive
- Medication is used in combination with BCG
- The individual has undergone transurethral resection of bladder tumor (TURBT) to remove all resectable disease (Ta and T1 components)
- The individual does NOT have muscle invasive (T2-T4), locally advanced, metastatic, or extravesical (i.e., urethra, ureter, or renal pelvis) urothelial carcinoma
- The individual's Eastern Cooperative Oncology Group (ECOG) performance score is less than or equal to 2.

*High-grade T1 at the first evaluation following induction BCG (3 months); recurrent high-grade Ta/T1 within 6 months of adequate BCG treatment; or recurrent CIS within 12 months of the last adequate BCG treatment.

**Adequate BCG therapy defined as having received at least two previous courses of BCG within a 12-month period defined as either:

- At least five of six induction BCG instillations AND at least two of three instillations of maintenance BCG; or

- At least two of six instillations of a second induction course where maintenance BCG is not given.

Continuation therapy

Continued therapy with nogapendekin alfa inbakicept-pmIn (Anktiva) is considered medically necessary and, therefore, covered when ALL of the following criteria are met while on the current regimen:

- There is no unacceptable toxicity.
- Clinical documentations demonstrate that the individual continues to show a positive clinical response to therapy (i.e., absence of recurrent high-grade NMIBC).

MANDATES

PENNSYLVANIA MEMBERS

In accordance with the Commonwealth of Pennsylvania's Act 6 of 2020 or Fair Access to Cancer Treatment Act, for members who are enrolled in Pennsylvania commercial products who have stage 4, advanced metastatic cancer, refer to the Medical Policy titled "Coverage of Anticancer Prescription Oral and Injectable Drugs and Biologics and Supportive Agents" (08.01.08) for additional information regarding the applicable coverage of drugs and biologics.

EXPERIMENTAL/INVESTIGATIONAL

All other uses for nogapendekin alfa inbakicept-pmIn (Anktiva) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the

participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Duration of authorization: 12 months

Version Effective Date: 04/21/2025

Title: Nutritional Formulas, Enteral Nutrition, Medical Foods, Low-Protein Modified Food Products, and Donated Breast Milk

MEDICALLY NECESSARY

NUTRITIONAL FORMULAS AND ENTERAL NUTRITION

Administration Through a Tube

Commercially available nutritional formulas (including enteral nutrition) and associated enteral supplies (including pump, tubing, feeding supply kits) prescribed by a professional provider are considered medically necessary and, therefore, covered for individuals of all ages when **all** of the following criteria **AND** the subsequent mandate criteria are met:

- The commercially available nutritional formula requires administration via a tube (e.g., percutaneous endoscopic gastrostomy [PEG] tube, jejunostomy tube [J-tube], percutaneous endoscopic jejunostomy [PEJ], nasogastric [NG] tube) into the alimentary canal.
- The tube feeding does not have to be the sole source of nutrition (i.e., more than 75% of estimated basal caloric requirements).
- Examples of nutritional formulas and enteral nutrition that can be administered through a tube include, but are not limited to, Boost, EleCare Infant or Jr., Glucerna, Isosource, Jevity, Nutren, Osmolite, PediaSure, Peptamen, Tolerex, Vivonex.

For Pennsylvania infant and child members, see Attachment A for PA Mandate Information.

For New Jersey members 12 months and under, see Attachment B for NJ Mandate Information.

For information regarding caloric requirements, see Attachment C.

Administration Orally

Infants and Children

Commercially available nutritional formulas prescribed by a professional provider are considered medically necessary and, therefore, covered for infants and children who require oral administration of an elemental formula (e.g., EleCare Infant or Jr., Neocate Splash, PurAmino, Neocate Junior or Infant, Tolerex, Vivonex) as the sole source of nutrition (i.e., the formula provides more than 75% of estimated basal caloric requirements) and who meet **one or more** of the following criteria **AND** meet the subsequent Mandate criteria:

- The individual suffers from severe systemic protein hypersensitivity (e.g., IgE-mediated: eosinophilic esophagitis, eosinophilic gastritis, eosinophilic gastroenteritis; non-IgE-mediated: food protein-induced entities such as enterocolitis) that is refractory to dietary and other treatments. Infants younger than 1 year of age must be shown to be refractory to treatment for at least 2 weeks with standard milk or soy protein formulas (e.g., Enfamil A.R., Similac with Iron, Similac for Diarrhea, Enfamil Prosobee), and refractory to treatment for at least 2 weeks with nonstandard, extensively hydrolyzed formulas (e.g., Nutramigen, Pregestimil, Similac Alimentum).
- The individual has a disorder(s) of gross anatomy impeding or obstructing passage of nutrition through the alimentary canal (e.g., stricture, tumor, blind pouches).

For Pennsylvania infant and child members, see Attachment A for PA Mandate Information.

NOTE: Members enrolled in a Pennsylvania Product are **not** required to meet the Company's definition of sole source of nutrition (i.e., the formula provides more than 75% of estimated basal caloric requirements); therefore, an estimated basal caloric requirement is not required.

For New Jersey members 12 months and under, see Attachment B for NJ Mandate Information. For information regarding caloric requirements, see Attachment C.

Adults

Commercially available nutritional

formulas (e.g., Boost, Ensure, Glucerna, Jevity, Osmolite) prescribed by a professional provider are considered medically necessary and, therefore, covered for adults who require oral administration of nutritional formulas as the sole source of nutrition (i.e., the formula provides more than 75% of estimated basal caloric requirements) when the individual has a disorder(s) of gross anatomy impeding or obstructing the passage of nutrition through the alimentary canal (e.g., stricture, tumor, blind pouches).

For information regarding caloric requirements, see Attachment C.

MEDICAL FOODS FOR INBORN ERRORS OF METABOLISM ADMINISTERED ORALLY OR THROUGH A TUBE

Medical foods prescribed by a professional provider and administered orally or via a tube into the alimentary canal for individuals diagnosed with genetic (inherited) inborn errors of metabolism (IEM), such as phenylketonuria (PKU), homocystinuria, branched-chain ketonuria, galactosemia, and maple syrup urine disease, are covered for individuals of all ages who need administration of a formula that is manufactured for individuals with IEMs.

- Medical foods are **not** required to meet the Company's definition of sole source of nutrition (i.e., the formula provides more than 75% of estimated basal caloric

requirements); therefore, an estimated basal caloric requirement is not required for IEMs.

- Examples of medical foods for individuals diagnosed with IEM include, but are not limited to, BCAD 1 or 2, OA 1 or 2, PFD 2 or Toddler, PhenylAde, Phenyl-Free 1 or 2 or 2HP, Ketonex 1 or 2.

For Pennsylvania members, see Attachment A for PA Mandate Information.

For New Jersey members, see Attachment B for NJ Mandate Information.

For information regarding caloric requirements, see Attachment C.

LOW-PROTEIN MODIFIED FOODS FOR INBORN ERRORS OF METABOLISM

New Jersey Products

Low-protein modified food products prescribed by a professional provider are covered by the Company in accordance with the state mandates for individuals enrolled in a New Jersey product subject to New Jersey's insurance law who are diagnosed with an inherited errors of metabolism, and the treatment is determined to be medically necessary by the individual's physician.

For New Jersey members, see Attachment B for NJ Mandate Information.

Pennsylvania Products

Low-protein modified food products are not covered by the Company for individuals enrolled in Pennsylvania products for IEM because they do not meet the Company's definition of medical foods or nutritional formulas. Therefore, they are not eligible for reimbursement consideration.

For Pennsylvania members, see Attachment A for PA Mandate Information.

IMMOBILIZED LIPASE CARTRIDGE (E.G., RELIZORB)

Initial Therapy

Immobilized lipase cartridge (e.g., Relizorb), up to six cartridges per day, is considered medically necessary and, therefore, covered for individuals 2 years of age and older when all of the

following criteria are met:

- The individual has a documented diagnosis of cystic fibrosis with exocrine pancreatic insufficiency
- The individual has continued malabsorption of fats (i.e., weight loss or inadequate weight gain) from enteral formula despite optimization of pancreatic enzyme replacement therapy (PERT)

Continuation Therapy

Immobilized lipase cartridge (e.g., Relizorb) is considered medically necessary and, therefore, covered for continuation therapy when the individual with cystic fibrosis and exocrine pancreatic insufficiency meets both of the following:

- There is documentation of a positive clinical response or stabilization due to the cartridge use (e.g., weight gain, BMI increase to—or maintained at—50th percentile, or decreased symptoms of malabsorption, such as diarrhea)
- The individual is not using more than six cartridges per day, per product labeling

NOT COVERED

Nutritional formulas, enteral nutrition, or medical foods not prescribed by a healthcare provider are not covered by the Company because they are a benefit contract exclusion. Therefore, they are not eligible for reimbursement consideration.

Infant, child, or adult nutritional formulas or enteral nutrition that do not meet the Company's coverage criteria are not covered by the Company, and are, therefore, not eligible for reimbursement consideration. Examples include the following:

- Extensively hydrolyzed formulas (e.g., Nestle Extensive HA, Nutramigen, Pregestimil, Similac Alimentum)
- Oral polymeric formulas (e.g., Boost, Enfamil EnfaCare, Ensure, NeoSure, PediaSure, Scandishake) for infants and children

- Oral nutritional formulas and enteral nutrition for individuals with a diagnosis of malnutrition due to anorexia or failure to thrive
- Oral organic formulas (e.g., Kate Farms Organic formula, Similac Organic formula)

Banked breast milk is not covered by the Company, and is therefore not eligible for reimbursement consideration. For members enrolled in New Jersey Products, donated banked breast milk may be covered through a New Jersey Mandate. Individual benefits must be verified.

Elemental semisolid foods (e.g., Neocate Nutra) are not covered by the Company, and are therefore not eligible for reimbursement consideration.

Products that are used to replace fluids and electrolytes (e.g., Electrolyte Gastro, Pedialyte), for adults and children, are not covered by the Company, and are therefore not eligible for reimbursement consideration.

Medical foods for non-IEM (e.g., Encala) are not covered by the Company because they are a benefit contract exclusion. Therefore, they are not eligible for reimbursement consideration.

Oral additives (e.g., Duocal, fiber, probiotics, supplements [e.g., PKU Easy Microtabs] or vitamins) and food thickeners (e.g., Thick-It, Resource ThickenUp) for adults and children, are not covered by the Company, and are therefore not eligible for reimbursement consideration.

- Most prescribed enteral formulas are nutritionally complete (i.e., they contain all vital nutrients, including vitamins and fiber). Therefore, additives and food thickeners are not eligible for separate reimbursement.
 - Nutritional formulas that are incomplete are described as such because they consist of specific nutrients to meet the nutritional needs of individuals with IEM.

Supplies associated with the oral administration of formula (e.g., bottles, nipples) are not covered by the Company, and are therefore not eligible for reimbursement consideration.

EXPERIMENTAL/INVESTIGATIONAL

All other uses for nutritional formulas, enteral nutrition, medical foods, low-protein modified food products, and immobilized lipase cartridge (e.g., Relizorb) are considered experimental/investigational and, therefore, not covered because their safety and/or effectiveness cannot be established by review of the available published peer-reviewed literature.

REQUIRED DOCUMENTATION

The Company may conduct reviews and audits of services to our members regardless of the participation status of the provider. Medical record documentation must be maintained on file to reflect the medical necessity of the care and services provided. These medical records may include but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

STANDARD ORDER

Before submitting a claim to the Company, the supplier must have on file a timely, appropriate, and complete order for each item billed that is signed and dated by the professional provider who is treating the member. Requesting a provider to sign a retrospective order at the time of an audit or after an audit for submission as an original order, reorder, or updated order will not satisfy the requirement to maintain a timely professional provider order on file.

PROOF OF DELIVERY

Medical record documentation must include a contemporaneously prepared delivery confirmation or member's receipt of supplies and equipment. The medical record documentation must include a copy of delivery confirmation if delivered by a commercial carrier and a signed copy of delivery confirmation by member/caregiver if delivered by the durable medical equipment (DME) supplier/provider. All documentation is to be prepared contemporaneous with delivery and be available to the Company upon request.

ASSOCIATED SUPPLIES (WHEN APPLICABLE)

The DME supplier must monitor the quantity of accessories and supplies an individual is actually using. Contacting the individual regarding replenishment of supplies should not be done earlier than approximately 30 days prior to the delivery/shipping date. Dated documentation of this contact with the individual is required in the individual's medical record. Delivery of the supplies should not be done earlier than approximately 10 days before the individual would exhaust their on-hand supply.

If required documentation is not available on file to support a claim at the time of an audit or

record request, the DME supplier may be required to reimburse the Company for overpayments.

The maximum number of supplies that can be dispensed at one time is no more than a 1-month supply (maximum 31-day supply). Supply allowance HCPCS codes (B4034, B4035, B4036, and B4148) are daily allowances that are considered all-inclusive and therefore refill requirements are not applicable to these HCPCS codes.

Duration of authorization: 12 months

Version Effective Date: 09/09/2024

Attachment A: [Nutritional Formulas, Enteral Nutrition, Medical Foods, Low-Protein Modified Food Products, and Donated Breast Milk](#)

Description: PA Mandates

Attachment B: [Nutritional Formulas, Enteral Nutrition, Medical Foods, Low-Protein Modified Food Products, and Donated Breast Milk](#)

Description: NJ Mandates

Attachment C: [Nutritional Formulas, Enteral Nutrition, Medical Foods, Low-Protein Modified Food Products, and Donated Breast Milk](#)

Description: Caloric Requirements

Policy Attachment

Attachment to Policy # 08.00.18q

Attachment: A

Policy #: 08.00.18q

Description: PA Mandates

Title: Nutritional Formulas, Enteral Nutrition, Medical Foods, Low-Protein Modified Food Products, and Donated Breast Milk

COMMONWEALTH OF PENNSYLVANIA MANDATE

Coverage is subject to the terms, conditions, and limitations of the member's contract. State mandates do not automatically apply to self-funded groups, but may be included or excluded at the option of the group; therefore, individual group benefits must be verified.

For members enrolled in a Pennsylvania product, The Medical Foods Insurance Coverage Act makes provision of insurance coverage for the following:

NUTRITIONAL FORMULAS AND ENTERAL NUTRITION

Pennsylvania mandates require coverage of orally or enterally administered amino acid-based elemental medical formulas (i.e., formula made of 100% free amino acids as the protein source) when ordered by a physician as medically necessary for infants and children with food protein allergies, food protein-induced enterocolitis syndrome, eosinophilic disorders and short bowel syndrome.

NOTE: Members described above are not required to meet the Company's definition of sole source of nutrition (i.e., the formula provides more than 75 percent of estimated basal caloric requirements); therefore, an estimated basal caloric requirement is not required.

MEDICAL FOODS FOR INBORN ERRORS OF METABOLISM ADMINISTERED ORALLY OR THROUGH A TUBE

Prescription medical foods (formulas) administered orally or via a tube into the alimentary canal for individuals diagnosed with a rare genetic (inherited) inborn errors of metabolism (IEM), such as phenylketonuria (PKU), homocystinuria, branched-chain ketonuria, and galactosemia are covered for individuals of all ages who need administration of a formula that is manufactured for the therapeutic treatment and dietary management of individuals with IEMs and is administered under the direction of a physician.

- Medical foods are not required to meet the Company's definition of sole source of nutrition (i.e., the formula provides more than 75 percent of estimated basal caloric requirements); therefore, an estimated basal caloric requirement is not required for IEMs.
- Medical foods are exempt from Deductible requirements.

LOW-PROTEIN MODIFIED FOOD PRODUCTS FOR INBORN ERRORS OF METABOLISM

Pennsylvania Mandate does not require coverage for low-protein modified food products such as breads, pasta, pastry shells, and rice pizza shells that can be purchased commercially without a prescription and are used in the dietary management of rare hereditary genetic metabolic disorders such as PKU, branched chain-ketonuria, galactosemia, and homocystinuria.

REFERENCES

Laws of PA. 1492. Act 1996-191. HB 1532. Approved 12/20/1996. Available at: <http://www.palrb.us/pamphletlaws/19001999/1996/0/act/0191.pdf> or <http://www.legis.state.pa.us/cfdocs/billinfo/billinfo.cfm?year=1995&sind=0&body=H&type=B&bn=1532>.

Amended Act of Oct. 22, 2014, P.L. 2564, No. 158. Cl. 40. PA HB 1436. Available at: <http://www.legis.state.pa.us/cfdocs/legis/li/uconsCheck.cfm?yr=2014&sessInd=0&act=158>.

Version Effective Date: 09/09/2024

Policy Attachment

Attachment to Policy # 08.00.18q

Attachment: B

Policy #: 08.00.18q

Description: NJ Mandates

Title: Nutritional Formulas, Enteral Nutrition, Medical Foods, Low-Protein Modified Food Products, and Donated Breast Milk

NEW JERSEY STATE MANDATES

Coverage is subject to the terms, conditions, and limitations of the member's contract. State mandates do not automatically apply to self-funded groups, but may be included or excluded at the option of the group; therefore, individual group benefits must be verified.

NEW JERSEY SPECIALTY INFANT FORMULA PROGRAM

For members enrolled in a New Jersey product, Coverage of Certain Infant Formulas Act 2001-2002, P.L. 2001, Ch 361, makes provision of insurance coverage for specialized nonstandard infant formulas, when the covered infant's physician has diagnosed the infant as having multiple food protein intolerance and has determined such formula to be medically necessary, and when the covered infant has not been responsive to trials of standard non-cow milk-based formulas, including soybean and goat milk.

In accordance with NJ Statute, P.L. 2001, c.361, specialized nonstandard infant formula is available only to infants (ages 0 through 12 months) enrolled in a New Jersey plan that includes coverage for prescription drugs or who have a freestanding prescription drug program. Coverage for specialized infant formulas is subject to utilization review, including periodic review, of the continued medical necessity of the specialized infant formula.

- http://www.njleg.state.nj.us/2000/Bills/PL01/361_.HTM

- http://www.njleg.state.nj.us/2000/Bills/S2000/1839_S1.PDF

New Jersey Members with a Pharmacy Benefit

Specialized nonstandard infant formulas are covered only through the pharmacy benefit when all of the following criteria are met:

- The individual is enrolled in a New Jersey product that includes coverage for prescription drugs.
- The individual requires these formulas from birth through 12 months of age.
- The individual has been diagnosed with multiple food protein intolerance and has failed standard non-cow milk-based formulas, including soybean and goat milk.
- The professional provider has determined that specialized infant formulas are medically necessary.
- Continued coverage for specialized infant formulas is subject to utilization review, including periodic review, of the continued medical necessity of the specialized non-standard infant formula.
- Examples of specialized non-standard infant formulas list includes, but is not limited to, the following: Elecare Infant or Jr.; Nutramigen; Progestimil; Neocate Junior or Infant; Portagen; Alimentum; NeoSure

For additional information addressing the New Jersey Specialty Infant Formula Program, contact the individual's Prescription Benefit Plan.

New Jersey Members without a Pharmacy Benefit

- If the individual has a pharmacy benefit with another company, the individual should be directed to seek coverage from that plan.
- If the individual does not have a pharmacy benefit with another plan, only nutritional formulas for individuals with inherited metabolic disorders are covered under the member's medical benefit when the medical necessity criteria contained within the policy are met.
- Coverage of these products is subject to periodic review for continued medical necessity.

All other requests for nutritional formulas are treated as a benefit exclusion.

MEDICAL FOODS AND LOW-PROTEIN MODIFIED FOOD PRODUCTS FOR INBORN ERRORS OF METABOLISM ADMINISTERED ORALLY OR THROUGH A TUBE

For members enrolled in a New Jersey product, An Act concerning coverage for foods and food products for inherited metabolic diseases (Chapter 338, Approved January 12, 1998) Ch 27, 17B:27-46.1r (1998) provides for insurance coverage for the following:

Coverage for the therapeutic treatment of inherited metabolic diseases, including the purchase of medical foods and low-protein modified food products, when the disease is diagnosed and the

treatment is determined to be medically necessary by the individual's physician.

"Low protein modified food product" means a food product that is specially formulated to have less than one gram of protein per serving and is intended to be used under the direction of a physician for the dietary treatment of an inherited metabolic disease, but does not include a natural food that is naturally low in protein; and "medical food" means a food that is intended for the dietary treatment of a disease or condition for which nutritional requirements are established by medical evaluation and is formulated to be consumed or administered enterally under direction of a physician.

NJ Approved January 12, 1998.

http://www.njleg.state.nj.us/9697/Bills/PL97/338_.HTM.

Medical foods and low protein modified foods are covered under the medical benefit when both of the following criteria are met:

- The individual is diagnosed with an inherited error of metabolism.
- The required medical necessity documentation is provided the individuals' physician.

DONATED HUMAN BREAST MILK

For members enrolled in a New Jersey product, An Act concerning coverage for donated human breast milk (Public Law 2017, c 301; Approved January 16, 2018) provides for insurance coverage for the following:

Expenses incurred in the provision of pasteurized donated human breast milk (including human milk fortifiers) are covered by the Company in accordance with the state mandates for individuals enrolled in a New Jersey product subject to New Jersey's insurance law.

Coverage of pasteurized donated human breast milk, which may include human milk fortifiers, is based on meeting criteria which include the following:

- I. The covered person is an infant under the age of six months
- II. The milk is obtained from a human milk bank that meets quality guidelines established by the Department of Health
- III. The licensed medical practitioner who is prescribing the milk must meet one of the following requirements:
 - a. The licensed medical practitioner has issued an order for an infant who is medically or physically unable to receive maternal breast milk or participate in breast feeding or whose mother is medically or physically unable to produce maternal breast milk in sufficient quantities or participate in breast feeding despite optimal lactation support; or
 - b. The licensed medical practitioner has issued an order for an infant who meets any of the following conditions:

- 1) a body weight below healthy levels determined by the licensed medical practitioner
- 2) a congenital or acquired condition that places the infant at a high risk for development of necrotizing enterocolitis
- 3) a congenital or acquired condition that may benefit from the use of donor breast milk as determined by the Department of Health

Coverage for donated human breast milk is subject to utilization review, including periodic review, of the continued medical necessity.

NOTE: If there is no supply of human breast milk that meets the above requirements, the insurer shall not be required to provide coverage of expenses pursuant to this section.

NJ Effective January 1, 2019.

<http://www.njleg.state.nj.us/2016/Bills/PL17/309 .PDF>.

Version Effective Date: 09/09/2024

Policy Attachment

Attachment to Policy # 08.00.18q

Attachment: C

Policy #: 08.00.18q

Description: Caloric Requirements

Title: Nutritional Formulas, Enteral Nutrition, Medical Foods, Low-Protein Modified Food Products, and Donated Breast Milk

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and

pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

This attachment contains several calculations for the energy requirements for individuals.

CALORIC REQUIREMENTS IN CHILDREN

SAMPLE ESTIMATED ENERGY REQUIREMENTS FOR HEALTHY BOYS AND GIRLS OF MEDIAN WEIGHT AND HEIGHT (FOR AGE AT 50TH PERCENTILE)

Age	Boys - estimated energy requirements (kcal/kg/day)			Girls - estimated energy requirements (kcal/kg/day)		
0–2 mo	107			104		
3 mo	95			95		
4–35 mo	82			82		
	Boys			Girls		
	Median Weight, Boys (kg)	Sedentary * (kcal/kg/d)	Active * (kcal/kg/d)	Median Weight, Girls (kg)	Sedentary * (kcal/kg/d)	Active * (kcal/kg/d)
3 yr	14.3	80	104	13.9	76	100
4 yr	16.2	74	97	15.8	70	93
5 yr	18.4	68	90	17.9	65	87

6 yr	20.7	63	84	20.2	61	81
7 yr	23.1	59	80	22.8	56	75
8 yr	25.6	56	75	25.6	52	71
9 yr	28.6	53	71	29.0	48	65
10 yr	31.9	49	67	32.9	44	60
11 yr	35.9	46	63	37.2	41	56
12 yr	40.5	44	60	41.6	38	52
13 yr	45.6	42	57	45.8	36	50
14 yr	51.0	40	55	49.4	34	47
15 yr	56.3	39	54	52.0	33	45
16 yr	60.9	38	52	53.9	32	44
17 yr	64.6	36	50	55.1	31	43
18 yr	67.2	35	49	56.2	30	42

* See definition of sedentary and active Physical Activity Level (PAL) below for further information.

References for Caloric Requirements in Children:

Engorn B, Flerlage J. The Harriet Lane Handbook. 20th ed. Philadelphia, PA: Elsevier Saunders; 2015.

Otten JJ, Hellwig JP, Meyers LD, eds. *Dietary Reference Intakes: The Essential Guide to Nutrient Requirements*. Washington, DC: National Academies Press, 2006.

***PHYSICAL ACTIVITY LEVELS (PAL) IN CHILDREN AND ADULTS:**

Physical Activity Coefficients (PA Values) for Use in EER Equations

	Sedentary (PAL* 1.0–1.39)	Low Active (PAL* 1.4–1.59)	Active (PAL* 1.6–1.89)	Very Active (PAL* 1.9–2.5)
	Typical daily living activities (e.g., household tasks, walking to the bus)	Typical daily living activities PLUS 30-60 minutes of daily moderate activity (e.g., walking 5-7 km/h)	Typical daily living activities PLUS at least 60 minutes of daily moderate activity	Typical daily living activities PLUS at least 60 minutes of daily moderate activity PLUS an additional 60 minutes of vigorous activity or 120 minutes of moderate activity
Boys 3–18 y	1.00	1.13	1.26	1.42
Girls 3–18 y	1.00	1.16	1.31	1.56
Men 19 y +	1.00	1.11	1.25	1.48
Women 19 y +	1.00	1.12	1.27	1.45

References for Caloric Requirements in Children:

Coulston A, Boushey CJ, Ferruzzi MG. Nutrition in the Prevention and Treatment of Disease, 3rd Ed. 2013.

Engorn B, Flerlage J. The Harriet Lane Handbook. 20th ed. Philadelphia, PA: Elsevier Saunders; 2015.

Escott-Stump S. Nutrition and Diagnosis - Related Care, 7th Ed. 2012. Wolters Kluwer/Lippincott Williams & Wilkins. Philadelphia, PA.

Otten JJ, Hellwig JP, Meyers LD, eds. *Dietary Reference Intakes: The Essential Guide to Nutrient Requirements*. Washington, DC: National Academies Press, 2006.

CALORIC REQUIREMENTS IN CHILDREN AND ADULTS:

1. Equations based on the following sources: Coulston 2013, Escott-Stump (2012), Otten (2006)

Infants and Young Children

Estimated Energy Requirement (EER) (kcal/day) = Total Energy Expenditure + Energy Deposition

0–3 months $EER^a = (89 \times \text{weight [kg]} - 100) + 175$

4–6 months $EER = (89 \times \text{weight [kg]} - 100) + 56$

7–12 months $EER = (89 \times \text{weight [kg]} - 100) + 22$

13–35 months $EER = (89 \times \text{weight [kg]} - 100) + 20$

Children and Adolescents 3–18 years

Estimated Energy Requirement (EER) (kcal/day) = Total Energy Expenditure + Energy Deposition

Boys

3–8 years $EER = 88.5 - (61.9 \times \text{age [y]}) + PAL \times [(26.7 \times \text{weight [kg]}) + (903 \times \text{height [m]})] + 20$

9–18 years $EER = 88.5 - (61.9 \times \text{age [y]}) + PAL \times [(26.7 \times \text{weight [kg]}) + (903 \times \text{height [m]})] + 25$

Girls

3–8 years $EER = 135.3 - (30.8 \times \text{age [y]}) + PAL \times [(10.0 \times \text{weight [kg]}) + (934 \times \text{height [m]})] + 20$

9–18 years $EER = 135.3 - (30.8 \times \text{age [y]}) + PAL \times [(10.0 \times \text{weight [kg]}) + (934 \times \text{height [m]})] + 25$

Adults 19 years and older

Estimated Energy Requirement (EER) (kcal/day) = Total Energy Expenditure

Men $EER = 662 - (9.53 \times \text{age [y]}) + PAL \times [(15.91 \times \text{weight [kg]}) + (539.6 \times \text{height [m]})]$

Women $EER = 354 - (6.91 \times \text{age [y]}) + PAL \times [(9.36 \times \text{weight [kg]}) + (726 \times \text{height [m]})]$

Pregnancy

Estimated Energy Requirement (EER) (kcal/day) = Nonpregnant EER + Pregnancy Energy Deposition

1st trimester $EER = \text{Nonpregnant EER} + 0$

2nd trimester $EER = \text{Nonpregnant EER} + 340$

3rd trimester $EER = \text{Nonpregnant EER} + 452$

Lactation

Estimated Energy Requirement (EER) (kcal/day) = Nonpregnant EER + Milk Energy Output – Weight Loss

0–6 months postpartum $EER = \text{Nonpregnant EER} + 500 - 170$

7–12 months postpartum $EER = \text{Nonpregnant EER} + 400 - 0$

NOTE: These equations provide an estimate of energy requirement. Relative body weight (i.e., loss, stable, gain) is the preferred indicator of energy adequacy.

* See definition of sedentary and active Physical Activity Level (PAL) above for further information.

References for Caloric Requirements in Children and Adults:

Coulston A, Boushey CJ, Ferruzzi MG. Nutrition in the Prevention and Treatment of Disease, 3rd Ed. 2013.

Escott-Stump S. Nutrition and Diagnosis - Related Care, 7th Ed. 2012. Wolters Kluwer/Lippincott Williams & Wilkins. Philadelphia, PA.

Otten JJ, Hellwig JP, Meyers LD, eds. *Dietary Reference Intakes: The Essential Guide to Nutrient Requirements*. Washington, DC: National Academies Press, 2006.

2. Harris-Benedict Equations (1919):

REE = Resting Energy Expenditure

Women: $REE \text{ (kcal/day)} = 655 + 9.56 \text{ (weight in kg)} + 1.85 \text{ (height in cm)} - 4.68 \text{ (age in years)}$

Men: $REE \text{ (kcal/day)} = 66.5 + 13.75 \text{ (weight in kg)} + 5 \text{ (height in cm)} - 6.76 \text{ (age in years)}$

References for Caloric Requirements in Children and Adults:

Coulston A, Boushey CJ, Ferruzzi MG. Nutrition in the Prevention and Treatment of Disease, 3rd Ed. 2013.

Harris JA, Benedict FG. [A Biometric Study of Basal Metabolism in Man](#). Washington, DC: Carnegie Institution, 1919.

3. Harris-Benedict Equations revised by Mifflin and St Jeor (1990):

REE = Resting Energy Expenditure.

Note: REE is usually multiplied by PAL*

Females: $REE = 10 \times \text{weight (kg)} + 6.25 \times \text{height (cm)} - 5 \times \text{age (y)} - 161$

Males: $REE = 10 \times \text{weight (kg)} + 6.25 \times \text{height (cm)} - 5 \times \text{age (y)} + 5$

References for Caloric Requirements in Children and Adults:

Mifflin MD, St Jeor ST, Hill LA, Scott BJ, Daugherty SA, Koh YO. [A new predictive equation for resting energy expenditure in healthy individuals](#). *Am J Clin Nutr*. 1990 Feb;51(2):241-7.

CALORIC REQUIREMENTS IN ADULTS:

Short methods for calculating energy needs:

1. Energy Needs Based on Level of Activity or Illness:

	Level of Activity or Illness		
Goal	Low	Moderate	High
Lose weight	15 kcal/kg	20 kcal/kg	25 kcal/kg
Maintain weight	20 kcal/kg	25 kcal/kg	30 kcal/kg
Gain weight	25 kcal/kg	30 kcal/kg	35 kcal/kg

2. Energy Needs Based on Gender:

Note: weight in lbs.

Men or active women	15 kcal/lb
Most women, sedentary men, adults over 55 years	13 kcal/lb
Sedentary women, obese adults	10 kcal/lb
Pregnant women	
1 st trimester	13-15 kcal/lb
2 nd and 3 rd trimester	16-17 kcal/lb
Lactating women	15-17 kcal/lb

References for Caloric Requirements Adults:

Escott-Stump S. Nutrition and Diagnosis - Related Care, 7th Ed. 2012. Wolters Kluwer/Lippincott Williams & Wilkins. Philadelphia, PA.

Version Effective Date: 09/09/2024

Title: Ocrelizumab (Ocrevus®) and Ocrelizumab and Hyaluronidase-ocsq (Ocrevus Zunovo™)

MEDICALLY NECESSARY

Ocrelizumab (Ocrevus®), administered as an intravenous (IV) infusion, or ocrelizumab and hyaluronidase-ocsq (Ocrevus Zunovo™), as a subcutaneous (SC) injection, are considered medically necessary and, therefore, covered for the treatment of adults with either relapsing forms of multiple sclerosis (RMS) (including clinically isolated syndrome [CIS], relapsing-remitting disease, and active secondary progressive disease) or primary progressive forms of multiple sclerosis (PPMS) when the individual is hepatitis B negative (i.e., has negative results for hepatitis B surface antigen [HBsAg] and anti-hepatitis B virus tests).

EXPERIMENTAL/INVESTIGATIONAL

All other uses for ocrelizumab (Ocrevus) or ocrelizumab and hyaluronidase-ocsq (Ocrevus Zunovo), including nonrelapsing secondary progressive MS, are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Duration of authorization: 12 months

Version Effective Date: 04/21/2025

Title: Octreotide Acetate (Sandostatin® LAR Depot)

MEDICALLY NECESSARY

Octreotide acetate (Sandostatin LAR Depot) is considered medically necessary and, therefore, covered for the long-term treatment of any of the following conditions in individuals who have already started therapy with octreotide acetate (Sandostatin) immediate-release formulation, when the corresponding Dosing and Frequency Requirements are met:

- Acromegaly
 - For the management of individuals who had inadequate response to surgery and/or radiotherapy, or for whom surgery and/or radiotherapy was not an option
 - Dosage and frequency up to 40 mg every 4 weeks
- Metastatic Carcinoid Tumors
 - For the management of severe diarrhea and flushing episodes associated with metastatic carcinoid tumors
 - Dosage and frequency up to 30 mg every 4 weeks
- Neuroendocrine and Adrenal Tumors (See corresponding Dosing and Frequency Requirements, listed after each condition)
 - Neuroendocrine Tumors of the GI Tract (well-differentiated Grade 1/2), Lung, and Thymus
 - As primary treatment for symptom and /or tumor control for unresected primary gastrinoma
 - For symptom control in individuals with carcinoid syndrome:
 - as a single agent
 - in combination with telotristat (Xermelo) for persistent diarrhea due to poorly controlled carcinoid syndrome
 - in combination with other systemic therapies (based on disease site) with or without telotristat (Xermelo) for persistent symptoms such as flushing or diarrhea due to poorly controlled carcinoid syndrome

- For symptom and/or tumor control of recurrent, locoregional advanced disease and/or distant metastases* of the gastrointestinal tract
 - as a single agent if unresectable and a low tumor burden
 - as a single agent for disease progression (if not already receiving) following resection of primary + metastases
 - as a single agent for disease progression (if not already receiving) following observation unresectable low tumor burden
 - as a single agent following resection of primary tumor if unresectable and locally symptomatic from primary tumor
 - as a single agent or in combination with alternative front-line therapy if clinically significant tumor burden
 - as a single agent as subsequent therapy at above label dosing after clinical, symptomatic, or radiographic progression (if SSTR-positive) on standard doses

- For symptom and/or tumor control of recurrent and/or locoregional unresectable bronchopulmonary/thymic disease* if somatostatin receptor positive and/or hormonal symptoms
 - as primary therapy
 - as subsequent therapy (as alternate primary therapy) if progression on primary therapy

- For symptom and/or tumor control of recurrent and/or distant metastatic bronchopulmonary/thymic disease* if somatostatin receptor positive and/or hormonal symptoms (preferred if clinically significant tumor burden and low grade (typical carcinoid), evidence of disease progression, intermediate grade (atypical carcinoid histology), or symptomatic.
 - as primary therapy
 - as subsequent therapy (as alternate primary therapy) if progression on primary therapy if clinically significant tumor burden and low grade (typical carcinoid), evidence of disease progression, intermediate grade (atypical carcinoid histology), or symptomatic
 - at above label dosing if clinically significant tumor burden and low grade (typical carcinoid), evidence of disease progression,

intermediate grade (atypical carcinoid histology), or symptomatic after clinical, symptomatic, or radiographic progression (if SSTR-positive and/or hormonal symptoms) on standard doses

- For symptom and/or tumor control of multiple lung nodules or tumorlets and evidence of diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH) chronic cough/dyspnea is not responsive to inhalers as primary therapy
- Dosage and frequency up to 30 mg every four weeks until disease progression or unacceptable toxicity
- Neuroendocrine Tumors of the Pancreas (Islet Cell Tumors) (well-differentiated Grade 1/2)
 - For the management of symptoms and /or tumor control of locoregional disease
 - for gastrinoma (usually duodenal or head of pancreas)
 - insulinoma only if tumor expresses somatostatin receptors
 - for glucagonoma (usually tail)
 - for VIPoma
 - For symptom and/or tumor control as subsequent therapy at above label dosing after clinical, symptomatic or radiographic progression on standard doses (if SSTR-positive)
 - For NCCN-Preferred for symptoms and /or tumor control in individuals** with recurrent or locoregional advanced disease and/or distant metastatic disease* if somatostatin receptor (SSTR) - positive
 - as a single agent for asymptomatic, low tumor burden and stable disease
 - as a single agent for symptomatic, clinically significant tumor burden, or clinically significant progression (if disease progression and not already receiving)
 - in combination with alternative front-line therapy for symptomatic, clinically significant tumor burden, or clinically

significant progression

- Dosage and frequency up to 30 mg every four weeks until disease progression or unacceptable toxicity
- Pheochromocytoma/Paraganglioma
 - As primary treatment of either of the following:
 - for hormone excess and symptom control of locally unresectable disease or distant metastases (if SSTR-positive) of secreting tumors
 - Dosage and frequency up to 30 mg every four weeks
- Neuroendocrine Tumors: well-differentiated Grade 3, as treatment of symptoms and /or tumor (if SSTR-positive and/or hormonal symptoms) for unresectable locally advanced/metastatic disease with favorable biology (e.g. relatively low Ki-67 [$<55\%$], positive SSTR-based PET imaging)
 - Dosage and frequency up to 30 mg every four weeks until disease progression or unacceptable toxicity
- Thymomas and Thymic Carcinomas
 - Preoperative systemic therapy if octreotide scan or dotatate PET/CT positive with or without prednisone for individuals who cannot tolerate first-line combination regimens for thymoma for surgically resectable disease if R0 resection is considered uncertain
 - Postoperative treatment if octreotide scan or dotatate PET/CT positive with or without prednisone for individuals who cannot tolerate first-line combination regimens for thymoma after R2 resection
 - First-line therapy if octreotide scan or dotatate PET/CT positive with or without prednisone for individuals who cannot tolerate first-line combination regimens for:
 - potentially resectable locally advanced disease
 - potentially resectable solitary metastasis or ipsilateral pleural metastasis
 - following surgery for solitary metastasis or ipsilateral pleural metastasis

- medically inoperable/unresectable solitary metastasis or ipsilateral pleural metastasis
 - extrathoracic metastatic disease
- Second-line therapy if octreotide scan or dotatate PET/CT positive with or without prednisone for:
 - unresectable locally advanced disease
 - solitary metastasis or ipsilateral pleural metastasis
 - extrathoracic metastatic disease
- Dosage and frequency up to 30 mg every four weeks until disease progression or unacceptable toxicity
- Central Nervous System Cancers - Meningiomas
 - in combination with everolimus for surgically inaccessible recurrent or progressive disease when radiation is not possible
 - Dosage and frequency up to 30 mg every 4 weeks until disease progression or unacceptable toxicity
- Vasoactive Intestinal Peptide (VIP)-secreting Tumors
 - For the management of profuse watery diarrhea associated with VIP-secreting tumors
 - Dosage and frequency up to 30 mg every four weeks

Per NCCN:

*If disease progression, treatment with octreotide LAR should be continued in individuals with functional tumors and may be used in combination with any of the systemic therapy options.

**For individuals with insulinoma, octreotide should be used only if somatostatin scintigraphy is positive.

EXPERIMENTAL/INVESTIGATIONAL

All other uses for octreotide acetate (Sandostatin LAR Depot), including dosage and frequency up to the covered amount specified, are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

MANDATES

PENNSYLVANIA MEMBERS

In accordance with the Commonwealth of Pennsylvania's Act 6 of 2020 or Fair Access to Cancer Treatment Act, for members who are enrolled in Pennsylvania commercial products who have Stage 4, advanced metastatic cancer, refer to the Medical Policy titled Coverage of Anticancer Prescription Oral and Injectable Drugs and Biologics and Supportive agents (08.01.08) for additional information regarding the applicable coverage of drugs and biologics.

DOSING AND FREQUENCY REQUIREMENTS

The Company reserves the right to modify the Dosing and Frequency Requirements listed in this policy to ensure consistency with the most recently published recommendations for the use of octreotide acetate (Sandostatin LAR Depot). Changes to these guidelines are based on a consensus of information obtained from resources such as, but not limited to: the US Food and Drug Administration (FDA); Company-recognized authoritative pharmacology compendia; or published peer-reviewed clinical research. The professional provider must supply supporting documentation (i.e., published peer-reviewed literature) in order to request coverage for an amount of octreotide acetate (Sandostatin LAR Depot) outside of the Dosing and Frequency Requirements listed in this policy. For a list of Company-recognized pharmacology compendia, view the Company's policy on off-label coverage for prescription drugs and biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of this drug. If the member's dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider must submit those changes to the Company for a new approval based on those changes as part of the precertification process. The Company reserves the right to conduct post-payment review and audit procedures for any claims submitted for octreotide acetate (Sandostatin LAR Depot).

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

When coverage of octreotide acetate (Sandostatin LAR Depot) is requested outside of the Dosing and Frequency Requirements listed in this policy, the prescribing professional provider must supply documentation (i.e., published peer-reviewed literature) to the Company that supports this request.

Duration of authorization: 12 months

Version Effective Date: 10/01/2024

Attachment A: [Octreotide Acetate \(Sandostatin® LAR Depot\)](#)

Description: ICD-10 CODES AND NARRATIVES

Policy Attachment

Attachment to Policy # 08.01.10j

Attachment: A

Policy #: 08.01.10j

Description: ICD-10 CODES AND NARRATIVES

Title: Octreotide Acetate (Sandostatin® LAR Depot)

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding

changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

ICD-10 CODES AND NARRATIVES

C25.4 Malignant neoplasm of endocrine pancreas

C37 Malignant neoplasm of thymus

C70.0 Malignant neoplasm of cerebral meninges

C70.1 Malignant neoplasm of spinal meninges

C70.9 Malignant neoplasm of meninges, unspecified

C74.01 Malignant neoplasm of cortex of right adrenal gland

C74.02 Malignant neoplasm of cortex of left adrenal gland

C74.11 Malignant neoplasm of medulla of right adrenal gland

C74.12 Malignant neoplasm of medulla of left adrenal gland

C74.91 Malignant neoplasm of unspecified part of right adrenal gland

C74.92 Malignant neoplasm of unspecified part of left adrenal gland

C75.5 Malignant neoplasm of aortic body and other paraganglia

C7A.00 Malignant carcinoid tumor of unspecified site

C7A.010 Malignant carcinoid tumor of the duodenum

C7A.011 Malignant carcinoid tumor of the jejunum

C7A.012 Malignant carcinoid tumor of the ileum

C7A.019 Malignant carcinoid tumor of the small intestine, unspecified portion

C7A.020 Malignant carcinoid tumor of the appendix

C7A.021 Malignant carcinoid tumor of the cecum

C7A.022 Malignant carcinoid tumor of the ascending colon

C7A.023 Malignant carcinoid tumor of the transverse colon

C7A.024 Malignant carcinoid tumor of the descending colon

C7A.025 Malignant carcinoid tumor of the sigmoid colon

C7A.026 Malignant carcinoid tumor of the rectum

C7A.029 Malignant carcinoid tumor of the large intestine, unspecified portion

C7A.090 Malignant carcinoid tumor of the bronchus and lung

C7A.091 Malignant carcinoid tumor of the thymus

C7A.092 Malignant carcinoid tumor of the stomach

C7A.093 Malignant carcinoid tumor of the kidney

C7A.094 Malignant carcinoid tumor of the foregut, unspecified

C7A.095 Malignant carcinoid tumor of the midgut, unspecified

C7A.096 Malignant carcinoid tumor of the hindgut, unspecified

C7A.098 Malignant carcinoid tumors of other sites

C7A.1 Malignant poorly differentiated neuroendocrine tumors

C7A.8 Other malignant neuroendocrine tumors

C7B.00 Secondary carcinoid tumors, unspecified site

C7B.01 Secondary carcinoid tumors of distant lymph nodes

C7B.02 Secondary carcinoid tumors of liver

C7B.03 Secondary carcinoid tumors of bone

C7B.04 Secondary carcinoid tumors of peritoneum

C7B.09 Secondary carcinoid tumors of other sites

C7B.8 Other secondary neuroendocrine tumors

D13.7 Benign neoplasm of endocrine pancreas

D15.0 Benign neoplasm of thymus

D32.0 Benign neoplasm of cerebral meninges

D32.1 Benign neoplasm of spinal meninges

D32.9 Benign neoplasm of meninges, unspecified

D35.01 Benign neoplasm of right adrenal gland

D35.02 Benign neoplasm of left adrenal gland

D3A.00 Benign carcinoid tumor of unspecified site

D3A.010 Benign carcinoid tumor of the duodenum

D3A.011 Benign carcinoid tumor of the jejunum

D3A.012 Benign carcinoid tumor of the ileum

D3A.019 Benign carcinoid tumor of the small intestine, unspecified portion

D3A.020 Benign carcinoid tumor of the appendix

D3A.021 Benign carcinoid tumor of the cecum

D3A.022 Benign carcinoid tumor of the ascending colon

D3A.023 Benign carcinoid tumor of the transverse colon

D3A.024 Benign carcinoid tumor of the descending colon

D3A.025 Benign carcinoid tumor of the sigmoid colon

D3A.026 Benign carcinoid tumor of the rectum

D3A.029 Benign carcinoid tumor of the large intestine, unspecified portion

D3A.090 Benign carcinoid tumor of the bronchus and lung

D3A.091 Benign carcinoid tumor of the thymus

D3A.092 Benign carcinoid tumor of the stomach

D3A.094 Benign carcinoid tumor of the foregut, unspecified

D3A.095 Benign carcinoid tumor of the midgut, unspecified

D3A.096 Benign carcinoid tumor of the hindgut, unspecified

D3A.098 Benign carcinoid tumors of other sites

D3A.8 Other benign neuroendocrine tumors

E16.1 Other hypoglycemia

E16.3 Increased secretion of glucagon

E16.4 Increased secretion of gastrin

E16.8 Other specified disorders of pancreatic internal secretion

E22.0 Acromegaly and pituitary gigantism

E34.00 Carcinoid syndrome, unspecified

E34.01 Carcinoid heart syndrome

E34.09 Other carcinoid syndrome

Title: Off-label Coverage for Prescription Drugs and/or Biologics

Policy

Coverage is subject to the terms, conditions, and limitations of the member's contract.

The Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition.

CRITERIA TO ESTABLISH MEDICAL NECESSITY FOR OFF-LABEL COVERAGE OF US FOOD AND DRUG ADMINISTRATION (FDA)--APPROVED DRUGS AND/OR BIOLOGICS

Off-label use of prescription drugs and/or biologics can include factors such as indications, dosages, frequencies, or routes of administration that are inconsistent with US Food and Drug Administration (FDA) labeling. For off-label use, additional clinical rationale is required to support coverage.

Off-label use of prescription drugs and/or biologics is considered medically necessary and, therefore, covered when the off-label use is supported by either the Company-recognized prescription drug and/or biologic compendia, or published research, as outlined below.

1. COMPENDIA FOR ONCOLOGIC USE (ANTI-CANCER CHEMOTHERAPY)

For coverage of an anti-cancer chemotherapy regimen, the off-label use is considered medically necessary and therefore covered when one of the following criteria is met:

- The narrative text in American Hospital Formulary Service--Drug Information (AHFS-DI®) is supportive of the use.
- The use is classified as Category 1 or 2A by National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium™.
- The use is classified as Class I or Class IIa in Micromedex® DrugDex® Compendium.

An anti-cancer chemotherapy regimen is considered experimental/investigational even when above criteria have been met, and when one of the following exists:

- The use is classified as Category 3 by NCCN® or Class III in Micromedex® DrugDex®.
- The narrative text in AHFS-DI® is not supportive of the use.

- Any of the compendia listed above state that the prescription drug and/or biologic is not indicated, is unsupported, is not recommended, or equivalent terms are used regarding the prescription drug and/or biologic

When a compendia is considered neither supportive nor non-supportive (ie, Category 2B in NCCN, Class IIb in Micromedex® DrugDex®, or an absence of narrative text or evidence classification from any Company-recognized compendium), please refer to the section in this policy entitled Published Clinical Research.

2. COMPENDIA FOR NON-ONCOLOGIC USE

For coverage of non-oncologic prescription drugs and/or biologics, the off-label use is considered medically necessary and therefore covered when one of the following exists:

- The narrative text in American Hospital Formulary Service--Drug Information (AHFS-DI®) is supportive of the use.
- The use is classified as Class I or Class IIa in Micromedex® DrugDex® Compendium.

Non-oncologic drugs and/or biologics are considered experimental/investigational and therefore not covered, even when the above criteria have been met, and when one of the following exists:

- The use is classified as Class III in Micromedex® DrugDex®.
- The narrative text in AHFS-DI® is not supportive of the use.
- Either of the compendia listed above state that the prescription drug and/or biologic is not indicated, is unsupported, is not recommended, or equivalent terms are used regarding the prescription drug and/or biologic.

When a compendia is considered neither supportive nor non-supportive (i.e., Class IIb in Micromedex® DrugDex®, or an absence of narrative text or evidence classification from any Company-recognized compendium), please refer to the section in this policy entitled Published Clinical Research.

3. PUBLISHED CLINICAL RESEARCH

In order for an off-label use to be supported by published clinical research, all of the following criteria must be met:

- The prescription drug and/or biologic must have been studied in at least two clinical trials conducted at different centers, and the results must have been published in national or international peer-reviewed journals with an editorial committee composed of physicians. Peer-reviewed medical literature includes scientific, medical, and pharmaceutical publications. It does not include in-house publications of pharmaceutical manufacturing companies or abstracts (including meeting abstracts).
 - A use is considered supported by clinical research when it appears in at least two Phase III clinical trials that have definitively demonstrated its safety and effectiveness as an appropriate medical treatment for the condition. If no Phase III trial evidence is available, at least two Phase II clinical trials with reasonably large patient samples showing consistent results of safety and efficacy may be considered in certain instances (e.g., in rare diseases in which a Phase III study might be difficult to complete in a reasonable period of time after completion of the Phase II studies, or when overwhelmingly good evidence of safety and effectiveness is noted in the Phase II studies).
- Reliable evidence must demonstrate that the proposed off-label use for the specified medical condition is safe and effective and that the beneficial effects of the treatment outweigh its risks.
- In determining whether there is supportive clinical evidence for a particular use of a prescription drug and/or biologic, the quality of the evidence in published, peer-reviewed medical literature is considered. Among other things, such consideration involves the assessment of the following:
 - The prevalence and life history of the disease when evaluating the adequacy of the number of subjects and the response rate
 - The effect on the individual's well-being and other responses to therapy that indicate effectiveness (e.g., reduction in mortality, morbidity, and signs and symptoms)
 - Whether the clinical characteristics of the beneficiary and the use are adequately represented in the published evidence
 - Whether the study is appropriate to address the clinical question, such as:
 - If the study design is appropriate to address investigative questions (e.g., in some clinical studies, it may be unnecessary or not feasible to use randomization, double-blind trials, placebos, or crossover)
 - If non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of prescription drug and/or biologic

- Generally, case reports are considered uncontrolled, are based on anecdotal information, and do not provide adequate supportive clinical evidence for determining accepted uses of prescription drugs and/or biologics
- The off-label use is supported by published clinical research, and the results have been published in major peer-reviewed medical journals such as, but not limited to:

• <i>American Journal of Medicine</i> • <i>Annals of Internal Medicine</i> • <i>Annals of Oncology</i> • <i>Annals of Surgical Oncology</i> • <i>Biology of Blood and Marrow Transplantation</i> • <i>Blood</i> • <i>Bone Marrow Transplantation</i> • <i>British Journal of Cancer</i> • <i>British Journal of Hematology</i> • <i>British Medical Journal</i> • <i>Cancer</i> • <i>Clinical Cancer Research</i> • <i>Drugs</i> • <i>European Journal of Cancer</i>	• <i>Gynecologic Oncology</i> • <i>International Journal of Radiation, Oncology, Biology, and Physics</i> • <i>Journal of Clinical Oncology</i> • <i>Journal of the National Cancer Institute</i> • <i>Journal of the National Comprehensive Cancer Network (NCCN)</i> • <i>Journal of Urology</i> • <i>Lancet</i> • <i>Lancet Oncology</i> • <i>Leukemia</i> • <i>Radiation Oncology</i> • <i>The Journal of the American Medical Association</i> • <i>The New England Journal of Medicine</i>

EXPERIMENTAL/INVESTIGATIONAL

Prescription drugs and/or biologics that are considered experimental/investigational are not covered because the safety and/or effectiveness of the prescription drug and/or biologic cannot be established by a review of the available published peer-reviewed literature. Prescription drugs and/or biologics are considered experimental/investigational for any of the following:

- The prescription drug and/or biologic has not received US Food and Drug Administration (FDA) approval for any use.
- The off-label use of the prescription drug and/or biologic does not meet the medical necessity criteria listed in this policy or in any other specific Company Medical Policy addressing a drug and/or biologic (i.e., the off-label use is not recognized by the appropriate compendia or published clinical research). This includes products granted orphan designation by the FDA.
- The FDA determines a prescription drug and/or biologic to be contraindicated for specific condition(s) or specific off-label use(s).
- The off-label use is not medically accepted or not indicated by a compendium for specific conditions (i.e., the use is a Category 3 in NCCN, Class III in Micromedex® DrugDex®, or when the narrative text in AHFS-DI® is not supportive.)
 - The absence of narrative text for an off-label use is considered neither supportive nor non-supportive.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the prescription drug and/or biologic.

Duration of authorization: 12 months

Version Effective Date: 09/18/2024

Title: olipudase alfa-rpcp (Xenpozyme®)

MEDICALLY NECESSARY

INITIAL THERAPY

Olipudase alfa-rpcp (Xenpozyme) is considered medically necessary and, therefore, covered for individuals with acid sphingomyelinase deficiency (ASMD) when all of the following criteria are met, including dosing and frequency requirements listed in Attachment A:

- Diagnosis of non–central nervous system manifestations of ASMD type B or type A/B is confirmed by one of the following:
 - Molecular genetic testing that reveals biallelic pathogenic variants in the *SMPD1* (sphingomyelin phosphodiesterase-1) gene
 - Residual acid sphingomyelinase activity that is less than 10% of controls (in peripheral blood lymphocytes or cultured skin fibroblasts)
- Prescribed by, or in consultation with, a metabolic disease specialist, geneticist, or a specialist in the treatment of lysosomal storage disorders

CONTINUATION THERAPY

Continuation of olipudase alfa-rpcp (Xenpozyme) is considered medically necessary and, therefore, covered for individuals who have a documentation of a positive clinical response to therapy (e.g., decrease in spleen size, decrease in liver size, increase in platelet count, improved lung function)

NOT MEDICALLY NECESSARY

When molecular genetic testing does not reveal a genetic etiology for ASMD type B or type A/B (e.g., results of testing show established benign variation(s), lack of biallelic pathogenic variation, or wild-type genotype in the *SMPD1* gene), olipudase alfa-rpcp (Xenpozyme) is considered not medically necessary and, therefore, not covered because the available published peer-reviewed literature does not support its use in the treatment of this disease.

EXPERIMENTAL/INVESTIGATIONAL

All other uses for olipudase alfa-rpcp (Xenpozyme) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

DOSING AND FREQUENCY REQUIREMENTS

Refer to Attachment A for dosing and frequency requirements for olipudase alfa-rpcp (Xenpozyme).

The Company reserves the right to modify the Dosing and Frequency Requirements listed in this policy to ensure consistency with the most recently published recommendations for the use of olipudase alfa-rpcp (Xenpozyme). Changes to these guidelines are based on a consensus of information obtained from resources such as, but not limited to: the US Food and Drug Administration (FDA); Company-recognized authoritative pharmacology compendia; or published peer-reviewed clinical research. The professional provider must supply supporting documentation (i.e., published peer-reviewed literature) in order to request coverage for an amount of olipudase alfa-rpcp (Xenpozyme) outside of the Dosing and Frequency Requirements listed in this policy. For a list of Company-recognized pharmacology compendia, view our policy on off-label coverage for prescription drugs and biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of this drug. If the member's dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider must submit those changes to the Company for a new approval based on those changes as part of the utilization management activities. The Company reserves the right to conduct post-payment review and audit procedures for any claims submitted for olipudase alfa-rpcp (Xenpozyme).

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the service.

When coverage of olipudase alfa-rpcp (Xenpozyme) is requested outside of the Dosing and Frequency Requirements listed in this policy, the prescribing professional provider must supply documentation (i.e., published peer-reviewed literature) to the Company that supports this request.

Duration of authorization: 12 months

Version Effective Date: 03/05/2025

Attachment A: [olipudase alfa-rpcp \(Xenpozyme®\)](#)

Description: Dosing and Frequency Requirements for olipudase alfa-rpcp (Xenpozyme)

Policy Attachment

Attachment to Policy # 08.01.96a

Attachment: A

Policy #: 08.01.96a

Description: Dosing and Frequency Requirements for olipudase alfa-rpcp (Xenpozyme)

Title: olipudase alfa-rpcp (Xenpozyme®)

DOSING AND FREQUENCY REQUIREMENTS FOR OLIPUDASE ALFA-RPCP (XENPOZYME)

The Company reserves the right to modify the Dosing and Frequency Requirements listed in this Policy to ensure consistency with the most recently published recommendations for the use of olipudase alfa-rpcp (Xenpozyme). Changes to these guidelines are based on a consensus of information obtained from resources such as, but not limited to: the US Food and Drug Administration (FDA); Company-recognized authoritative pharmacology compendia; or published peer-reviewed clinical research. The professional provider must supply supporting documentation (i.e., published peer-reviewed literature) in order to request coverage for an amount of olipudase alfa-rpcp (Xenpozyme) outside of the Dosing and Frequency Requirements listed in this Policy. For a list of Company-recognized pharmacology compendia, view our policy on off-label coverage for prescription drugs and biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of this drug. If the member's dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider **must** submit those changes to the Company for a new approval based on those changes as part of the precertification process. The Company reserves the right to conduct post-payment review and audit procedures for any claims submitted for olipudase alfa-rpcp (Xenpozyme).

Olipudase alfa-rpcp (Xenpozyme) is administered via intravenous infusion every 2 weeks. Dosages are based on body mass index (BMI):

- BMI $\leq$ 30, the dosage is based on actual body weight (kg)
- BMI > 30, the dosage is based on adjusted body weight (kg). Calculation: Adjusted body weight (kg) = (actual height in meters)² x 30

PEDIATRIC DOSING:

Dose Escalation Phase:	Pediatric (ages 0-17 years)
First dose (Day 1/Week 0)	0.03 mg/kg
Second dose (Week 2)	0.1 mg/kg
Third dose (Week 4)	0.3 mg/kg
Fourth dose (Week 6)	0.3 mg/kg
Fifth dose (Week 8)	0.6 mg/kg
Sixth dose (Week 10)	0.6 mg/kg
Seventh dose (Week 12)	1 mg/kg

Eighth dose (Week 14)	2 mg/kg
Ninth dose (Week 16)	3 mg/kg
Maintenance Phase:	3 mg/kg every 2 weeks

ADULT DOSING:

Dose Escalation Phase:	Adult (ages 18 years and older)
First dose (Day 1/Week 0)	0.1 mg/kg
Second dose (Week 2)	0.3 mg/kg
Third dose (Week 4)	0.3 mg/kg
Fourth dose (Week 6)	0.6 mg/kg
Fifth dose (Week 8)	0.6 mg/kg
Sixth dose (Week 10)	1 mg/kg
Seventh dose (Week 12)	2 mg/kg
Eighth dose (Week 14)	3 mg/kg
Maintenance Phase:	3 mg/kg every 2 weeks

Dosing modifications, withholdings, or slowing of infusion rate may be necessary for adverse reactions or missed doses. See the product's prescribing information for more details.

Version Effective Date: 03/05/2025

Title: Omalizumab (Xolair®)-Medical

MEDICALLY NECESSARY

INITIAL THERAPY

Allergic Asthma

Omalizumab (Xolair) is considered medically necessary and, therefore, covered as an adjunctive treatment of moderate-to-severe persistent asthma in individuals who are at least 6 years of age when **all** of the following criteria and the Dosing and Frequency Requirements listed in Attachment A are met:

- The individual has a positive skin test or in vitro reactivity to a perennial aeroallergen.
 - The individual has a baseline serum immunoglobulin E (IgE) level of between 30 IU/mL and 1500 IU/mL.
 - High-dose inhaled corticosteroids (ICS) taken in combination with a long-acting beta-agonist (LABA) have been tried but failed to adequately control the individual's asthma symptoms.
 - Omalizumab (Xolair) will not be used in combination with other biologics for asthma/allergic conditions (e.g., benralizumab [Fasenra], dupilumab [Dupixent], mepolizumab [Nucala], reslizumab [Cinqair]).
- Dosing and Frequency Requirements: See Attachment A.

Chronic Urticaria

Omalizumab (Xolair) is considered medically necessary and, therefore, covered for the treatment of chronic urticaria in individuals who are at least 12 years of age when **all** of the following criteria, including Dosing and Frequency Requirements listed below, are met:

- Documented failure, contraindication, or intolerance to a 4-week trial of one second-generation nonsedating H1 antihistamine at the maximum recommended doses (e.g., cetirizine [Zyrtec], fexofenadine [Allegra], loratadine [Claritin, Alavert], desloratadine [Clarinex], levocetirizine [Xyzal])
- Documented failure, contraindication, or intolerance to at least a 2-week trial of **any** of the following medications:
 - Leukotriene receptor antagonist (e.g., zafirlukast [Accolate], montelukast [Singulair], zileuton [Zyflo]) in addition to the nonsedating H1 antihistamine

- Histamine H2-receptor antagonist (e.g., cimetidine [Tagamet], famotidine [Pepcid], nizatidine) in addition to the nonsedating H1 antihistamine
- First-generation (sedating) H1 antihistamine (e.g., chlorpheniramine [Chlor-Trimeton], cyproheptadine, diphenhydramine [Benadryl]) in addition to the nonsedating H1 antihistamine
- Systemic glucocorticosteroids administered as a short-term therapy (may treat for less than a 2-week trial) in addition to the nonsedating H1 antihistamine
- Addition of, or substitution to, a different second-generation nonsedating H1 antihistamine
- Cyclosporine, in addition to the nonsedating H1 antihistamine
- Omalizumab (Xolair) will not be used in combination with other biologics for asthma/allergic conditions (e.g., benralizumab [Fasenra], dupilumab [Dupixent], mepolizumab [Nucala], reslizumab [Cinqair])
- Dosing and Frequency: Omalizumab (Xolair) 150 or 300 mg by subcutaneous injection every 4 weeks. Dosing is not dependent on serum IgE levels or body weight.

IgE-Mediated Food Allergy

Omalizumab (Xolair) is considered medically necessary and, therefore, covered for the treatment of IgE-mediated food allergy (Type I) in individuals who are 1 year of age or older for the reduction of allergic reactions, including anaphylaxis, that may occur with accidental exposure to one or more foods when all of the following criteria, including Dosing and Frequency Requirements listed below and in Attachment A are met:

- IgE mediated food allergy has been confirmed by at least one of the following:
 - Positive skin prick test (greater than or equal to 4mm wheal greater than saline control)
 - Positive food specific serum IgE (greater than or equal to 6 IU/mL)
 - A positive physician controlled oral food challenge (e.g., moderate to severe skin, respiratory, or gastrointestinal [GI] symptoms)
 - Baseline (pre-Xolair treatment) serum total IgE level is greater than or equal to 30 IU/mL and less than or equal to 1850 UE/mL
- Xolair is used in conjunction with food allergen avoidance.

- Xolair will not be used as the emergency treatment for allergic reactions (including anaphylaxis, asthma, rhinitis, conjunctivitis, dermatitis) and individual has access to epinephrine.
- Omalizumab (Xolair) will not be used in combination with other biologics for asthma/allergic conditions (e.g., benralizumab [Fasenra], dupilumab [Dupixent], mepolizumab [Nucala], reslizumab [Cinqair]).
- Dosing and Frequency Requirements: See Attachment A.

Immune Checkpoint Inhibitor–Related Pruritus

Omalizumab (Xolair) is considered medically necessary and, therefore, covered for the management of severe (Grade 3) pruritus related to immunotherapy (e.g., ipilimumab [Yervoy], nivolumab [Opdivo], pembrolizumab [Keytruda]) in adult individuals when **all** of the following criteria, including the Dosing and Frequency Requirements below, are met:

- The individual is refractory to antihistamines and corticosteroids
- The individual has an elevated baseline serum IgE level
- Omalizumab (Xolair) will not be used in combination with other biologics for asthma/allergic conditions (e.g., benralizumab [Fasenra], dupilumab [Dupixent], mepolizumab [Nucala], reslizumab [Cinqair])
- Dosing and Frequency: Omalizumab (Xolair) doses up to 300 mg by subcutaneous injection every 4 weeks

Chronic Rhinosinusitis with Nasal Polyps

Omalizumab (Xolair) is considered medically necessary and, therefore, covered as add-on maintenance therapy of chronic rhinosinusitis with nasal polyps in adults when **all** of the following criteria, including Dosing and Frequency Requirements listed in Attachment A, are met:

- The individual is diagnosed with persistent bilateral nasal polyps characterized by **all** of the following:

- Signs and symptoms of rhinosinusitis persisting at least 12 weeks (e.g., nasal and sinus inflammation, nasal drainage/congestion, facial pressure/pain, reduction in sense of smell)
- Evidence of nasal polyps identified via one of the following visualization techniques: anterior rhinoscopy, nasal endoscopy, sinus computed tomography (CT) or magnetic resonance imaging (MRI)
- The individual has a Nasal Polyp Score (NPS) of 5 or higher (NPS >2 for each nostril) at baseline
- The individual has a weekly self-reported Nasal Congestion Score (NCS) average of >1 at baseline
- The individual has a baseline serum IgE level of between 30 IU/mL and 1500 IU/mL
- Documented failure, contraindication, or intolerance to at least a 4-week trial of intranasal corticosteroids
- Omalizumab (Xolair) will be used in combination with intranasal corticosteroids, unless documented failure, contraindication, or intolerance.
- Omalizumab (Xolair) will not be used in combination with other biologics for asthma/allergic conditions (e.g., benralizumab [Fasenra], dupilumab [Dupixent], mepolizumab [Nucala], reslizumab [Cinqair])
- Dosing and Frequency Requirements: See Attachment A

Systemic Mastocytosis

Prophylactic Treatment for Chronic Mast Cell Mediator–Related Cardiovascular and Pulmonary Symptoms

Omalizumab (Xolair) is considered medically necessary and, therefore, covered for the following conditions in individuals who are at least 12 years of age, when all of the following criteria, including the Dosing and Frequency Requirements listed below, are met:

- As a component of stepwise prophylactic treatment for chronic mast cell mediator–related cardiovascular and pulmonary symptoms (e.g., pre-syncope, tachycardia, wheezing, throat swelling), that are insufficiently controlled by H1- and H2-blockers and corticosteroids
- Omalizumab (Xolair) will not be used in combination with other biologics for asthma/allergic conditions (e.g., benralizumab [Fasenra], dupilumab [Dupixent], mepolizumab [Nucala], reslizumab [Cinqair])
- Dosing and Frequency: Omalizumab (Xolair) doses up to 300 mg by subcutaneous injection every 4 weeks

Prevention of Anaphylaxis

Omalizumab (Xolair) is considered medically necessary and, therefore, covered for the following conditions in individuals who are at least 12 years of age, when all of the following criteria, including the Dosing and Frequency Requirements listed below, are met:

- Prevention of one of the following conditions:
 - Unprovoked anaphylaxis
 - Hymenoptera (insect venom, e.g., bee or wasp sting) or food-induced anaphylaxis, with negative specific IgE or negative skin test
 - To improve tolerance while on immunotherapy
- Omalizumab (Xolair) will not be used in combination with other biologics for asthma/allergic conditions (e.g., benralizumab [Fasenra], dupilumab [Dupixent], mepolizumab [Nucala], reslizumab [Cinqair])
- Dosing and Frequency: Omalizumab (Xolair) doses up to 300 mg by subcutaneous injection every 2 weeks.

CONTINUATION THERAPY

Continuation of omalizumab (Xolair) is considered medically necessary and, therefore, covered when **all** of the following criteria are met:

- The individual has a documented clinical improvement or stabilization in their disease (e.g., reduction in the frequency of exacerbations, reduction in the reported signs and symptoms)
- The individual continues to receive concomitant drugs, if applicable
- Omalizumab (Xolair) will not be used in combination with other biologics for asthma/allergic conditions (e.g., benralizumab [Fasenra], dupilumab [Dupixent], mepolizumab [Nucala], reslizumab [Cinqair])
- The Dosing and Frequency Requirements are met

EXPERIMENTAL/INVESTIGATIONAL

All other uses for omalizumab (Xolair) including, but not limited to, acute bronchospasm or status asthmaticus, are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the medical policy on off-label coverage for prescription drugs and biologics.

DOSING AND FREQUENCY REQUIREMENTS

Refer to this Policy Section (above) or to Attachment A for the Dosing and Frequency Requirements for omalizumab (Xolair).

The Company reserves the right to modify the Dosing and Frequency Requirements listed in this policy to ensure consistency with the most recently published recommendations for the use of omalizumab (Xolair). Changes to these guidelines are based on a consensus of information obtained from resources such as, but not limited to: the US Food and Drug Administration (FDA); Company-recognized authoritative pharmacology compendia; or published peer-reviewed clinical research. The professional provider must supply supporting documentation (i.e., published peer-reviewed literature) in order to request coverage for an amount of omalizumab (Xolair) outside of the Dosing and Frequency Requirements listed in this policy. For a list of Company-recognized pharmacology compendia, view our policy on off-label coverage for prescription drugs and biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of this drug. If the member's dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider must submit those changes to the Company for a new approval based on those changes as part of the precertification process. The Company reserves the right to conduct postpayment review and

audit procedures for any claims submitted for omalizumab (Xolair).

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

When coverage of omalizumab (Xolair) is requested outside of the Dosing and Frequency Requirements listed in this policy, the prescribing professional provider must supply documentation (i.e., published peer-reviewed literature) to the Company that supports this request.

Duration of authorization: 12 months

Version Effective Date: 01/06/2025

Attachment A: [Omalizumab \(Xolair®\)](#)

Description: Dosing and Frequency Requirements for Omalizumab (Xolair®)

Policy Attachment

Attachment to Policy # 08.00.55I

Attachment: A

Policy #: 08.00.55I

Description: Dosing and Frequency Requirements for Omalizumab (Xolair®)

Title: Omalizumab (Xolair®)

DOSING AND FREQUENCY REQUIREMENTS

Refer to Attachment A for the Dosing and Frequency Requirements for omalizumab (Xolair).

The Company reserves the right to modify the Dosing and Frequency Requirements listed in this

Accurate member information is necessary for the Company to approve the requested dose and frequency of this drug. If the member's dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider must submit those changes to the Company for a new approval based on those changes as part of the precertification process. The Company reserves the right to conduct post-payment review and audit procedures for any claims submitted for omalizumab (Xolair).

Dosing for Allergic Asthma: Dosing and frequency is determined by serum total IgE level (IU/mL), measured before the start of treatment, and body weight (kg). Doses may need to be adjusted for significant changes in body weight. See dosing information below:

Dosing and Frequency for Individuals 6 Years of Age and Older:

Pretreat- ment Serum IgE (IU/mL)	Dosing Freq.	Body Weight									
		20- 25 kg	>25- 30 kg	>30-40 kg	>40-50 kg	>50- 60 kg	>60- 70 kg	>70- 80 kg	>80- 90 kg	>90- 125 kg	>125- 150 kg
		Dose (mg)									

30-100	Every 4 weeks	75	75	+75 *150	150	150	150	150	150	300	300
>100-200		150	150	+150 *300	300	300	300	300	300	225	+300 *225
>200-300		150	150	+225 *300	300	300	225	225	225	300	+375 *300
>300-400		225	225	+300	225	225	225	300	300	450	525
				*225							
>400-500		225	300	+225 *300	+225 *300	300	300	375	375	525	600
>500-600		300	300	+225 *300	300	300	375	450	450	600	
>600-700	300	225	+225 *375	+300 *375	375	450	450	525			
>700-800	Every 2 weeks	225	225	300	375	450	450	525	600		
>800-900		225	225	300	375	450	525	600			
>900-1000		225	300	375	450	525	600				
>1000-1100		225	300	375	450	600		Insufficient data to recommend a dose			
>1100-1200		300	300	450	525	600					
>1200-1300		300	375	450	525						
>1300-1500		300	375	525	600						

Sources: U.S. Prescribing Information, European Prescribing Information, Kornmann 2014, Zielen 2013, Lowe 2015.

Note: There are some dosing differences between age groups that are identified by the following symbols:

+ Individuals 6 – 12 years of age

* Individuals 12 years of age and older

CHRONIC RHINOSINUSITIS WITH NASAL POLYPS

Dosing for Chronic Rhinosinusitis with Nasal Polyps: Dosing and frequency is determined by serum total IgE level (IU/mL), measured before the start of treatment, and body weight (kg). Doses may need to be adjusted for significant changes in body weight. See dosing information below:

Dosing and Frequency for Individuals 18 Years of Age and Older:

Pre-treatment Serum IgE (IU/mL)	Dosing Freq.	Body Weight							
		>30-40 kg	>40-50 kg	>50-60 kg	>60-70 kg	>70-80 kg	>80-90 kg	>90-125 kg	>125-150 kg
		Dose (mg)							
30-100	Every 4 weeks	75	150	150	150	150	150	300	300
>100-200		150	300	300	300	300	300	450	600
>200-300		225	300	300	450	450	450	600	375
>300-400		300	450	450	450	600	600	450	525
>400-500		450	450	600	600	375	375	525	600
>500-600		450	600	600	375	450	450	600	
>600-700		450	600	375	450	450	525		
>700-800		300	375	450	450	525	600		

>800-900	Every 2 weeks	300	375	450	525	600	Insufficient Data to Recommend a Dose
>900-1000		375	450	525	600		
>1000-1100		375	450	600			
>1100-1200		450	525	600			
>1200-1300		450	525				
>1300-1500		525	600				

Refs: U.S. Prescribing Information

IgE- MEDIATED FOOD ALLERGY

Dosing for IgE-Mediated food allergy: Dosing and frequency is determined by serum total IgE level (IU/mL), measured before the start of treatment, and body weight (kg). Doses may need to be adjusted for significant changes in body weight. Total IgE levels are elevated during treatment and remain elevated for up to one year after the discontinuation of treatment. Therefore, re-testing of IgE levels during XOLAIR treatment cannot be used as a guide for dose determination. Interruptions lasting less than one year: Dose based on serum IgE levels obtained at the initial dose determination. Interruptions lasting one year or more: Re-test total serum IgE levels for dose determination. See dosing information below:

Peer-reviewed literature and clinical trials recommend a dose of 75mg to 600 mg by subcutaneous injection every 2 or 4 weeks.

Dosing and Frequency for Individuals 1 year of Age and Older:

Pre-treatment Serum IgE (IU/mL)	Dosing Freq.	Body Weight (kg)												
		≥10-12	>12-15	>15-20	>20-25	>25-30	>30-40	>40-50	>50-60	>60-70	>70-80	>80-90	>90-125	>125-150
		Dose (mg)												
>30-100	Every 4 weeks	75	75	75	75	75	75	150	150	150	150	150	300	300
>100-200		75	75	75	150	150	150	300	300	300	300	300	450	600
>200-300		75	75	150	150	150	225	300	300	450	450	450	600	375
>300-400		150	150	150	225	225	300	450	450	450	600	600	450	525
>400-500		150	150	225	225	300	450	450	600	600	375	375	525	600
>500-600		150	150	225	300	300	450	600	600	375	450	450	600	
>600-700		150	150	225	300	225	450	600	375	450	450	525		
>700-800	Every 2 weeks	150	150	150	225	225	300	375	450	450	525	600		
>800-900		150	150	150	225	225	300	375	450	525	600			
>900-1000		150	150	225	225	300	375	450	525	600				
>1000-1100		150	150	225	225	300	375	450	600					
>1100-1200		150	150	225	300	300	450	525	600					
>1200-1300		150	225	225	300	375	450	525						
>1300-1500		150	225	300	300	375	525	600						
>1500-1850			225	300	375	450	600							

Refs: U.S. Prescribing Information

	Subcutaneous doses to be administered every 4 weeks
	Subcutaneous doses to be administered every 2 weeks
	Insufficient data to Recommend a Dose

Version Effective Date: 01/06/2025

Title: Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound)/(Abraxane® for Injectable Suspension)

MEDICALLY NECESSARY

Paclitaxel protein-bound particles for injectable suspension (albumin-bound) (Abraxane® for injectable suspension) are considered medically necessary and, therefore, covered for any of the following indications:

AMPULLARY ADENOCARCINOMA

- Subsequent therapy for disease progression in individuals with good performance status (PS) (Eastern Cooperative Oncology Group [ECOG] 0-1, with good biliary drainage and adequate nutritional intake) and pancreaticobiliary and mixed type if previously treated with fluoropyrimidine-based therapy in combination with gemcitabine
- Subsequent as therapy for disease progression in select individuals (poor PS and ECOG PS 2) with pancreaticobiliary and mixed type in combination with gemcitabine
- First-line therapy in combination with gemcitabine for pancreaticobiliary and mixed-type disease for the following indications:
 - Unresectable localized
 - Stage IV resected ampullary cancer
 - Metastatic disease at initial presentation
 - for individuals with good PS and ECOG 0-1, with good biliary drainage and adequate nutritional intake*
 - for individuals with poor PS and ECOG PS 2
- Neoadjuvant therapy, with or without subsequent chemoradiation, in combination with gemcitabine for pancreaticobiliary and mixed-type localized disease, in high-risk individuals (i.e., imaging findings, markedly elevated CA 19-9, markedly elevated carcinoembryonic antigen [CEA], large primary tumors, large regional lymph nodes, excessive weight loss, extreme pain)

*May be followed by chemoradiation for palliative indications (National Comprehensive Cancer Network [NCCN] recommended).

BREAST CANCER, INVASIVE

NOTE: The medical necessity of this drug is based on meeting the requirements of the human epidermal growth factor 2 (HER2) testing, as well as the medical necessity criteria below:

- Single-agent or in combination with carboplatin for the treatment of individuals with high tumor burden, rapidly progressing disease, and visceral crisis for individuals for recurrent unresectable (local or regional) or stage IV (M1) HER2-negative disease that is hormone receptor–positive with a visceral crisis or endocrine therapy refractory as one of the following:
 - First-line therapy if no germline BRCA 1/2 mutation
 - Second-line therapy if not a candidate for fam-trastuzumab deruxtecan-nxki
 - Third-line therapy and beyond
- Single-agent therapy or in combination with carboplatin (useful in certain circumstances, in select individuals with high tumor burden, rapidly progressing disease, and visceral crisis) for recurrent unresectable (local or regional) or stage IV (M1) triple-negative breast cancer (TNBC) as one of the following:
 - First-line therapy if PD-L1 CPS <10 and no germline BRCA 1/2 mutation
 - Second-line therapy
 - Third-line therapy and beyond
- In combination with pembrolizumab for PD-L1 positive (PD-L1 CPS ≥10) triple-negative recurrent unresectable (local or regional) or stage IV (M1) disease:
 - As NCCN-preferred first-line therapy
 - As second and subsequent lines of therapy if PD-L1 inhibitor has not been previously used
- As a forth third-line therapy and beyond in combination with trastuzumab (Herceptin®) for HER2-positive disease recurrent unresectable (local or regional) or stage IV (M1) disease that is:

- Hormone receptor–negative
- Hormone receptor–positive with or without endocrine therapy refractory
- As a substitute for paclitaxel (i.e., Taxol®, Onxol®) or docetaxel (i.e., Taxotere) for individuals with hypersensitivity reactions

BREAST CANCER, INFLAMMATORY

- Single-agent or in combination with carboplatin for the treatment of individuals with high tumor burden, rapidly progressing disease, and visceral crisis in individuals with no response to preoperative systemic therapy, or for recurrent unresectable (local or regional) or stage IV (M1) HER2-negative disease that is hormone receptor–positive with a visceral crisis or endocrine therapy refractory for any line of therapy:
 - First-line therapy if no germline BRCA 1/2 mutation
 - Second-line therapy if not a candidate for fam-trastuzumab deruxtecan-nxki
 - Third-line therapy and beyond
- Single-agent therapy or in combination with carboplatin (useful in certain circumstances, in select individuals with high tumor burden, rapidly progressing disease, and visceral crisis) for individuals with no response to preoperative systemic therapy, or recurrent unresectable (local or regional) or stage IV (M1) triple-negative breast cancer (TNBC) as one of the following:
 - First-line therapy if PD-L1 CPS <10 and no germline BRCA 1/2 mutation
 - Second-line therapy
 - Third-line therapy and beyond
- Fourth-line therapy and beyond in combination with trastuzumab for HER2-positive disease in individuals with no response to preoperative systemic therapy, or recurrent unresectable (local or regional) or stage IV (M1) disease that is one of the following:
 - Hormone receptor–negative
 - Hormone receptor–positive with or without endocrine therapy

- In combination with pembrolizumab for PD-L1 (PD-L1 CPS ≥ 10) positive triple-negative disease for individuals with no response to preoperative systemic therapy, or recurrent unresectable (local or regional) or stage IV (M1) disease:
 - As NCCN-preferred first line of therapy
 - As second and subsequent lines of therapy if PD-1/PD-L1 inhibitor has not been previously used
- As a substitute for paclitaxel (i.e., Taxol[®], Onxol[®]) or docetaxel (i.e., Taxotere) for hypersensitivity reactions

BREAST CANCER, METASTATIC

- Treatment of metastatic breast cancer after failure of combination chemotherapy for metastatic disease or relapse within 6 months of adjuvant chemotherapy. Prior chemotherapy must have included an anthracycline unless clinically contraindicated.

CERVICAL CANCER

- Second-line or subsequent therapy as a single agent for any of the following:
 - Local/regional recurrence
 - Stage IVB or recurrence with distant metastases
 - Persistent, recurrent, or metastatic small cell neuroendocrine carcinoma of the cervix (NECC)

BILIARY CANCERS

Intrahepatic Cholangiocarcinoma, Extrahepatic Cholangiocarcinoma

- In combination with gemcitabine as primary treatment for unresectable or resected gross residual (R2), or metastatic disease
- In combination with gemcitabine as subsequent therapy for the treatment of progression on or after systemic therapy in individuals with unresectable or resected gross residual (R2), or metastatic disease

Gallbladder Cancer

- As neoadjuvant systemic therapy in combination with gemcitabine for resectable locoregionally advanced disease that presents as one of the following:
 - Incidental finding of suspicious mass during surgery where hepatobiliary surgery expertise unavailable
 - Incidental finding on pathologic review (cystic duct node–positive)
 - Mass on imaging
- The primary treatment for unresectable or resected gross residual (R2) disease, or metastatic disease in combination with gemcitabine
- Subsequent treatment for progression on or after systemic treatment for unresectable or resected gross residual (R2) disease, or metastatic disease in combination with gemcitabine

KAPOSI SARCOMA

Subsequent systemic therapy, given alone (no HIV) or with antiretroviral therapy (ART) for individuals with HIV (PWH), for relapsed/refractory advanced cutaneous, oral, visceral, or nodal disease that has progressed on or not responded to first-line systemic therapy, and progressed on alternate first-line systemic therapy.

NOTE: includes classic Kaposi, posttransplant, and iatrogenic variant of Kaposi sarcoma.

no HIV = HIV negative. PWH = HIV positive.

MELANOMA, CUTANEOUS

Single-agent therapy or in combination with carboplatin for metastatic or unresectable disease as second-line or subsequent therapy for disease progression intolerance, and/or projected risk of progression with BRAF-targeted therapy

MELANOMA, UVEAL

As single-agent therapy for distant metastatic or unresectable disease.

NON-SMALL CELL LUNG CANCER (NSCLC)

- Treatment for recurrent, advanced, or metastatic disease as first-line therapy for PD-L1 expression–positive ($\geq 1\%$) tumors that are negative for actionable molecular biomarkers* (may be KRAS G12C mutation–positive) and no contraindications** to PD-1 or PD-L1 inhibitors and PS 0-2 (excluding locoregional recurrence or symptomatic local

disease [except for mediastinal lymph node recurrence with prior radiation therapy] with no evidence of disseminated disease, or for PD-L1 $\geq 50\%$ as one of the following:

- In combination with tremelimumab-actl, durvalumab, and carboplatin)
- In combination with pembrolizumab and carboplatin for squamous cell histology (preferred)
- In combination with carboplatin and atezolizumab for nonsquamous cell histology
- In combination with tremelimumab-actl, durvalumab, and carboplatin
- Treatment for recurrent, advanced, or metastatic disease (except for locoregional recurrence or symptomatic local disease [excluding mediastinal lymph node recurrence with prior radiation therapy] with no evidence of disseminated disease)
- In combination with carboplatin for those with PS 0-2 (useful in certain circumstances if contraindications** to PD-1 or PD-L1 inhibitors and PS 0-1 for both nonsquamous cell histology and squamous cell histology, or other recommended regimen for nonsquamous cell histology and PS 2, or preferred for squamous cell histology and PS 2)
- As a single agent for PS 2 (useful in certain circumstances for both nonsquamous cell histology and squamous cell histology)
 - The above regimens are used as one of the following:
 - initial systemic therapy for PD-L1 expression positive ($\geq 1\%$) and negative for actionable molecular biomarkers* (may be KRAS G12C mutation–positive) with contraindications to PD-1 or PD-L1 inhibitors
 - initial systemic therapy for PD-L1 $< 1\%$ and negative for actionable molecular biomarkers* (may be KRAS G12C mutation–positive)
 - first-line therapy for EGFR exon 20 insertion mutation–positive tumors
 - first-line or subsequent therapy for BRAF V600E mutation–positive tumors
 - first-line (useful in certain circumstances) or subsequent therapy for NTRK1/2/3 gene fusion–positive tumors
 - first-line (useful in certain circumstances) or subsequent therapy for MET exon 14 skipping mutation–positive tumors
 - first-line or subsequent therapy for RET rearrangement–positive tumors
 - first-line therapy for ERBB2 (HER2) mutation–positive tumors

- subsequent therapy for EGFR exon 19 deletion or exon 21 L858R tumors and prior erlotinib ± (ramucirumab or bevacizumab), afatinib, gefitinib, osimertinib, or dacomitinib therapy
- subsequent therapy for EGFR S768I, L861Q, and/or G719X mutation–positive tumors and prior afatinib, osimertinib, erlotinib, gefitinib, or dacomitinib therapy
- subsequent therapy for ALK rearrangement–positive tumors and prior crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib therapy
- subsequent therapy for ROS1 rearrangement–positive tumors and prior crizotinib, entrectinib, repotrectinib, ceritinib, or lorlatinib therapy
- subsequent therapy for PD-L1 expression–positive ($\geq 1\%$) tumors and negative for actionable molecular biomarkers* after prior PD-1/PD-L1 inhibitor but no prior platinum-containing chemotherapy
- Treatment for recurrent, advanced, or metastatic disease for individuals with PS 0-1 and no contraindications** to PD-1 or PD-L1 inhibitors, in combination with one of the following:
 - Atezolizumab and carboplatin for nonsquamous cell histology (except for locoregional recurrence or symptomatic local disease [excluding mediastinal lymph node recurrence with prior radiation therapy] with no evidence of disseminated disease)
 - Carboplatin and pembrolizumab for squamous cell histology (preferred)
 - Tremelimumab-actl, durvalumab, and carboplatin
 - The above regimens are used as one of the following:
 - initial systemic therapy for PD-L1 $< 1\%$ and negative for actionable molecular biomarkers* (may be KRAS G12C mutation–positive)
 - first-line therapy for EGFR exon 20 insertion mutation–positive tumors
 - first-line or subsequent therapy for BRAF V600E mutation positive tumors
 - first-line (useful in certain circumstances) or subsequent therapy for NTRK1/2/3 gene fusion positive tumors
 - first-line (useful in certain circumstances) or subsequent therapy for MET exon 14 skipping mutation–positive tumors
 - first-line or subsequent therapy for RET rearrangement–positive tumors

- first-line therapy for ERBB2 (HER2) mutation–positive tumors
- subsequent therapy for EGFR exon 19 deletion or exon 21 L858R tumors and prior erlotinib ± (ramucirumab or bevacizumab), afatinib, gefitinib, osimertinib, or dacomitinib therapy
- subsequent therapy for EGFR S768I, L861Q, and/or G719X mutation–positive tumors and prior afatinib, osimertinib, erlotinib, gefitinib, or dacomitinib therapy
- subsequent therapy for ALK rearrangement–positive tumors and prior crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib therapy
- subsequent therapy for ROS1 rearrangement–positive tumors and prior crizotinib, entrectinib, repotrectinib, ceritinib, or lorlatinib therapy
- For the treatment of individuals who are not candidates for curative surgery or radiation as first-line therapy for locally advanced or metastatic NSCLC, in combination with carboplatin.
- As subsequent systemic therapy as a single agent (if not already given) for recurrent, advanced, or metastatic disease in individuals with PS 0-2 (except for progression after subsequent systemic therapy and for locoregional recurrence or symptomatic local disease [excluding mediastinal lymph node recurrence with prior radiation therapy] with no evidence of disseminated disease
- As a substitute for either paclitaxel or docetaxel in individuals who have experienced hypersensitivity reactions after receiving paclitaxel or docetaxel despite premedication, or for individuals in whom standard hypersensitivity premedications are contraindicated

*Complete genotyping for EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET, RET, and ERBB2 (HER2), via biopsy and/or plasma testing. If a clinically actionable marker is found, it is reasonable to start therapy based on the identified marker. Treatment is guided by available results and, if unknown, these individuals are treated as though they do not have driver oncogenes.

**Contraindications for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or current use of immunosuppressive agents, or presence of an oncogene (e.g., EGFR [exon 19 deletions, p.L858R point mutation in exon 21], ALK rearrangements, RET rearrangements), which would predict lack of benefit.

OVARIAN CANCER / FALLOPIAN TUBE CANCER / PRIMARY PERITONEAL CANCER

Epithelial Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer

Carcinosarcoma (Malignant Mixed Müllerian Tumors)

Clear Cell Carcinoma of the Ovary

Mucinous Carcinoma of the Ovary

Peritoneal Cancer - Grade 1 Endometrioid Carcinoma

- Therapy for persistent disease or recurrence in combination with carboplatin if platinum-sensitive persistent disease or recurrence for individuals with confirmed taxane hypersensitivity in individuals with complete remission and relapse within 6 months after completing prior chemotherapy
- As a single-agent therapy for persistent disease or recurrence (excluding immediate treatment for biochemical relapse)
 - For progression on primary, maintenance, or recurrence therapy (platinum-resistant disease)
 - For stable or persistent disease (if not on maintenance therapy) (platinum-resistant disease)
 - For complete remission and relapse 6 months after completing chemotherapy (platinum-resistant disease)
 - For radiographic and/or clinical relapse in individuals with previous complete remission and relapse, within 6 months, after completing prior chemotherapy (platinum-sensitive disease)
- May be a substitute for paclitaxel in individuals who experience a hypersensitivity reaction to paclitaxel

Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer - Low-Grade Serous Carcinoma

- Useful in certain circumstances in combination with carboplatin if platinum-sensitive recurrence for individuals with confirmed taxane hypersensitivity
- May be a substitute for paclitaxel in individuals who experience a hypersensitivity reaction to paclitaxel
- Single-agent therapy for platinum-sensitive or platinum-resistant recurrence

*Platinum agents have limited activity when the disease has demonstrated growth through a platinum-based regimen, and platinum rechallenge is generally not recommended in this setting

PANCREATIC ADENOCARCINOMA

- First-line therapy, or as continuation (maintenance) therapy if no disease progression (after at least 4–6 months of chemotherapy, assuming acceptable tolerance) after first-line therapy in individuals with metastatic disease and good PS in combination with either of the following or both of the following:
 - Gemcitabine (preferred) if ECOG PS 0-2
 - Gemcitabine and cisplatin if ECOG PS 0-1
- First-line chemotherapy, or induction therapy followed by chemoradiation in selected individuals, without systemic metastases, for individuals with locally advanced disease and good PS (ECOG PS 0-1) with good biliary drainage and adequate nutritional intake) in combination with one of the following:
 - Gemcitabine (NCCN-preferred regimen)
- Neoadjuvant treatment (NCCN-preferred regimen) in combination with gemcitabine, with or without subsequent chemoradiation for one of the following:
 - Resectable disease in high-risk individuals (i.e., very highly elevated CA 19-9, large primary tumors, large regional lymph nodes, excessive weight loss, extreme pain)
 - Biopsy-positive borderline resectable disease
- As NCCN-preferred first-line therapy followed by chemoradiation without systemic metastases for locally advanced disease and intermediate PS (ECOG PS 2) for metastatic disease in individuals with good PS (ECOG PS 0-2), in combination with gemcitabine
- Subsequent treatment in combination with gemcitabine for locally advanced or metastatic disease for individuals with good PS (ECOG PS 0-1) and disease progression who were previously treated with fluoropyrimidine-based therapy in combination with gemcitabine
- Therapy in individuals with good PS if less than 6 months from completion of primary therapy and previously treated with fluoropyrimidine-based therapy in combination with gemcitabine if ECOG PS 0-2 with or without chemoradiation for local recurrence in the

pancreatic operative bed after resection for recurrent metastatic disease with or without local recurrence after resection

- Therapy in individuals with good PS if 6 or more months from completion of primary therapy in combination with gemcitabine*** if ECOG PS 0-2 with* or without chemoradiation for local recurrence in the pancreatic operative bed after resection for recurrent metastatic disease with or without local recurrence after resection
- First-line therapy for metastatic disease with good PS (defined as ECOG PS 0-1, with good biliary drainage and adequate nutritional intake) in combination with any of the following:
 - Gemcitabine (preferred regimen)
 - Gemcitabine and cisplatin
 - First-line therapy for metastatic disease with intermediate PS (ECOG PS 2) in combination with gemcitabine (preferred regimen)
 - Subsequent therapy for locally advanced or metastatic disease and disease progression if intermediate PS (ECOG PS 2) and previously treated with fluoropyrimidine-based therapy in combination with gemcitabine

*If not previously done.

**As repeat systemic therapy previously administered.

***As alternate systemic therapy not previously used.

SMALL BOWEL ADENOCARCINOMA

- As a single agent or in combination with gemcitabine for advanced or metastatic small bowel adenocarcinoma for one of the following:
 - As initial therapy if an individual has received previous FOLFOX/CAPEOX in the adjuvant setting within the past 12 months or is contraindicated
 - As second-line and subsequent therapy (if not previously given)

UTERINE NEOPLASMS

- Single-agent second-line therapy for the treatment of recurrent disease
 - For isolated metastases

- For disseminated metastases with or without sequential palliative external beam radiation therapy (EBRT)
- With sequential EBRT and with or without brachytherapy for locoregional recurrence in individuals with no prior radiotherapy to the site of recurrence, or previous brachytherapy only
- After surgical exploration, with sequential EBRT for locoregional recurrence in individuals with disease confined to the vagina or paravaginal soft tissue, or in pelvic, or para-aortic, or common iliac lymph nodes
- After surgical exploration, with or without sequential EBRT for locoregional recurrence in individuals with upper abdominal or peritoneal disease
- With or without sequential palliative EBRT or brachytherapy for locoregional recurrence in individuals who have received prior EBRT to the site of recurrence

VAGINAL CANCER

- Second-line or subsequent therapy as a single agent for one of the following:
 - Local/regional recurrence
 - Stage IVB or recurrent distant metastases

EXPERIMENTAL/INVESTIGATIONAL

All other uses for paclitaxel protein-bound particles for injectable suspension (albumin-bound) (Abraxane® for injectable suspension) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the medical policy on off-label coverage for prescription drugs and biologics.

MANDATES

PENNSYLVANIA MEMBERS

In accordance with the Commonwealth of Pennsylvania's Act 6 of 2020 or Fair Access to Cancer Treatment Act, for members who are enrolled in Pennsylvania commercial products who have stage 4, advanced metastatic cancer, refer to the Medical Policy titled "Coverage of Anticancer Prescription Oral and Injectable Drugs and Biologics and Supportive Agents" (08.01.08) for additional information regarding the applicable coverage of drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Duration of authorization: 12 months

Version Effective Date: 01/01/2025

Attachment A: [Paclitaxel Protein-Bound Particles for Injectable Suspension \(Albumin-Bound\)/\(Abraxane® for Injectable Suspension\)](#)

Description: ICD-10 codes

Policy Attachment

Attachment to Policy # 08.00.90s

Attachment: A

Policy #: 08.00.90s

Description: ICD-10 codes

Title: Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound)/(Abraxane® for Injectable Suspension)

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

C17.0 Malignant neoplasm of duodenum

C17.1 Malignant neoplasm of jejunum

C17.2 Malignant neoplasm of ileum

C17.3 Meckel's diverticulum, malignant

C17.8 Malignant neoplasm of overlapping sites of small intestine

C17.9 Malignant neoplasm of small intestine, unspecified

C22.1 Intrahepatic bile duct carcinoma

C23 Malignant neoplasm of gallbladder

C24.0 Malignant neoplasm of extrahepatic bile duct

C24.1 Malignant neoplasm of ampulla of Vater

C24.8 Malignant neoplasm of overlapping sites of biliary tract

C24.9 Malignant neoplasm of biliary tract, unspecified

C25.0 Malignant neoplasm of head of pancreas

C25.1 Malignant neoplasm of body of pancreas

C25.2 Malignant neoplasm of tail of pancreas

C25.3 Malignant neoplasm of pancreatic duct

C25.4 Malignant neoplasm of endocrine pancreas

C25.7 Malignant neoplasm of other parts of pancreas

C25.8 Malignant neoplasm of overlapping sites of pancreas

C25.9 Malignant neoplasm of pancreas, unspecified

C33 Malignant neoplasm of trachea

C34.01 Malignant neoplasm of right main bronchus

C34.02 Malignant neoplasm of left main bronchus

C34.11 Malignant neoplasm of upper lobe, right bronchus or lung

C34.12 Malignant neoplasm of upper lobe, left bronchus or lung

C34.2 Malignant neoplasm of middle lobe, bronchus or lung

C34.31 Malignant neoplasm of lower lobe, right bronchus or lung

C34.32 Malignant neoplasm of lower lobe, left bronchus or lung

C34.81 Malignant neoplasm of overlapping sites of right bronchus and lung

C34.82 Malignant neoplasm of overlapping sites of left bronchus and lung

C34.91 Malignant neoplasm of unspecified part of right bronchus or lung

C34.92 Malignant neoplasm of unspecified part of left bronchus or lung

C43.0 Malignant melanoma of lip

C43.111 Malignant melanoma of right upper eyelid, including canthus

C43.112 Malignant melanoma of right lower eyelid, including canthus

C43.121 Malignant melanoma of left upper eyelid, including canthus

C43.122 Malignant melanoma of left lower eyelid, including canthus

C43.21 Malignant melanoma of right ear and external auricular canal

C43.22 Malignant melanoma of left ear and external auricular canal

C43.30 Malignant melanoma of unspecified part of face

C43.31 Malignant melanoma of nose

C43.39 Malignant melanoma of other parts of face

C43.4 Malignant melanoma of scalp and neck

C43.51 Malignant melanoma of anal skin

C43.52 Malignant melanoma of skin of breast

C43.59 Malignant melanoma of other part of trunk

C43.61 Malignant melanoma of right upper limb, including shoulder

C43.62 Malignant melanoma of left upper limb, including shoulder

C43.71 Malignant melanoma of right lower limb, including hip

C43.72 Malignant melanoma of left lower limb, including hip

C43.8 Malignant melanoma of overlapping sites of skin

C43.9 Malignant melanoma of skin, unspecified

C44.90 Unspecified malignant neoplasm of skin, unspecified

C46.0 Kaposi's sarcoma of skin

C46.1 Kaposi's sarcoma of soft tissue

C46.2 Kaposi's sarcoma of palate

C46.3 Kaposi's sarcoma of lymph nodes

C46.4 Kaposi's sarcoma of gastrointestinal sites

C46.51 Kaposi's sarcoma of right lung

C46.52 Kaposi's sarcoma of left lung

C46.7 Kaposi's sarcoma of other sites

C46.9 Kaposi's sarcoma, unspecified

C48.1 Malignant neoplasm of specified parts of peritoneum

C48.2 Malignant neoplasm of peritoneum, unspecified

C48.8 Malignant neoplasm of overlapping sites of retroperitoneum and peritoneum

C50.011 Malignant neoplasm of nipple and areola, right female breast

C50.012 Malignant neoplasm of nipple and areola, left female breast

C50.021 Malignant neoplasm of nipple and areola, right male breast

C50.022 Malignant neoplasm of nipple and areola, left male breast

C50.111 Malignant neoplasm of central portion of right female breast

C50.112 Malignant neoplasm of central portion of left female breast

C50.121 Malignant neoplasm of central portion of right male breast

C50.122 Malignant neoplasm of central portion of left male breast

C50.211 Malignant neoplasm of upper-inner quadrant of right female breast

C50.212 Malignant neoplasm of upper-inner quadrant of left female breast

C50.221 Malignant neoplasm of upper-inner quadrant of right male breast

C50.222 Malignant neoplasm of upper-inner quadrant of left male breast

C50.311 Malignant neoplasm of lower-inner quadrant of right female breast

C50.312 Malignant neoplasm of lower-inner quadrant of left female breast

C50.321 Malignant neoplasm of lower-inner quadrant of right male breast

C50.322 Malignant neoplasm of lower-inner quadrant of left male breast

C50.411 Malignant neoplasm of upper-outer quadrant of right female breast

C50.412 Malignant neoplasm of upper-outer quadrant of left female breast
C50.421 Malignant neoplasm of upper-outer quadrant of right male breast
C50.422 Malignant neoplasm of upper-outer quadrant of left male breast
C50.511 Malignant neoplasm of lower-outer quadrant of right female breast
C50.512 Malignant neoplasm of lower-outer quadrant of left female breast
C50.521 Malignant neoplasm of lower-outer quadrant of right male breast
C50.522 Malignant neoplasm of lower-outer quadrant of left male breast
C50.611 Malignant neoplasm of axillary tail of right female breast
C50.612 Malignant neoplasm of axillary tail of left female breast
C50.621 Malignant neoplasm of axillary tail of right male breast
C50.622 Malignant neoplasm of axillary tail of left male breast
C50.811 Malignant neoplasm of overlapping sites of right female breast
C50.812 Malignant neoplasm of overlapping sites of left female breast
C50.821 Malignant neoplasm of overlapping sites of right male breast
C50.822 Malignant neoplasm of overlapping sites of left male breast
C50.911 Malignant neoplasm of unspecified site of right female breast
C50.912 Malignant neoplasm of unspecified site of left female breast
C50.921 Malignant neoplasm of unspecified site of right male breast
C50.922 Malignant neoplasm of unspecified site of left male breast
C52 Malignant neoplasm of vagina

C53.0 Malignant neoplasm of endocervix
C53.1 Malignant neoplasm of exocervix
C53.8 Malignant neoplasm of overlapping sites of cervix uteri
C53.9 Malignant neoplasm of cervix uteri, unspecified
C54.0 Malignant neoplasm of isthmus uteri
C54.1 Malignant neoplasm of endometrium
C54.2 Malignant neoplasm of myometrium
C54.3 Malignant neoplasm of fundus uteri

C54.8 Malignant neoplasm of overlapping sites of corpus uteri

C54.9 Malignant neoplasm of corpus uteri, unspecified

C55 Malignant neoplasm of uterus, part unspecified

C56.1 Malignant neoplasm of right ovary

C56.2 Malignant neoplasm of left ovary

C56.3 Malignant neoplasm of bilateral ovaries

C57.01 Malignant neoplasm of right fallopian tube

C57.02 Malignant neoplasm of left fallopian tube

C57.11 Malignant neoplasm of right broad ligament

C57.12 Malignant neoplasm of left broad ligament

C57.21 Malignant neoplasm of right round ligament

C57.22 Malignant neoplasm of left round ligament

C57.3 Malignant neoplasm of parametrium

C57.4 Malignant neoplasm of uterine adnexa, unspecified

C57.7 Malignant neoplasm of other specified female genital organs

C57.8 Malignant neoplasm of overlapping sites of female genital organs

C57.9 Malignant neoplasm of female genital organ, unspecified

C69.31 Malignant neoplasm of right choroid

C69.32 Malignant neoplasm of left choroid

C69.41 Malignant neoplasm of right ciliary body

C69.42 Malignant neoplasm of left ciliary body

C69.61 Malignant neoplasm of right orbit

C69.62 Malignant neoplasm of left orbit

C69.91 Malignant neoplasm of unspecified site of right eye

C69.92 Malignant neoplasm of unspecified site of left eye

C79.81 Secondary malignant neoplasm of breast

D03.51 Melanoma in situ of anal skin

D03.52 Melanoma in situ of breast (skin) (soft tissue)

Version Effective Date: 01/01/2025

Title: Palivizumab (Synagis)

MEDICALLY NECESSARY

Immune prophylaxis using palivizumab (Synagis) is considered medically necessary and, therefore, covered for a maximum of five doses in an annual respiratory syncytial virus (RSV) season for the prevention of serious lower respiratory tract infection caused by RSV in the following high-risk individuals, when the criteria for the indications listed below are met:

- **Chronic lung disease (CLD) of prematurity**
 - Infants and children younger than 24 months of age with CLD of prematurity who were born at a gestational age of less than 32 weeks, 0 days, and required more than 21% oxygen for at least the first 28 days after birth:
 - During the first year of life
 - During the second year of life for individuals who require medical therapy for CLD within the 6 months before the start of the RSV season. (Medical therapy includes any of the following: a requirement for supplemental oxygen, diuretics, or corticosteroids.)
- **Congenital abnormalities of the airway or certain neuromuscular diseases**
 - Infants and children 12 months of age or younger at the start of the RSV season with **EITHER** of the following indications:
 - Congenital abnormalities of the airway
 - Neuromuscular disease that compromises mobilization of respiratory secretions
- **Congenital heart disease (CHD)**
 - Infants and children with congenital heart disease (CHD) younger than 12 months of age at the start of the RSV season who meet **ANY** of the following criteria:
 - Hemodynamically significant acyanotic CHD, when the individual is receiving medication to control congestive heart failure and will require cardiac surgical procedures
 - Hemodynamically significant cyanotic CHD, after consultation with a pediatric cardiologist
 - Diagnosis of moderate-to-severe pulmonary hypertension
- **Cystic fibrosis with nutritional compromise and/or chronic lung disease (CLD)**

- Infants and children younger than 24 months of age with cystic fibrosis who have nutritional compromise and/or manifestations of severe lung disease (previous hospitalizations for pulmonary exacerbation in the first year of life or abnormalities on chest radiography or chest computed tomography that persists when stable)
- **Immunocompromised status**
 - Infants and children younger than 24 months of age who are profoundly immunocompromised (e.g., due to transplantation or chemotherapy) during the RSV season
- **Prematurity**
 - Infants and children born before 29 weeks gestation (29 weeks, 0 days) who are younger than 12 months of age at the start of the RSV season

An additional postoperative dose of palivizumab (Synagis) is considered medically necessary and, therefore, covered for infants or children younger than 24 months of age who are currently receiving palivizumab (Synagis) when they are medically stable, meet the above criteria for immune prophylaxis, and have undergone **ONE** of the following procedures during the current RSV season:

- Surgical procedures that use cardiopulmonary bypass
- Cardiac transplantation

According to the American Academy of Pediatrics (AAP) (2021), RSV season onset can be determined in real time by identifying the first week of two consecutive weeks that RSV real time-polymerase chain reaction (RT-PCR) test positivity is 3% or greater or antigen detection positivity is 10% or greater. Because five monthly doses of palivizumab will provide more than 6 months of serum palivizumab (Synagis) concentrations above the threshold for protection for most infants, administration of more than five monthly doses is not recommended within the continental United States. For qualifying infants born during the RSV season, fewer than five doses will be needed to provide protection until the RSV season ends in their region.

Medical necessity criteria for immune prophylaxis for RSV in at-risk infants and young children are subject to change based on updated recommendations as outlined in the AAP policy statement and Red Book.

NOT MEDICALLY NECESSARY

If an infant or child receiving monthly prophylaxis with palivizumab (Synagis) experiences a breakthrough RSV hospitalization, monthly prophylaxis with palivizumab (Synagis) is not medically necessary, and therefore not covered, due to the low likelihood of a second RSV hospitalization in the same season.

The administration of palivizumab (Synagis) after the administration of nirsevimab-alip (Beyfortus) in the same RSV season is not medically necessary, and therefore not covered.

EXPERIMENTAL/INVESTIGATIONAL

All other indications for palivizumab (Synagis) are considered experimental/investigational and, therefore, not covered.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Duration of authorization: 12 months

Version Effective Date: 08/21/2024

Title: patisiran (Onpattro®) and vutrisiran (Amvuttra®)

MEDICALLY NECESSARY

INITIAL THERAPY

Patisiran (Onpattro) or vutrisiran (Amvuttra) are considered medically necessary and, therefore, covered for individuals 18 years of age or older with hereditary transthyretin-mediated (hATTR) amyloidosis with polyneuropathy when all of the following criteria, including Dosing and Frequency Requirements listed below, are met:

- Diagnosis of hATTR amyloidosis with polyneuropathy is confirmed by molecular genetic testing that reveals pathogenic variation(s) in the transthyretin (TTR) gene (e.g., variation of V30M, which is the most common pathogenic variant consisting of a point mutation)
- Documentation of one of the following baseline ambulation parameters in either the Familial Amyloid Polyneuropathy (FAP) Stage or Polyneuropathy Disability (PND) Score (see Guidelines Section for description of scores):
 - Stage 1 (unimpaired ambulation) or 2 (assisted ambulation) on the FAP staging tool
 - Score 0, I, II, IIIa, or IIIb on the PND scoring tool
- Documented presence of cardiac or renal manifestations, or motor, sensory, or autonomic neuropathy related to the hATTR amyloidosis with polyneuropathy (e.g., neuropathic pain, muscle weakness that affects daily living, orthostatic hypotension, diarrhea, nausea, vomiting, heart failure, arrhythmias, proteinuria, renal failure; vision disorders, such as vitreous opacity, dry eyes, glaucoma, or pupils with an irregular or scalloped appearance)
- Prescribed by or in consultation with a neurologist, geneticist, or professional provider specializing in the treatment of amyloidosis
- Individual has not had a liver transplant or is unlikely to be a candidate
- Patisiran (Onpattro) or vutrisiran (Amvuttra) will not be used in combination with any other RNA interference agents (e.g., eplontersen [Wainua], inotersen [Tegsedi]), or transthyretin stabilizers (e.g., tafamidis [Vyndaqel, Vyndamax])

CONTINUATION THERAPY (AFTER 18 MONTHS OF THERAPY)

Patisiran (Onpattro) or vutrisiran (Amvuttra) are considered medically necessary and, therefore, covered for continuation therapy following at least 18 months of therapy for the treatment of hATTR amyloidosis with polyneuropathy when the individual meets both of the following criteria:

- Recent documentation of one of the following ambulation parameters (see Guidelines section for description of scores):
 - Stage 1 (unimpaired ambulation) or 2 (assisted ambulation) on the FAP staging tool
 - Score 0, I, II, IIIa, or IIIb on the PND scoring tool
- Documented improvement or stability in the signs and symptoms of hATTR amyloidosis with polyneuropathy (e.g., neuropathic pain, muscle weakness that affects daily living, orthostatic hypotension, diarrhea, nausea, vomiting, heart failure, arrhythmias, proteinuria, renal failure; vision disorders, such as vitreous opacity, dry eyes, glaucoma, or pupils with an irregular or scalloped appearance), based on objective or standard evaluation scales

NOTE:

Evio has been selected by the Company to administer clinical outcomes monitoring for patients receiving certain high-cost drug therapies. Patisiran (Onpattro) and vutrisiran (Amvuttra) are included in the portfolio of high-cost drug therapies for which Evio will be tracking clinical outcomes. If a patient meets all medical policy provisions and is approved to receive treatment, the requesting professional provider or member must attest and agree to providing clinical outcomes data and information via Evio's secure web portal as requested.

DOSING AND FREQUENCY REQUIREMENTS

PATISIRAN (ONPATTRO)

The following dosing and frequency information was taken from the prescribing information for this product:

- Individuals weighing less than 100 kg: the dosage is 0.3 mg/kg once every 3 weeks via intravenous infusion
- Individuals weighing 100 kg or more: the dosage is 30 mg once every 3 weeks via intravenous infusion

VUTRISIRAN (AMVUTTRA)

The following dosing and frequency information was taken from the prescribing information for this product: the recommended dosage is 25 mg administered by subcutaneous injection by a professional provider once every 3 months.

REQUIREMENTS

The Company reserves the right to modify the dosing and frequency requirements listed in this policy to ensure consistency with the most recently published recommendations for the use of patisiran (Onpattro) or vutrisiran (Amvuttra). Changes to these guidelines are based on a consensus of information obtained from resources such as, but not limited to, the US Food and Drug Administration (FDA); Company-recognized authoritative pharmacology compendia; or published peer-reviewed clinical research. The professional provider must supply supporting documentation (i.e., published peer-reviewed literature) in order to request coverage for an amount of patisiran (Onpattro) or vutrisiran (Amvuttra) outside of the dosing and frequency requirements listed in this policy. For a list of Company-recognized pharmacology compendia, view our policy on off-label coverage for prescription drugs and biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of this drug. If the member's dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider must submit those changes to the Company for a new approval based on those changes as part of the utilization management activities. The Company reserves the right to conduct postpayment review and audit procedures for any claims submitted for patisiran (Onpattro) or vutrisiran (Amvuttra).

NOT MEDICALLY NECESSARY

When molecular genetic testing reveals results showing established benign variation(s) or wild-type genotype in the TTR gene, patisiran (Onpattro) or vutrisiran (Amvuttra) are considered not medically necessary and, therefore, not covered because the available published peer-reviewed literature does not support their uses as treatments.

EXPERIMENTAL/INVESTIGATIONAL

When molecular genetic testing reveals likely pathogenic or variations of unknown significance (VUS) in the TTR gene, the use of patisiran (Onpattro) or vutrisiran (Amvuttra) are considered experimental/investigational and, therefore, not covered because the safety and/or effectiveness of this service cannot be established by review of the available published peer-reviewed literature.

The use of patisiran (Onpattro) or vutrisiran (Amvuttra) for hATTR amyloidosis with cardiomyopathy in those who are not experiencing polyneuropathy is considered experimental/investigational and, therefore, not covered because the safety and/or effectiveness of this service cannot be established by review of the available published peer-reviewed literature.

All other uses for patisiran (Onpattro) and vutrisiran (Amvuttra) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

When coverage of patisiran (Onpattro) or vutrisiran (Amvuttra) are requested outside of the dosing and frequency requirements listed in this policy, the prescribing professional provider must supply documentation (i.e., published peer-reviewed literature) to the Company that supports this request.

Duration of authorization: 12 months

Version Effective Date: 10/21/2024

Title: Pegloticase (Krystexxa®)

MEDICALLY NECESSARY

INITIAL THERAPY

Pegloticase (Krystexxa) is considered medically necessary and, therefore, covered for the treatment of symptomatic chronic gout in adult individuals when all of the following criteria, including Dosing and Frequency Requirements, are met:

- Failure to normalize uric acid levels to less than 6 mg/dL after at least three months of one xanthine oxidase inhibitor (XOI) (e.g., allopurinol or febuxostat) at the maximum recommended dose (alone or in combination with probenecid), unless the individual is intolerant to, has had a toxic reaction to, or has a contraindication to taking XOI.
- Individual has at least one of the following:
 - at least two gout flares in the previous 12 months
 - at least one gout tophus
 - gouty arthritis
- Pegloticase (Krystexxa) must be used in combination with weekly oral methotrexate, unless intolerant, contraindicated, or not clinically appropriate
- Dosing and frequency: 8 mg IV infusion every 2 weeks

CONTINUATION THERAPY

Pegloticase (Krystexxa) is considered medically necessary and, therefore, covered for the continued treatment of symptomatic chronic gout in adult individuals when both of the following are met:

- There is documented improvement in clinical signs and symptoms, such as reduction of uric acid levels to less than 6 mg/dL, gout flare reduction, tophus reduction/resolution, reduction in joint pain/swelling.
- Dosing and frequency: 8 mg IV infusion every 2 weeks

DOSING AND FREQUENCY REQUIREMENTS

The Company reserves the right to modify the Dosing and Frequency Requirements listed in this policy to ensure consistency with the most recently published recommendations for the use of pegloticase (Krystexxa). Changes to these guidelines are based on a consensus of information obtained from resources such as, but not limited to: the US Food and Drug Administration

(FDA); Company-recognized authoritative pharmacology compendia; or published peer-reviewed clinical research. The professional provider must supply supporting documentation (i.e., published peer-reviewed literature) in order to request coverage for an amount of pegloticase (Krystexxa) outside of the Dosing and Frequency Requirements listed in this policy. For a list of Company-recognized pharmacology compendia, view our policy on off-label coverage for prescription drugs and biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of this drug. If the member's dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider must submit those changes to the Company for a new approval based on those changes as part of the utilization management activities. The Company reserves the right to conduct post-payment review and audit procedures for any claims submitted for pegloticase (Krystexxa).

EXPERIMENTAL INVESTIGATIONAL

The use of pegloticase (Krystexxa) for non-adults or for individuals with asymptomatic hyperuricemia is considered experimental/investigational and, therefore, not covered because the safety and/or effectiveness of this use cannot be established by review of the available published peer-reviewed literature.

All other uses for pegloticase (Krystexxa) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

When coverage of pegloticase (Krystexxa) is requested outside of the Dosing and Frequency Requirements listed in this policy, the prescribing professional provider must supply documentation (i.e., published peer-reviewed literature) to the Company that supports this request.

Duration of authorization: 12 months

Version Effective Date: 04/30/2025

Attachment A: [Pegloticase \(Krystexxa®\)](#)

Description: ICD-10 Codes and Narratives

Policy Attachment

Attachment to Policy # 08.01.02h

Attachment: A

Policy #: 08.01.02h

Description: ICD-10 Codes and Narratives

Title: Pegloticase (Krystexxa®)

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

ICD-10 CODES AND NARRATIVES

MEDICALLY NECESSARY

M1A.0110 Idiopathic chronic gout, right shoulder, without tophus (tophi)

M1A.0111 Idiopathic chronic gout, right shoulder, with tophus (tophi)

M1A.0120 Idiopathic chronic gout, left shoulder, without tophus (tophi)

M1A.0121 Idiopathic chronic gout, left shoulder, with tophus (tophi)

M1A.0210 Idiopathic chronic gout, right elbow, without tophus (tophi)

M1A.0211 Idiopathic chronic gout, right elbow, with tophus (tophi)

M1A.0220 Idiopathic chronic gout, left elbow, without tophus (tophi)

M1A.0221 Idiopathic chronic gout, left elbow, with tophus (tophi)

M1A.0310 Idiopathic chronic gout, right wrist, without tophus (tophi)

M1A.0311 Idiopathic chronic gout, right wrist, with tophus (tophi)

M1A.0320 Idiopathic chronic gout, left wrist, without tophus (tophi)

M1A.0321 Idiopathic chronic gout, left wrist, with tophus (tophi)

M1A.0410 Idiopathic chronic gout, right hand, without tophus (tophi)

M1A.0411 Idiopathic chronic gout, right hand, with tophus (tophi)

M1A.0420 Idiopathic chronic gout, left hand, without tophus (tophi)

M1A.0421 Idiopathic chronic gout, left hand, with tophus (tophi)

M1A.0510 Idiopathic chronic gout, right hip, without tophus (tophi)

M1A.0511 Idiopathic chronic gout, right hip, with tophus (tophi)

M1A.0520 Idiopathic chronic gout, left hip, without tophus (tophi)

M1A.0521 Idiopathic chronic gout, left hip, with tophus (tophi)

M1A.0610 Idiopathic chronic gout, right knee, without tophus (tophi)

M1A.0611 Idiopathic chronic gout, right knee, with tophus (tophi)

M1A.0620 Idiopathic chronic gout, left knee, without tophus (tophi)

M1A.0621 Idiopathic chronic gout, left knee, with tophus (tophi)

M1A.0710 Idiopathic chronic gout, right ankle and foot, without tophus (tophi)

M1A.0711 Idiopathic chronic gout, right ankle and foot, with tophus (tophi)

M1A.0720 Idiopathic chronic gout, left ankle and foot, without tophus (tophi)

M1A.0721 Idiopathic chronic gout, left ankle and foot, with tophus (tophi)

M1A.08x0 Idiopathic chronic gout, vertebrae, without tophus (tophi)

M1A.08x1 Idiopathic chronic gout, vertebrae, with tophus (tophi)

M1A.09x0 Idiopathic chronic gout, multiple sites, without tophus (tophi)

M1A.09x1 Idiopathic chronic gout, multiple sites, with tophus (tophi)

M1A.1110 Lead-induced chronic gout, right shoulder, without tophus (tophi)

M1A.1111 Lead-induced chronic gout, right shoulder, with tophus (tophi)

M1A.1120 Lead-induced chronic gout, left shoulder, without tophus (tophi)

M1A.1121 Lead-induced chronic gout, left shoulder, with tophus (tophi)

M1A.1210 Lead-induced chronic gout, right elbow, without tophus (tophi)

M1A.1211 Lead-induced chronic gout, right elbow, with tophus (tophi)

M1A.1220 Lead-induced chronic gout, left elbow, without tophus (tophi)

M1A.1221 Lead-induced chronic gout, left elbow, with tophus (tophi)

M1A.1310 Lead-induced chronic gout, right wrist, without tophus (tophi)

M1A.1311 Lead-induced chronic gout, right wrist, with tophus (tophi)

M1A.1320 Lead-induced chronic gout, left wrist, without tophus (tophi)

M1A.1321 Lead-induced chronic gout, left wrist, with tophus (tophi)

M1A.1410 Lead-induced chronic gout, right hand, without tophus (tophi)

M1A.1411 Lead-induced chronic gout, right hand, with tophus (tophi)

M1A.1420 Lead-induced chronic gout, left hand, without tophus (tophi)

M1A.1421 Lead-induced chronic gout, left hand, with tophus (tophi)

M1A.1510 Lead-induced chronic gout, right hip, without tophus (tophi)

M1A.1511 Lead-induced chronic gout, right hip, with tophus (tophi)

M1A.1520 Lead-induced chronic gout, left hip, without tophus (tophi)

M1A.1521 Lead-induced chronic gout, left hip, with tophus (tophi)

M1A.1610 Lead-induced chronic gout, right knee, without tophus (tophi)

M1A.1611 Lead-induced chronic gout, right knee, with tophus (tophi)

M1A.1620 Lead-induced chronic gout, left knee, without tophus (tophi)

M1A.1621 Lead-induced chronic gout, left knee, with tophus (tophi)

M1A.1710 Lead-induced chronic gout, right ankle and foot, without tophus (tophi)

M1A.1711 Lead-induced chronic gout, right ankle and foot, with tophus (tophi)

M1A.1720 Lead-induced chronic gout, left ankle and foot, without tophus (tophi)

M1A.1721 Lead-induced chronic gout, left ankle and foot, with tophus (tophi)

M1A.18x0 Lead-induced chronic gout, vertebrae, without tophus (tophi)

M1A.18x1 Lead-induced chronic gout, vertebrae, with tophus (tophi)

M1A.19x0 Lead-induced chronic gout, multiple sites, without tophus (tophi)

M1A.19x1 Lead-induced chronic gout, multiple sites, with tophus (tophi)

M1A.2110 Drug-induced chronic gout, right shoulder, without tophus (tophi)

M1A.2111 Drug-induced chronic gout, right shoulder, with tophus (tophi)

M1A.2120 Drug-induced chronic gout, left shoulder, without tophus (tophi)

M1A.2121 Drug-induced chronic gout, left shoulder, with tophus (tophi)

M1A.2210 Drug-induced chronic gout, right elbow, without tophus (tophi)

M1A.2211 Drug-induced chronic gout, right elbow, with tophus (tophi)

M1A.2220 Drug-induced chronic gout, left elbow, without tophus (tophi)

M1A.2221 Drug-induced chronic gout, left elbow, with tophus (tophi)

M1A.2310 Drug-induced chronic gout, right wrist, without tophus (tophi)

M1A.2311 Drug-induced chronic gout, right wrist, with tophus (tophi)

M1A.2320 Drug-induced chronic gout, left wrist, without tophus (tophi)

M1A.2321 Drug-induced chronic gout, left wrist, with tophus (tophi)

M1A.2410 Drug-induced chronic gout, right hand, without tophus (tophi)

M1A.2411 Drug-induced chronic gout, right hand, with tophus (tophi)

M1A.2420 Drug-induced chronic gout, left hand, without tophus (tophi)

M1A.2421 Drug-induced chronic gout, left hand, with tophus (tophi)

M1A.2510 Drug-induced chronic gout, right hip, without tophus (tophi)

M1A.2511 Drug-induced chronic gout, right hip, with tophus (tophi)

M1A.2520 Drug-induced chronic gout, left hip, without tophus (tophi)

M1A.2521 Drug-induced chronic gout, left hip, with tophus (tophi)

M1A.2610 Drug-induced chronic gout, right knee, without tophus (tophi)

M1A.2611 Drug-induced chronic gout, right knee, with tophus (tophi)

M1A.2620 Drug-induced chronic gout, left knee, without tophus (tophi)

M1A.2621 Drug-induced chronic gout, left knee, with tophus (tophi)

M1A.2710 Drug-induced chronic gout, right ankle and foot, without tophus (tophi)

M1A.2711 Drug-induced chronic gout, right ankle and foot, with tophus (tophi)

M1A.2720 Drug-induced chronic gout, left ankle and foot, without tophus (tophi)

M1A.2721 Drug-induced chronic gout, left ankle and foot, with tophus (tophi)

M1A.28x0 Drug-induced chronic gout, vertebrae, without tophus (tophi)

M1A.28x1 Drug-induced chronic gout, vertebrae, with tophus (tophi)

M1A.29x0 Drug-induced chronic gout, multiple sites, without tophus (tophi)

M1A.29x1 Drug-induced chronic gout, multiple sites, with tophus (tophi)

M1A.3110 Chronic gout due to renal impairment, right shoulder, without tophus (tophi)

M1A.3111 Chronic gout due to renal impairment, right shoulder, with tophus (tophi)

M1A.3120 Chronic gout due to renal impairment, left shoulder, without tophus (tophi)

M1A.3121 Chronic gout due to renal impairment, left shoulder, with tophus (tophi)

M1A.3210 Chronic gout due to renal impairment, right elbow, without tophus (tophi)

M1A.3211 Chronic gout due to renal impairment, right elbow, with tophus (tophi)

M1A.3220 Chronic gout due to renal impairment, left elbow, without tophus (tophi)

M1A.3221 Chronic gout due to renal impairment, left elbow, with tophus (tophi)

M1A.3310 Chronic gout due to renal impairment, right wrist, without tophus (tophi)

M1A.3311 Chronic gout due to renal impairment, right wrist, with tophus (tophi)

M1A.3320 Chronic gout due to renal impairment, left wrist, without tophus (tophi)

M1A.3321 Chronic gout due to renal impairment, left wrist, with tophus (tophi)

M1A.3410 Chronic gout due to renal impairment, right hand, without tophus (tophi)

M1A.3411 Chronic gout due to renal impairment, right hand, with tophus (tophi)

M1A.3420 Chronic gout due to renal impairment, left hand, without tophus (tophi)

M1A.3421 Chronic gout due to renal impairment, left hand, with tophus (tophi)

M1A.3510 Chronic gout due to renal impairment, right hip, without tophus (tophi)

M1A.3511 Chronic gout due to renal impairment, right hip, with tophus (tophi)

M1A.3520 Chronic gout due to renal impairment, left hip, without tophus (tophi)

M1A.3521 Chronic gout due to renal impairment, left hip, with tophus (tophi)

M1A.3610 Chronic gout due to renal impairment, right knee, without tophus (tophi)

M1A.3611 Chronic gout due to renal impairment, right knee, with tophus (tophi)

M1A.3620 Chronic gout due to renal impairment, left knee, without tophus (tophi)

M1A.3621 Chronic gout due to renal impairment, left knee, with tophus (tophi)

M1A.3710 Chronic gout due to renal impairment, right ankle and foot, without tophus (tophi)

M1A.3711 Chronic gout due to renal impairment, right ankle and foot, with tophus (tophi)

M1A.3720 Chronic gout due to renal impairment, left ankle and foot, without tophus (tophi)

M1A.3721 Chronic gout due to renal impairment, left ankle and foot, with tophus (tophi)

M1A.38x0 Chronic gout due to renal impairment, vertebrae, without tophus (tophi)

M1A.38x1 Chronic gout due to renal impairment, vertebrae, with tophus (tophi)

M1A.39x0 Chronic gout due to renal impairment, multiple sites, without tophus (tophi)

M1A.39x1 Chronic gout due to renal impairment, multiple sites, with tophus (tophi)

M1A.4110 Other secondary chronic gout, right shoulder, without tophus (tophi)

M1A.4111 Other secondary chronic gout, right shoulder, with tophus (tophi)

M1A.4120 Other secondary chronic gout, left shoulder, without tophus (tophi)

M1A.4121 Other secondary chronic gout, left shoulder, with tophus (tophi)

M1A.4210 Other secondary chronic gout, right elbow, without tophus (tophi)

M1A.4211 Other secondary chronic gout, right elbow, with tophus (tophi)

M1A.4220 Other secondary chronic gout, left elbow, without tophus (tophi)

M1A.4221 Other secondary chronic gout, left elbow, with tophus (tophi)

M1A.4310 Other secondary chronic gout, right wrist, without tophus (tophi)

M1A.4311 Other secondary chronic gout, right wrist, with tophus (tophi)

M1A.4320 Other secondary chronic gout, left wrist, without tophus (tophi)
M1A.4321 Other secondary chronic gout, left wrist, with tophus (tophi)
M1A.4410 Other secondary chronic gout, right hand, without tophus (tophi)
M1A.4411 Other secondary chronic gout, right hand, with tophus (tophi)
M1A.4420 Other secondary chronic gout, left hand, without tophus (tophi)
M1A.4421 Other secondary chronic gout, left hand, with tophus (tophi)
M1A.4510 Other secondary chronic gout, right hip, without tophus (tophi)
M1A.4511 Other secondary chronic gout, right hip, with tophus (tophi)
M1A.4520 Other secondary chronic gout, left hip, without tophus (tophi)
M1A.4521 Other secondary chronic gout, left hip, with tophus (tophi)
M1A.4610 Other secondary chronic gout, right knee, without tophus (tophi)
M1A.4611 Other secondary chronic gout, right knee, with tophus (tophi)
M1A.4620 Other secondary chronic gout, left knee, without tophus (tophi)
M1A.4621 Other secondary chronic gout, left knee, with tophus (tophi)
M1A.4710 Other secondary chronic gout, right ankle and foot, without tophus (tophi)
M1A.4711 Other secondary chronic gout, right ankle and foot, with tophus (tophi)
M1A.4720 Other secondary chronic gout, left ankle and foot, without tophus (tophi)
M1A.4721 Other secondary chronic gout, left ankle and foot, with tophus (tophi)
M1A.48x0 Other secondary chronic gout, vertebrae, without tophus (tophi)
M1A.48x1 Other secondary chronic gout, vertebrae, with tophus (tophi)
M1A.49x0 Other secondary chronic gout, multiple sites, without tophus (tophi)
M1A.49x1 Other secondary chronic gout, multiple sites, with tophus (tophi)
M1A.9xx0 Chronic gout, unspecified, without tophus (tophi)
M1A.9xx1 Chronic gout, unspecified, with tophus (tophi)

EXPERIMENTAL INVESTIGATIONAL

E79.0 Hyperuricemia without signs of inflammatory arthritis and tophaceous disease
[asymptomatic]

Version Effective Date: 04/30/2025

Title: Pembrolizumab (Keytruda®)

MEDICALLY NECESSARY

AMPULLARY ADENOCARCINOMA

Pembrolizumab (Keytruda®) is considered medically necessary and, therefore, covered for the treatment of ampullary adenocarcinoma for the following indications:

- As therapy for disease progression as a single agent if no prior immunotherapy and microsatellite instability–high (MSI-H), mismatch repair deficient (dMMR), or tumor mutational burden–high (TMB-H) greater than or equal to 10 mutations/megabase [mut/Mb])
- First-line therapy as a single agent (may be followed by chemoradiation for palliative indications in individuals with good performance status [Eastern Cooperative Oncology Group (ECOG) 0–1], with good biliary drainage and adequate nutritional intake) if MSI-H, dMMR, or TMB-H ≥ 10 mut/Mb) for:
 - Unresectable localized disease
 - Stage IV resected ampullary cancer
 - Metastatic disease at initial presentation

ANAL CARCINOMA

Pembrolizumab (Keytruda®) is considered medically necessary and, therefore, covered as a single agent for metastatic anal carcinoma as National Comprehensive Cancer Network (NCCN)-preferred second-line and subsequent therapy for metastatic disease if no prior immunotherapy received.

DIFFUSE LARGE B-CELL LYMPHOMA/PRIMARY MEDIASTINAL LARGE B-CELL LYMPHOMA

Pembrolizumab (Keytruda®) is considered medically necessary and, therefore, covered as a single agent for the treatment of adult and pediatric individuals with refractory primary mediastinal large B-cell lymphoma (PMBCL) or individuals whose disease has relapsed after two or more prior lines of therapy.

US Food and Drug Administration (FDA) note: pembrolizumab (Keytruda®) is not recommended for the treatment of individuals with PMBCL who require urgent cytoreductive therapy.

BLADDER CANCER

Urothelial carcinoma of bladder

Pembrolizumab (Keytruda®) is considered medically necessary and, therefore, covered for the treatment of bladder cancer for the following indications:

- Treatment of individuals with Bacillus Calmette-Guérin (BCG)—unresponsive, high-risk, non—muscle-invasive bladder cancer with stage Tis (carcinoma in situ [CIS]) (with or without papillary) tumors who are ineligible for, or who have elected not to undergo cystectomy for any of the following indications:
 - As initial management
 - For cytology-positive, imaging- and cystoscopy-negative, bladder-positive recurrent or persistent disease
 - After incomplete response following a different intravesical agent for BCG-unresponsive recurrent or persistent disease that is cytology-positive, imaging- and cystoscopy-negative, and bladder positive
- First-line systemic therapy, as a single agent (NCCN preferred) for the treatment of cisplatin-ineligible individuals, who have locally advanced or metastatic disease and are not eligible for any platinum-containing chemotherapy for any of the following indications:
 - Stage II (cT2, N0) disease or stage IIIA (cT3, N0; cT4a, N0; cT1-T4a, N1) disease if the tumor is present following reassessment of tumor status 2 to 3 months after primary treatment with bladder-preserving concurrent chemoradiotherapy and maximal transurethral resection of bladder tumor (TURBT)
 - Stage II (cT2, N0) disease or stage IIIA (cT3, N0; cT4a, N0; cT1-T4a, N1) disease if the tumor is present following reassessment of tumor status 2 to 3 months after primary treatment with bladder-preserving concurrent chemoradiotherapy, radiotherapy alone, or TURBT
 - Stage IIIB (cT1-T4a, N2,3) disease as downstaging systemic therapy

- Stage IIIB (cT1-T4a, N2,3) disease following partial response (PR) or progression after primary treatment with concurrent chemoradiotherapy
- Stage IVA (cT4b, any N, M0; any T, any N, M1a) disease
- Stage IVA (cT4b, any N, M0) disease as consolidation therapy if no tumor present following reassessment of tumor status 2 to 3 months after primary treatment with concurrent chemoradiotherapy
- Stage IVA (cT4b, any N, M0) disease if tumor present following reassessment of tumor status 2 to 3 months after primary treatment with concurrent chemoradiotherapy
- Metastatic stage IVB (any T, any N, M1b) disease
- Muscle-invasive local recurrence or persistent disease in a preserved bladder treated with curative intent
- Metastatic or local recurrence postcystectomy treated with curative intent
- Second-line systemic therapy, as a single agent (NCCN preferred) postplatinum or other chemotherapy for the following indications:
 - Stage II (cT2, N0) or stage IIIA (cT3, N0; cT4a, N0; cT1-T4a, N1) disease if a tumor is present following reassessment of tumor status 2 to 3 months after primary treatment with concurrent bladder-preserving chemoradiotherapy and maximal TURBT
 - Stage IIIB (cT1-T4a, N2,3) disease following PR or progression after primary treatment with downstaging systemic therapy or concurrent chemoradiotherapy
 - Stage IVA (cT4b, any N, M0) disease if a tumor is present following reassessment of tumor status after primary treatment with first-line systemic therapy or concurrent chemoradiotherapy
 - Stage IVA (any T, any N, M1a) disease if stable disease or progression following reassessment of tumor status after primary treatment with first-line systemic therapy
 - Metastatic stage IVB (any T, any N, M1b) disease

- Muscle-invasive local recurrence or persistent disease in a preserved bladder treated with curative intent
- Metastatic or local recurrence post cystectomy treated with curative intent
- First-line systemic therapy in cisplatin-ineligible individuals who are not eligible for any platinum-containing chemotherapy
- First-line systemic therapy in combination with enfortumab vedotin-ejfv as first-line systemic therapy (NCCN preferred)
- Second-line systemic therapy postplatinum (NCCN preferred) or other chemotherapy
- Individuals with locally advanced or metastatic urothelial cancer in combination with enfortumab vedotin
- Individuals who are not eligible for cisplatin-containing chemotherapy and whose tumors express PD-L1 with combined positive score (CPS) 10 or less, as determined by an FDA-approved test
- Individuals who are not eligible for any platinum-containing chemotherapy regardless of PD-L1 status
- Individuals with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy
- Individuals with BCG-unresponsive, high-risk, non–muscle invasive bladder cancer (NMIBC) with CIS with or without papillary tumors who are ineligible for or have elected not to undergo cystectomy

Upper genitourinary tract tumors

Pembrolizumab (Keytruda®) for the treatment of upper genitourinary (GU) tumors is considered medically necessary and, therefore, covered as a single-agent therapy for the following indications:

- Therapy for metastatic disease in combination with enfortumab vedotin-ejfv as first-line systemic therapy (NCCN preferred)
- As first-line systemic therapy in cisplatin-ineligible individuals or who are not eligible for any platinum-containing chemotherapy

- As a second-line systemic therapy postplatinum or for individuals who received a therapy other chemotherapy (NCCN preferred)

Primary carcinoma of the urethra

Pembrolizumab (Keytruda®) for the treatment of primary carcinoma of the urethra is considered medically necessary and, therefore, covered as a single-agent therapy for the following indications:

- Primary therapy for the treatment of individuals with clinical stage T3-4, cN1-2 disease or cN1-2 palpable inguinal lymph nodes as first-line systemic therapy (NCCN preferred) in cisplatin-ineligible individuals or who are not eligible for any platinum-containing chemotherapy
- Therapy for metastatic disease in combination with enfortumab vedotin-ejfv as first-line systemic therapy (NCCN preferred)
- For recurrent or metastatic disease (except for recurrence of clinical stage T3-4 disease or palpable inguinal lymph nodes) as:
 - First-line systemic therapy in cisplatin-ineligible individuals or who are not eligible for any platinum-containing chemotherapy
 - Second-line systemic therapy postplatinum or other chemotherapy (NCCN preferred)

Urothelial carcinoma of the prostate

- Therapy for metastatic disease in combination with enfortumab vedotin-ejfv as first-line systemic therapy (NCCN preferred)
- Therapy for metastatic disease for
 - first-line systemic therapy as a single agent in cisplatin-ineligible patients who are not eligible for any platinum-containing chemotherapy
 - second-line systemic therapy as a single agent postplatinum or other chemotherapy (NCCN preferred)

BONE CANCERS

Pembrolizumab (Keytruda®) is considered medically necessary and, therefore, covered as a single-agent therapy for the treatment of individuals with unresectable or metastatic disease that has progressed following prior treatment and who have no satisfactory alternative treatment options for the following indications:

- Chondrosarcoma and any of the following:
 - MSI-H or dMMR tumors (NCCN preferred)
 - TMB-H tumors with 10 or more mut/Mb
- Chordoma and any of the following:
 - For MSI-H or dMMR (NCCN preferred)
 - For TMB-H tumors with 10 or more mut/Mb
- Ewing sarcoma (except for mesenchymal chondrosarcoma) and any of the following:
 - For MSI-H or dMMR tumors that have progressed following prior treatment (NCCN preferred)
 - For TMB-H tumors with 10 or more mut/Mb
- Osteosarcoma (except for dedifferentiated chondrosarcoma and for high-grade undifferentiated pleomorphic sarcoma [UPS]) and any of the following:
 - For MSI-H or dMMR tumors that have progressed following prior treatment (NCCN preferred)
 - For TMB-H tumors with 10 or more mut/Mb

BREAST CANCER

Triple-negative breast cancer

Pembrolizumab (Keytruda®) is considered medically necessary and, therefore, covered for the treatment of individuals with triple-negative breast cancer (TNBC) for any of the following indications:

- The treatment of individuals with high-risk early-stage TNBC in combination with chemotherapy as neoadjuvant treatment, and then continued as a single agent as adjuvant treatment after surgery.

- In combination with chemotherapy, for the treatment of individuals with locally recurrent unresectable or metastatic TNBC whose tumors express PD-L1 (CPS ≥ 10) as determined by an FDA-approved test.

Inflammatory breast cancer

Pembrolizumab (Keytruda®) is considered medically necessary and, therefore, covered for the treatment of individuals with inflammatory breast cancer for any of the following indications:

- As a single-agent therapy for inflammatory breast cancer with no response to preoperative systemic therapy, or recurrent unresectable (local or regional) or stage IV (M1) disease that is MSI-H or dMMR, or TMB-H tumors (≥ 10 mut/mb) that have progressed following prior treatment and have no satisfactory alternative treatment options
 - As third-line therapy and beyond for hormone receptor positive and human epidermal growth factor receptor 2 (HER2)-negative with visceral crisis or endocrine therapy refractory or for triple negative breast cancer (TNBC)
 - As fourth-line and beyond for HER2-positive disease
- As (NCCN preferred) therapy for individuals with high-risk (stage II-III) TNBC as part of the following regimen: preoperative pembrolizumab in combination with carboplatin and paclitaxel, followed by preoperative pembrolizumab in combination with cyclophosphamide and either doxorubicin or epirubicin, followed by surgery, followed by adjuvant single-agent pembrolizumab*

NCCN note: *There are no data on sequencing or combining adjuvant pembrolizumab with capecitabine or olaparib in individuals who meet criteria for treatment with one or more of these agents. However, their sequential/combined use may be considered given high-risk of recurrence in individuals with residual disease

- Therapy for individuals with TNBC in combination with either albumin-bound paclitaxel, paclitaxel, or gemcitabine with carboplatin for PD-L1–positive triple-negative for individuals with no response to preoperative systemic therapy, or recurrent unresectable (local or regional) or stage IV (M1) disease for one of the following:
 - As first-line therapy (NCCN preferred)

- As second and subsequent lines of therapy if PD-1/PD-L1 inhibitor has not been previously used

Invasive breast cancer

Pembrolizumab (Keytruda®) is considered medically necessary and, therefore, covered for the treatment of individuals with invasive breast cancer for any of the following indications:

- NCCN-preferred for high-risk (stage II-III) TNBC when used as part of the following regimen: preoperative therapy for individuals with locally advanced c≥T2 or cN+ and M0 disease, or cT1c, cN0 disease with pembrolizumab in combination with carboplatin and paclitaxel, followed by preoperative pembrolizumab in combination with cyclophosphamide and either doxorubicin or epirubicin, followed by mastectomy or breast-conserving surgery (BCS) with surgical axillary staging, followed by adjuvant single-agent pembrolizumab* if ypT0N0 or pCR, or if ypT1-4, N0 or ypN≥1

NCCN note: *There are no data on sequencing or combining adjuvant pembrolizumab with capecitabine or olaparib in individuals who meet criteria for treatment with one or more of these agents. However, their sequential/combined use may be considered given the high risk of recurrence in individuals with residual disease.

- Single-agent therapy for recurrent unresectable (local or regional) or stage IV (M1) disease that is MSI-H or mismatch repair deficient (dMMR), or TMB-H tumors (≥10 mut/mb) that have progressed following prior treatment and has no satisfactory alternative treatment options
 - As third-line therapy and beyond for hormone receptor positive and HER2-negative with visceral crisis or endocrine therapy refractory or for TNBC
 - As fourth-line and beyond for HER2-positive disease
- Therapy for individuals with TNBC in combination with either albumin-bound paclitaxel, paclitaxel, or gemcitabine with carboplatin for PD-L1–positive (PD-L1; CPS ≥10) triple-negative recurrent unresectable (local or regional) or stage IV (M1) disease for one of the following:
 - As first-line therapy (NCCN preferred)

- As second and subsequent lines of therapy if PD-L1 inhibitor has not been previously used
- Single-agent therapy for recurrent unresectable (local or regional) or stage IV (M1) disease that is MSI-H or dMMR, or TMB-H tumors (≥ 10 mut/mb) that have progressed following prior treatment and have no satisfactory alternative treatment options

CENTRAL NERVOUS SYSTEM CANCERS

Pembrolizumab (Keytruda®) is considered medically necessary and, therefore, covered as a single-agent therapy for the treatment of extensive OR limited brain metastases in individuals with any of the following conditions:

- BRAF-nonspecific melanoma or PD-L1–positive (Tumor Proportion Score [TPS] $\geq 1\%$) non–small cell lung cancer and limited brain metastases, in one of the following scenarios:
 - Initial treatment in select individuals (e.g., individuals with small asymptomatic brain metastases)
 - For recurrent brain metastases
 - Relapsed disease with either stable systemic disease or reasonable systemic treatment options
- BRAF non-specific melanoma or PD-L1–positive (TPS $\geq 1\%$) non–small cell lung cancer and extensive brain metastases OR as NCCN-preferred single-agent treatment for extensive brain metastases in MSI-H/dMMR) or TMB-H (≥ 10 mut/Mb) tumors for isolated brain metastases in one of the following scenarios:
 - Primary treatment in select individuals (e.g., individuals with small asymptomatic brain metastases)
 - Recurrent disease with stable systemic disease or reasonable systemic treatment options
- Single-agent treatment for extensive brain metastases in BRAF nonspecific melanoma or PD-L1–positive (TPS $\geq 1\%$) non–small cell lung cancer
 - As primary treatment in select cases (e.g., small asymptomatic brain metastases)
 - As treatment for recurrent disease with stable systemic disease or reasonable systemic treatment options

CERVICAL CANCER

Pembrolizumab (Keytruda®) for the treatment of cervical cancer is considered medically necessary and, therefore, covered as a single agent for the following indications:

- As primary treatment in combination with chemoradiation (cisplatin or carboplatin, if individual is cisplatin intolerant) only for individuals with FIGO 2014 stage III-IVA disease
- As a second-line therapy (NCCN preferred) for the treatment of individuals with progression on or after chemotherapy in individuals whose tumors express PD-L1 (CPS ≥ 1) as determined by an FDA-approved test or a validated test performed in a CLIA-certified laboratory, or if MSI-H or dMMR tumors for any of the following:
 - Local/regional recurrence
 - Stage IVB or distant metastases
- As NCCN preferred first-line, second-line, or subsequent therapy as clinically appropriate (if not used previously as first-line) in combination with cisplatin or carboplatin, paclitaxel, and with or without bevacizumab and continued for maintenance therapy[†] for PD-L1 positive (CPS ≥ 1) as determined by an FDA-approved test or a validated test performed in a CLIA-certified laboratory for:
 - Local/regional recurrence
 - Stage IVB or recurrence with distant metastases
- As NCCN-preferred second-line or subsequent treatment of individuals with unresectable or metastatic TMB-H (≥ 10 mut/Mb) tumors, as determined by an FDA-approved test or a validated test performed in a CLIA-certified laboratory, that have progressed following prior treatment and who have no satisfactory alternative treatment options
- In combination with chemoradiotherapy, for the treatment of individuals with FIGO 2014 Stage III-IVA cervical cancer
- For the treatment of individuals with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy whose tumors express PD-L1 (CPS ≥ 1) as determined by an FDA-approved test
- For the treatment of individuals with persistent, recurrent, or metastatic cervical cancer whose tumors express PD-L1 (CPS ≥ 1) as determined by an FDA-approved test in combination with chemotherapy, with or without bevacizumab.

NCCN note: [†]Pembrolizumab may be continued as a maintenance therapy. Refer to the original study protocol for maintenance therapy dosing schedules.

CHRONIC LYMPHOCYTIC LEUKEMIA/SMALL LYMPHOCYTIC LYMPHOMA

- As a single agent or in combination with ibrutinib for histologic (Richter) transformation to diffuse large B-cell lymphoma (clonally related or unknown clonal status) in individuals with del(17p)/TP53 mutation, or who are chemotherapy refractory or unable to receive chemoimmunotherapy.

COLON CANCER

Pembrolizumab (Keytruda®) for the treatment of colon cancer is considered medically necessary and, therefore, covered as a single-agent therapy for the following indications:

- Therapy as a single agent (dMMR/MSI-H or polymerase epsilon/delta [POLE/POLD1] mutation) (candidate for immunotherapy and no prior immunotherapy received)
 - As treatment for locally unresectable or medically inoperable disease (NCCN preferred)
 - As primary treatment for synchronous abdominal/peritoneal metastases that are nonobstructing, or following local therapy for individuals with existing or imminent obstruction
 - For synchronous unresectable metastases of other sites
 - As treatment for unresectable metachronous metastases
 - As treatment for (NCCN preferred) for dMMR/MSI-H only for neoadjuvant therapy for clinical T4b disease (NCCN preferred)
- Treatment as a single agent (dMMR/MSI-H) or POLE/POLD1 mutation)
 - As neoadjuvant therapy for resectable synchronous liver and/or lung metastases (if no previous treatment with a checkpoint inhibitor) (NCCN-preferred)
 - As initial treatment for resectable metachronous metastases if no previous immunotherapy
- Systemic therapy for advanced or metastatic appendiceal adenocarcinoma (dMMR/MSI-H or POLE/POLD1 mutation) as a single agent if candidate for immunotherapy and no prior immunotherapy received

COLORECTAL CANCER (CRC) MICROSATELLITE INSTABILITY–HIGH OR MISMATCH REPAIR DEFICIENT

Pembrolizumab (Keytruda®) is considered medically necessary and, therefore, covered as first-line therapy for the treatment of individuals with unresectable or metastatic MSI-H or dMMR CRC as determined by an FDA-approved test.

CUTANEOUS SQUAMOUS CELL CARCINOMA (cSCC)

Pembrolizumab (Keytruda®) is considered medically necessary and, therefore, covered for the treatment of individuals with recurrent or metastatic cutaneous squamous cell carcinoma (cSCC) or locally advanced cSCC that is not curable by surgery or radiation.

ESOPHAGEAL AND GASTROESOPHAGEAL JUNCTION CANCERS

Pembrolizumab (Keytruda®) is considered medically necessary and, therefore, covered for the treatment of individuals with carcinoma and the following indications:

- For recurrent locally advanced or metastatic esophageal or gastroesophageal junction (GEJ) tumors that are located in an epicenter 1 to 5 centimeters above the GEJ that is not amenable to surgical resection or definitive chemoradiation for any of the following regimens:
 - In combination with platinum- and fluoropyrimidine-based chemotherapy
 - As a single agent after one or more prior lines of systemic therapy for individuals with tumors of squamous cell tumor with histology that expresses PD-L1 (CPS ≥ 10) as determined by an FDA-approved test
- Palliative therapy for individuals who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease and Karnofsky performance score $\geq 60\%$ or ECOG performance score ≤ 2 and if no prior tumor progression while on therapy with a checkpoint inhibitor:
 - As NCCN-preferred first-line therapy as a single agent or in combination with oxaliplatin and fluorouracil or capecitabine if MSI-H or dMMR tumor and independent of PD-L1 status
 - As NCCN-preferred second-line therapy as a single agent for esophageal squamous cell carcinoma (SCC) with PD-L1 expression by CPS of levels ≥ 10
 - As NCCN-preferred second-line or subsequent therapy as a single agent for MSI-H or dMMR tumors

- As second-line or subsequent therapy as a single agent for TMB high (≥ 10 mut/Mb) tumors
- Palliative therapy for individuals with squamous cell carcinoma who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease and Karnofsky performance score $\geq 60\%$ or ECOG performance score ≤ 2 as NCCN-preferred first-line therapy in combination with one of the following:
 - Oxaliplatin and fluorouracil or capecitabine (if no prior tumor progression while on therapy with a checkpoint inhibitor)
 - Cisplatin and fluorouracil or capecitabine (if no prior tumor progression while on therapy with a checkpoint inhibitor)
- Palliative therapy for the treatment of individuals with adenocarcinoma that is HER2 overexpression-positive individuals who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease and Karnofsky performance score $\geq 60\%$ or ECOG performance score ≤ 2 as NCCN-preferred first-line therapy in combination with one of the following:
 - Fluorouracil, cisplatin or oxaliplatin, and trastuzumab (if no prior tumor progression while on therapy with a checkpoint inhibitor) in individuals with (PD-L1 CPS ≥ 10)
 - Capecitabine, cisplatin or oxaliplatin, and trastuzumab (if no prior tumor progression while on therapy with a checkpoint inhibitor) in individuals with (PD-L1 CPS ≥ 10)
- As induction systemic therapy in individuals with **Adenocarcinoma, Squamous cell carcinoma** for relieving dysphagia in select individuals with HER2 overexpression positive adenocarcinoma and PD-L1 CPS ≥ 1 who are medically fit and planned for esophagectomy with cT2, N0 (high-risk lesions: lymphovascular invasion, ≥ 3 cm, poorly differentiated), cT1b-cT2, N+ or cT3-cT4a, Any N disease for the following regimens:
 - In combination with cisplatin, trastuzumab and capecitabine or fluorouracil (NCCN-preferred)
 - In combination with oxaliplatin, trastuzumab and capecitabine or fluorouracil (NCCN-preferred)
- As induction systemic therapy for relieving dysphagia in select individuals (except with PD-L1 CPS ≥ 1) who are medically fit and planned for esophagectomy with cT2, N0 (high-risk lesions: lymphovascular invasion, ≥ 3 cm, poorly differentiated), cT1b-cT2, N+ or cT3-cT4a, Any N disease in combination with
 - Oxaliplatin and capecitabine or fluorouracil (NCCN-preferred)

- Cisplatin and capecitabine or fluorouracil (NCCN-preferred)
- As induction systemic therapy for relieving dysphagia in select individuals with MSI-H or dMMR tumors (independent of PD-L1 status) who are medically fit and planned for esophagectomy with cT2, N0 (high-risk lesions: lymphovascular invasion, ≥ 3 cm, poorly differentiated), cT1b-cT2, N+ or cT3-cT4a, Any N disease
 - As a single agent (NCCN-preferred)
 - In combination with oxaliplatin and capecitabine or fluorouracil (NCCN-preferred)
- For the treatment of individuals with locally advanced or metastatic esophageal or gastroesophageal junction (GEJ) (tumors with epicenter 1 to 5 centimeters above the GEJ) carcinoma that is not amenable to surgical resection or definitive chemoradiation either: **(FDA)**
 - In combination with platinum- and fluoropyrimidine-based chemotherapy,
 - As a single agent after one or more prior lines of systemic therapy for individuals with tumors of squamous cell histology that express PD-L1 (CPS ≥ 10) as determined by an FDA-approved test.

Adenocarcinoma

- As neoadjuvant or perioperative immunotherapy as a single agent for adenocarcinoma if tumor is MSI-H or dMMR
 - As primary treatment in individuals who are medically fit for surgery with cT2, N0 (high-risk lesions: lymphovascular invasion, ≥ 3 cm, poorly differentiated), cT1b-cT2, N+ or cT3-cT4a, Any N disease
 - As postoperative management following R0 resection in individuals who have received preoperative therapy with the same regimen
- Palliative therapy for individuals with HER2 overexpression negative adenocarcinoma (except PD-L1 CPS ≥ 1) who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease and Karnofsky performance score $\geq 60\%$ or ECOG performance score ≤ 2 as (NCCN-preferred) first-line therapy in combination with one of the following regimens:
 - Oxaliplatin and fluorouracil or capecitabine (if no prior tumor progression while on therapy with a checkpoint inhibitor)
 - Cisplatin and fluorouracil or capecitabine (if no prior tumor progression while on therapy with a checkpoint inhibitor)

GASTRIC CANCER

Pembrolizumab (Keytruda®) for the treatment of gastric cancer is considered medically necessary and, therefore, covered for the following indications:

- In combination with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy, for the first-line treatment of individuals with locally advanced unresectable or metastatic HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma whose tumors express PD-L1 (CPS ≥ 1) as determined by an FDA-approved test
- In combination with fluoropyrimidine- and platinum-containing chemotherapy, for the first-line treatment of adults with locally advanced unresectable or metastatic HER2-negative gastric or gastroesophageal junction (GEJ) adenocarcinoma. **(FDA)**
- Primary treatment for medically fit individuals with surgically unresectable locoregional HER2 overexpression–positive adenocarcinoma and PD-L1 CPS ≥ 1 in combination with:
 - Cisplatin, trastuzumab, and fluorouracil or capecitabine (NCCN-preferred)
 - Oxaliplatin, trastuzumab, and fluorouracil or capecitabine (NCCN-preferred)
- Primary treatment for individuals who are medically fit for surgery but with surgically unresectable locoregional HER2 overexpression negative disease in combination with:
 - Oxaliplatin and fluorouracil or capecitabine (NCCN-preferred)
 - Cisplatin and fluorouracil or capecitabine (NCCN-preferred)
- Primary treatment for individuals with MSI-H or dMMR tumors (independent of PD-L1 status) who are medically fit for surgery but with surgically unresectable locoregional disease
 - As a single agent (NCCN-preferred)
 - In combination with oxaliplatin and fluorouracil or capecitabine (NCCN-preferred)

- Palliative therapy for individuals who are not surgical candidates or have an unresectable locally advanced, recurrent, or metastatic disease (including peritoneal only metastatic disease, including positive cytology) with HER2 overexpression–positive adenocarcinoma with PD-L1 CPS ≥ 1 and Karnofsky performance score $\geq 60\%$ or ECOG performance score ≤ 2 as first-line therapy in combination with:
 - Cisplatin, trastuzumab, and fluorouracil or capecitabine (if no prior tumor progression while on therapy with a checkpoint inhibitor) (NCCN-preferred)
 - Oxaliplatin, trastuzumab, and fluorouracil or capecitabine (if no prior tumor progression while on therapy with a checkpoint inhibitor) (NCCN-preferred)
- Palliative therapy for HER2 overexpression negative individuals who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease (including peritoneal only metastatic disease, including positive cytology) and Karnofsky performance score $\geq 60\%$ or ECOG performance score ≤ 2 as first-line therapy in combination with
 - oxaliplatin and fluorouracil or capecitabine (if no prior tumor progression while on therapy with a checkpoint inhibitor)
 - cisplatin and fluorouracil or capecitabine (if no prior tumor progression while on therapy with a checkpoint inhibitor)
- Palliative therapy for individuals with MSI-H or dMMR tumors (independent of PD-L1 status) who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease (including peritoneal only metastatic disease, including positive cytology) and Karnofsky performance score $\geq 60\%$ or ECOG performance score ≤ 2 as NCCN-preferred first-line therapy
 - as a single agent (if no prior tumor progression while on therapy with a checkpoint inhibitor)
 - in combination with oxaliplatin and fluorouracil or capecitabine (if no prior tumor progression while on therapy with a checkpoint inhibitor)
- Palliative therapy for locoregional disease in individuals who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease (including peritoneal only metastatic disease, including positive cytology) and Karnofsky performance score $\geq 60\%$ or ECOG performance score ≤ 2 as second-line or subsequent

therapy as a single agent for MSI-H or dMMR tumors or TMB high (≥ 10 mut/Mb) tumors (if no prior tumor progression while on therapy with a checkpoint inhibitor)

- For individuals with early-stage gastric HER2 overexpression **positive** adenocarcinoma and PD-L1 CPS ≥ 1 with endoscopic features suggestive of deep submucosal invasion including converging folds, irregular surface pattern, and ulceration in a large gastric mass with favorable histology and completed an endoscopic resection, consider systemic therapy in combination with
 - cisplatin, trastuzumab and fluorouracil or capecitabine (NCCN-preferred)
 - oxaliplatin, trastuzumab and fluorouracil or capecitabine (NCCN-preferred)
- For individuals with early-stage gastric HER2 overexpression **negative** adenocarcinoma and PD-L1 CPS ≥ 1 with endoscopic features suggestive of deep submucosal invasion including converging folds, irregular surface pattern, and ulceration in a large gastric mass with favorable histology and completed an endoscopic resection, consider systemic therapy in combination with
 - oxaliplatin and fluorouracil or capecitabine (NCCN-preferred)
 - cisplatin and fluorouracil or capecitabine (NCCN-preferred)
- For individuals with early-stage gastric adenocarcinoma and MSI-H or dMMR tumors (independent of PD-L1 status) with endoscopic features suggestive of deep submucosal invasion including converging folds, irregular surface pattern, and ulceration in a large gastric mass with favorable histology and completed an endoscopic resection, consider systemic therapy in combination with one of the following:
 - As a single agent (NCCN-preferred)
 - In combination with oxaliplatin and fluorouracil or capecitabine (NCCN-preferred)
- As neoadjuvant or perioperative immunotherapy as a single agent for individuals with MSI-H or dMMR tumors for one of the following:
 - As primary treatment prior to surgery for potentially resectable locoregional disease (cT2 or higher, any N) if medically fit for surgery
 - As postoperative management following R0 resection in individuals who have received preoperative therapy with the same regimen

GESTATIONAL TROPHOBLASTIC NEOPLASIA

Pembrolizumab (Keytruda®) for the treatment of gestational trophoblastic neoplasia is

considered medically necessary and, therefore, covered as single-agent therapy for multiagent chemotherapy-resistant:

- High-risk disease (NCCN preferred)
- A recurrent or progressive intermediate trophoblastic tumor (placental site trophoblastic tumor or epithelioid trophoblastic tumor) following treatment with a platinum/etoposide-containing–based regimen

HEAD AND NECK CANCERS

Pembrolizumab (Keytruda®) is considered medically necessary and, therefore, covered for very advanced head and neck cancer for the following regimens:

- Systemic therapy as NCCN-preferred alternate single agent subsequent-line option if immunotherapy not previously used, for non-nasopharyngeal cancer if disease progression on or after platinum therapy in individuals with:
 - Performance status (PS) 0-3 and persistent or progressive metastatic disease (M1) at initial presentation following first-line therapy
 - PS 3 and unresectable locoregional recurrence without prior radiation therapy (RT) or unresectable persistent disease without prior RT
 - PS 0-3 and unresectable locoregional recurrence with prior RT, unresectable second primary with prior RT, unresectable persistent disease with prior RT, or recurrent/persistent disease with distant metastases
- First-line systemic therapy or if not previously used, may be considered as subsequent-line systemic therapy for the treatment of individuals with cancer of the nasopharynx in combination with cisplatin and gemcitabine for T1-4, N0-3, M1 (If complete response [CR]) or near CR, consider continued systemic therapy):
 - Oligometastatic disease and PS 0-2
 - Widely metastatic disease and good PS (0-2)
- Subsequent-line single-agent systemic therapy for the treatment of cancer of the nasopharynx if previously treated, PD-L1–positive, recurrent or metastatic disease, or for TMB-H tumors (≥ 10 mut/Mb) for T1-4, N0-3, M1 (if CR or near CR, consider continued systemic therapy)
 - Oligometastatic disease and PS 0-2
 - Widely metastatic disease and good PS 0-2

- As a systemic therapy option as a single agent for non-nasopharyngeal cancer in individuals with MSI-H, dMMR, or TMB-H (≥ 10 mut/Mb) tumors as:
 - First-line option for PS 3 for newly diagnosed T4b, N0-3, M0 disease, newly diagnosed unresectable nodal disease with no metastases, newly diagnosed nonmetastatic disease for individuals who are unfit for surgery
 - First-line or alternate subsequent-line option for PS 0-3 for metastatic (M1) disease at initial presentation
 - First-line or subsequent-line option for PS 3 and unresectable locoregional recurrence without prior RT or unresectable persistent disease without prior RT
 - First-line or alternate subsequent-line option for PS 0-3 and unresectable locoregional recurrence with prior RT, unresectable second primary with prior RT, unresectable persistent disease with prior RT, or recurrent/persistent disease with distant
- - metastases
- ne, if not previously used, may be considered in subsequent lines), fluorouracil and cisplatin (NCCN preferred first-line, if not previously used, may be considered in subsequent lines), docetaxel and carboplatin, docetaxel and cisplatin, paclitaxel and carboplatin, paclitaxel and cisplatin, cetuximab for any of the following indications (except for use of combination systemic therapy):
 - Metastatic (M1) disease at initial presentation
 - Recurrent/persistent disease with distant metasta
 - ses
 - Unresectable locoregional recurrence with prior RT
 - Unresectable second primary with prior RT
 - Unresectable persistent disease with prior RT
- Systemic therapy as a first-line or subsequent-line option if not previously given in individuals with nasopharyngeal cancer and PS 0-1 for unresectable locoregional recurrence with prior radiation therapy (RT), unresectable second primary with prior RT,

unresectable persistent disease with prior RT, or recurrent/persistent disease with distant metastases in combination with cisplatin and gemcitabine

- As combination systemic therapy in non-nasopharyngeal cancer for resectable locoregional recurrence or persistent disease without prior RT given with:
 - Fluorouracil and carboplatin (NCCN preferred first-line, if not previously used, may be considered in subsequent lines)
 - Fluorouracil and cisplatin (NCCN preferred first-line, if not previously used, may be considered in subsequent lines)
 - Docetaxel and carboplatin
 - Docetaxel and cisplatin
 - Paclitaxel and carboplatin
 - Paclitaxel and cisplatin
 - Cetuximab
- As (NCCN preferred) systemic therapy as a single agent for non-nasopharyngeal cancer tumors that express PD-L1 with CPS ≥ 1 as :
 - First-line option for PS 3 for newly diagnosed T4b, N0-3, M0 disease, newly diagnosed unresectable nodal disease with no metastases, newly diagnosed non-metastatic disease for individuals who are unfit for surg
 - ery
 - First-line or alternate subsequent line if not previously used option for PS 0-3 for metastatic (M1) disease at initial presentation
 - First-line or subsequent line, if not previously used option for PS 3 and unresectable locoregional recurrence without prior RT or unresectable persistent disease without prior RT
 - First-line or alternate subsequent line, if not previously used option for PS 0-3 and unresectable locoregional recurrence with prior RT, unresectable second primary with prior RT, unresectable persistent disease with prior RT, or recurrent/persistent disease with distant metastases
- individuals with TMB-H (≥ 10 mut/Mb) or previously treated, nasopharyngeal cancer and performance status (PS) of 0-3 for unresectable locoregional recurrence with prior radiation therapy (RT), unresectable second primary with prior RT, unresectable persistent disease with prior RT, or

recurrent/persistent disease with distant metastases

- If not previously used, may be considered as subsequent-line systemic therapy for cancer of the nasopharynx (If CR or near CR, consider continued systemic therapy) in combination with cisplatin and gemcitabine for T1-4, N0-3, M1 for any of the following:
 - Oligometastatic disease and PS 0-2
 - Widely metastatic disease and good PS (0-2)
- Systemic therapy for salivary gland tumors as single agent for MSI-H, dMMR, or TMB-H (≥ 10 mut/Mb) or PD-L1 positive recurrent disease with:
 - Distant metastases in individuals with a PS 0-3
 - Unresectable locoregional recurrence or second primary with prior RT

HEAD AND NECK SQUAMOUS CELL CARCINOMA (HNSCC)

- Pembrolizumab (Keytruda®) is considered medically necessary and, therefore, covered systemic therapy for the treatment of head and neck squamous cell carcinoma (HNSCC) for the following regimens:
 - In combination with platinum and fluorouracil for the first-line treatment of individuals with metastatic or unresectable, recurrent HNSCC
 - As a single agent for the first-line treatment of individuals with metastatic or with unresectable, recurrent HNSCC whose tumors express PD-L1 (CPS ≥ 1) as determined by an FDA-approved test.
 - As a single agent for the treatment of individuals with recurrent or metastatic HNSCC with disease progression on or after platinum-containing chemotherapy.

BILIARY CANCERS

Gallbladder Cancer, Extrahepatic Cholangiocarcinoma, Intrahepatic Cholangiocarcinoma

Pembrolizumab (Keytruda®) for the treatment of gallbladder cancer

- As neoadjuvant systemic therapy and one of the following:
 - In combination with cisplatin and gemcitabine
 - As a single agent for disease that is MSI-H and/or dMMR

- The above regimens may be used for resectable locoregionally advanced disease that presents as
 - incidental finding of suspicious mass during surgery where hepatobiliary surgery expertise unavailable
 - incidental finding on pathologic review (cystic duct node positive)
 - mass on imaging
- As NCCN preferred therapy in combination with cisplatin and gemcitabine as primary treatment for unresectable or resected gross residual (R2) disease, or metastatic disease
- Primary treatment of unresectable or resected gross residual (R2) disease, or metastatic disease that is MSI-H and/or dMMR
- Subsequent treatment for progression on or after systemic treatment for unresectable or resected gross residual (R2) disease, or metastatic disease in combination with cisplatin and gemcitabine that is MSI-H and/or dMMR or TMB-H in individuals who have not been previously treated with a checkpoint inhibitor
- Subsequent treatment as a single agent for progression on or after systemic treatment for unresectable or resected gross residual (R2) disease, or metastatic disease that is MSI-H and/or deficient mismatch repair (dMMR) or TMB-H in those who have not been previously treated with a checkpoint inhibitor

Intrahepatic cholangiocarcinoma/Extrahepatic cholangiocarcinoma

- NCCN-preferred therapy in combination with cisplatin and gemcitabine as primary treatment for unresectable or resected gross residual (R2) disease, or metastatic disease
- Primary treatment as a single agent for unresectable or resected gross residual (R2) disease, or metastatic disease that is MSI-H and/or dMMR
- Subsequent treatment for progression on or after systemic treatment for unresectable or resected gross residual (R2) disease, or metastatic disease in combination with cisplatin and gemcitabine in those who have not been previously treated with a checkpoint inhibitor
- Subsequent treatment as a single agent for progression on or after systemic treatment for unresectable or resected gross residual (R2) disease, or metastatic disease that is MSI-H and/or dMMR or TMB-H in those who have not been previously treated with a checkpoint inhibitor

Hepatocellular Carcinoma (HCC)

Pembrolizumab (Keytruda®) is considered medically necessary and, therefore, covered for the treatment of individuals with hepatocellular carcinoma (HCC) and one of the following:

- For the treatment of individuals with HCC secondary to hepatitis B who have received prior systemic therapy other than a PD1/PD-L1-containing regimen **(FDA)**
- Subsequent-line systemic therapy as a single agent if progression on or after systemic therapy in those who have not been previously treated with a checkpoint inhibitor*, who may or may not have microsatellite instability high (MSI-H) tumors, and one of the following conditions:
 - Liver-confined, unresectable disease and are deemed ineligible for transplant
 - Extrahepatic/metastatic disease and are deemed ineligible for resection, transplant, or locoregional therapy

NCCN note: *There is a lack of data for subsequent use of single-agent immunotherapy in those who have previously been treated with a checkpoint inhibitor.

CLASSIC HODGKIN LYMPHOMA (cHL)

Pediatric Hodgkin Lymphoma

Pembrolizumab (Keytruda®) for the treatment of cHL is considered medically necessary and, therefore, covered as single agent therapy for:

- Subsequent therapy (if not previously used) as a single agent for relapsed or refractory disease as a consideration in pediatric individuals (18 years and younger) with heavily pretreated disease (with platinum or anthracycline-based chemotherapy), or if a decrease in cardiac function observed, or who have relapsed after two or more prior lines of therapy

Classic Hodgkin Lymphoma (Age 18 – 60 years)

Pembrolizumab (Keytruda®) for the treatment of cHL is considered medically necessary and, therefore, covered as single agent therapy for:

- Treatment of adult individuals with relapsed or refractory cHL

- Treatment of individuals who are younger than 60 years of age as palliative therapy for one of the following indications:
 - Relapsed or progressed disease after HDT/ASCR
 - Relapsed/refractory disease in individuals who are transplant-ineligible based on comorbidity or failure of second-line chemotherapy
 - Post-allogeneic transplant
- Second-line systemic therapy for relapsed or refractory disease as one of the following:
 - Single agent or
 - In combination with GVD (gemcitabine, vinorelbine, liposomal doxorubicin)
 - In combination with ICE (ifosfamide, carboplatin, etoposide)
- Subsequent systemic therapy (if not previously used) for relapsed or refractory (only if Deauville 4 or 5 following restaging with FDG-PET/CT) disease as one of the following:
 - Single agent
 - In combination with GVD (gemcitabine, vinorelbine, liposomal doxorubicin)
 - In combination with ICE (ifosfamide, carboplatin, etoposide)
- Subsequent systemic therapy (if not previously used) in combination with
 - GVD (gemcitabine, vinorelbine, liposomal doxorubicin)
 - ICE (ifosfamide, carboplatin, etoposide)
 - The above regimens are used for primary refractory disease or suspected relapse:
 - within 3 months and candidate for high-dose therapy and autologous stem cell rescue (HDT/ASCR) (only if Deauville 4 or 5 following restaging with FDG-PET/CT)
 - after ≥ 3 months and candidate for HDT/ASCR
 - and not a candidate for HDT/ASCR
- Subsequent systemic therapy (if not previously used) for primary refractory disease or suspected relapse and not a candidate for high-dose therapy and autologous stem cell rescue (HDT/ASCR) as a single agent palliative therapy option
- Therapy for disease refractory to at least 3 prior lines of subsequent therapy in combination with

- decitabine
- vorinostat
- As a single agent post-allogeneic hematopoietic cell transplant

Management of CHL in Adults more than 60 years of age or Adults Unfit for Intensive Therapy

Pembrolizumab (Keytruda®) for the treatment of cHL is considered medically necessary and, therefore, covered as single agent therapy for:

- Primary treatment for individuals any age and not a candidate for anthracycline as a single agent + ISRT (if contraindications to brentuximab vedotin)

KAPOSI SARCOMA

Pembrolizumab (Keytruda®) for the treatment of Kaposi sarcoma is considered medically necessary and, therefore, covered as single-agent therapy for subsequent systemic therapy* for endemic or classic Kaposi sarcoma for disease that has progressed on or not responded to first-line systemic therapy, and progressed on alternate first-line systemic therapy for any of the following:

- relapsed/refractory advanced cutaneous
- oral
- visceral
- nodal disease

NCCN note: *immune checkpoint inhibitors should not be used in individuals with multicentric Castelman disease (MCD) or KSHV–associated inflammatory cytokine syndrome (KICS) due to risk of flare of these conditions. If the individual has a history of KSHV-associated diseases, ICIs should be used with caution and consideration of more frequent monitoring for signs and symptoms of KICS or MCD.

KIDNEY CANCER/RENAL CELL CARCINOMA (RCC)

Pembrolizumab (Keytruda®) for the treatment of advanced RCC is considered medically necessary and, therefore, covered as combination therapy:

- With axitinib or lenvatinib for relapsed or stage IV disease with clear cell histology for the follow
- ing:
 - As NCCN preferred first-line therapy and stage IV, then M1 or unresectable T4, M0 only
 - As subsequent therapy if immuno-oncology therapy naïve
 - As Subsequent therapy if prior history includes immuno-oncology therapy
- First-line therapy in combination with axitinib for the treatment of adult individuals with advanced RCC
- In combination with lenvatinib for the first-line treatment of adult individuals with advanced RCC
- For the adjuvant treatment of individuals with RCC at intermediate-high or high risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions
- As a single-agent therapy for relapse or stage IV disease as systemic therapy for non-clear cell histology (if first-line therapy and stage IV, then M1 or unresectable T4, M0 only)
- Single-agent adjuvant treatment following nephrectomy for resectable stage IV (T4, M0) disease with clear cell histology
- Single-agent adjuvant treatment for clear cell histology following
 - Nephrectomy in stage II disease (grade 4, with or without sarcomatoid features)
 - Nephrectomy in stage III disease
 - Metastasectomy with complete resection of disease within 1 year of nephrectomy for relapse or stage IV disease
- Used in combination with lenvatinib for stage IV or relapsed disease as:
 - As first-line therapy and stage IV, then M1 or unresectable T4, M0 only for clear cell histology (NCCN-preferred)

- As subsequent therapy for clear cell histology if immuno-oncology therapy naive
- As subsequent therapy for clear cell histology if prior history includes immuno-oncology therapy
- As systemic therapy for non-clear cell histology (NCCN-preferred) (if first-line therapy and stage IV, then M1 or unresectable T4, M0 only)

NCCN note: *if first-line therapy.

CUTANEOUS MELANOMA

Pembrolizumab (Keytruda®) is considered medically necessary and, therefore, covered as single-agent therapy for the treatment of individuals with unresectable or metastatic melanoma for one of the following regimens:

- Adjuvant systemic therapy option as a single agent for pathologically staged IIB/IIC disease following wide excision alone or wide excision with negative sentinel lymph node (SLN) biopsy
- First-line systemic therapy* option as a single agent for metastatic or unresectable disease**
 - As a single agent (NCCN preferred)As re-induction therapy as a single agent if prior anti-PD-1 therapy resulted in disease control (CR, PR, or stable disease) and no residual toxicity, and disease progression/relapse occurred >3 months after treatment discontinuation
- In combination with trametinib and dabrafenib if BRAF V600 mutation positive:
 - As second-line or subsequent therapy for metastatic or unresectable disease following disease progression or intolerance if BRAF/MEK and/or PD(L)-1 checkpoint inhibition not previously used
 - As re-induction therapy if prior combination BRAF/MEK + PD(L)-1 checkpoint inhibition resulted in disease control (CR, PR, or stable disease) with no residual toxicity, and disease progression/relapse >3 months after treatment discontinuation
- NCCN preferred adjuvant systemic therapy option as a single agent for: (except if NED after initial treatment with local or regional therapy)

- Clinical stage IIIB/C/D disease following wide excision alone or wide excision with negative SLN biopsy after microscopic satellites found in biopsy specimen from primary lesion
- Clinical stage IIIB/C/D disease that is SLN negative or SLN biopsy not performed after microscopic satellites found in wide excision specimen
- For resected stage III sentinel node positive disease (based on risk of recurrence) during radiographic surveillance or after completion lymph node dissection (CLND)
- For stage III disease with clinically positive node(s) following wide excision of primary tumor with therapeutic lymph node dissection (TLND)
- For stage III disease with clinical satellite/in-transit metastases if no evidence of disease (NED) after complete excision to clear margins or consider if NED after initial treatment with local or regional therapy
- For local satellite/in-transit recurrence if NED after complete excision to clear margins
- For resectable disease limited to nodal recurrence following excision of the recurrence with TLND
- If NED following metastasis-directed therapy (complete resection, stereotactic ablative therapy, or T-VEC/intralesional therapy) or systemic therapy followed by resection for oligometastatic disease
- NCCN preferred neoadjuvant systemic therapy option as a single agent as any of the following regimens:
 - As primary treatment for stage III clinically positive, resectable nodal disease
 - As initial and/or subsequent treatment for limited resectable stage III disease with clinical satellite/in-transit metastases
 - As initial and/or subsequent treatment for limited resectable local satellite/in-transit recurrence
 - As treatment for resectable disease limited to nodal recurrence
- Second-line (NCCN preferred) or subsequent systemic therapy* option as a single agent for metastatic or unresectable disease** after disease progression, intolerance, and/or projected risk of progression with BRAF-targeted therapy:
 - As a single agent if anti-PD-1 immunotherapy was not previously used

- In combination with low-dose ipilimumab for individuals who progress on single-agent anti-PD-1 immunotherapy (if combination ipilimumab/anti-PD-1 immunotherapy not previously used)
- As re-induction therapy as a single agent if prior anti-PD-1 immunotherapy resulted in disease control (CR, PR, or stable disease) and no residual toxicity, and disease progression/relapse occurred >3 months after treatment discontinuation
- As re-induction therapy in combination with low-dose ipilimumab if prior combination ipilimumab/anti-PD-1 immunotherapy resulted in disease control (CR, PR, or stable disease) and no residual toxicity, and disease progression/relapse occurred >3 months after treatment discontinuation
- As a subsequent systemic therapy option in combination with lenvatinib for metastatic or unresectable disease that has progressed following treatment with anti-PD-1/PD-L1-based therapy, including in combination with anti-CTLA-4 for ≥ 2 doses

NCCN note: *Systemic therapy is preferred for unresectable metastatic disease.

**Metastatic disease includes stage III unresectable/borderline resectable disease with clinically positive node(s) or clinical satellite/in-transit metastases, as well as unresectable/borderline resectable local satellite/in-transit recurrence, unresectable nodal recurrence, and widely disseminated distant metastatic disease

UVEAL MELANOMA

Pembrolizumab (Keytruda®) is considered medically necessary and, therefore, covered as single-agent therapy for the treatment of uveal melanoma in individuals with metastatic or unresectable disease.

MELANOMA

Pembrolizumab (Keytruda®) is considered medically necessary and, therefore, covered as single-agent therapy for the treatment of melanoma for the following indications:

- For the treatment of individuals with unresectable or metastatic melanoma.
- For the adjuvant treatment of adult and pediatric (12 years and older) individuals with stage IIB, IIC, or III melanoma following complete resection.

MERKEL CELL CARCINOMA

Pembrolizumab (Keytruda®) for the treatment of Merkel cell carcinoma is considered medically necessary and, therefore, covered for the treatment of one of the following indications:

- Treatment of adult and pediatric individuals with recurrent locally advanced or metastatic disease
- Single-agent treatment (NCCN preferred)
 - For primary clinical N0 locally advanced disease if curative surgery and curative radiation therapy (RT) are not feasible or for progression on neoadjuvant nivolumab
 - For recurrent N0 locally advanced disease if curative surgery and curative RT are not feasible
 - For recurrent N+ regional disease if curative surgery and curative RT are not feasible
 - For M1 disseminated disease

MESOTHELIOMA

Pembrolizumab (Keytruda®) is considered medically necessary and, therefore, covered for the treatment of mesothelioma for the following indications:

Mesothelioma Peritoneal

- Used in combination with (cisplatin or carboplatin) and pemetrexed as NCCN-preferred first-line systemic therapy for*%
 - Adjuvant treatment of medically operable and complete cytoreduction achievable; with pre-operative low-risk features^ following cytoreductive surgery (CRS) + hyperthermic intraperitoneal chemotherapy (HIPEC), if presence of any surgical/pathologic high-risk features‡
 - Medically operable disease and complete cytoreduction achievable; with pre-operative low risk features^ if progression following CRS + HIPEC if no prior adjuvant systemic therapy given
 - Medically inoperable disease; complete cytoreduction not achievable, or presence of any high-risk features‡

NCCN note: *May also be used for pericardial mesothelioma and tunica vaginalis testis mesothelioma

% Best supportive care is recommended for individuals presenting with PS=3-4

^Low-risk features: epithelioid histology; absence of any high-risk features

‡High-risk features: biphasic/sarcomatoid histology, nodal metastasis, Ki-67 >9%, thrombocytosis, PS=2, bivalvular disease, high disease burden/incomplete cytoreduction (Peritoneal Cancer Index [PCI] >17, completeness of cytoreduction [cc] score >1)

Mesothelioma: Pleural

- NCCN-preferred induction systemic therapy*^ in combination with (cisplatin or carboplatin) and pemetrexed prior to surgical exploration for clinical stage I disease and epithelioid histology
- Used in combination with (cisplatin or carboplatin) and pemetrexed as NCCN-preferred first-line systemic therapy*^ for
 - Clinical stage I disease and epithelioid histology as initial treatment
 - Clinical stage II-IV and epithelioid histology, sarcomatoid or biphasic histology (any stage), or if medically inoperable as initial treatment
 - Clinical stage I disease and epithelioid histology following surgical exploration (if induction systemic therapy not given)

NCCN note: *May also be used for pericardial mesothelioma and tunica vaginalis testis mesothelioma.

^Best supportive care is recommended for individuals presenting with PS 3-4.

MICROSATELLITE INSTABILITY–HIGH OR MISMATCH REPAIR DEFICIENT CANCER

Pembrolizumab (Keytruda®) is considered medically necessary and, therefore, covered as single-agent therapy for the treatment of adult and pediatric individuals with unresectable or metastatic, MSI-H or dMMR disease for one of the following indications:

- Solid tumors that have progressed following prior treatment and there are no satisfactory alternative treatment options, as determined by an FDA-approved test, that have progressed following prior treatment and who have no satisfactory alternative treatment options
- For the treatment of individuals with unresectable or metastatic MSI-H or dMMR colorectal cancer (CRC) as determined by an FDA-approved test

FDA note: The safety and effectiveness of Pembrolizumab (Keytruda®) in pediatric individuals with MSI-H central nervous system cancers have not been established.

NEUROENDOCRINE AND ADRENAL TUMORS

Extrapulmonary poorly differentiated neuroendocrine carcinoma/large or small cell carcinoma/mixed neuroendocrine-non-neuroendocrine neoplasm/well-differentiated grade 3 neuroendocrine tumors/adrenal gland tumors

Pembrolizumab (Keytruda®) is considered medically necessary and, therefore, covered for the treatment of individuals with any of the following indications:

- As subsequent therapy for Extrapulmonary Poorly Differentiated Neuroendocrine Carcinoma/Large or Small Cell Carcinoma/Mixed Neuroendocrine-Non-Neuroendocrine Neoplasm locoregional unresectable or metastatic disease as treatment for individuals with dMMR, MSI-H, or advanced TMB-H (≥ 10 mut/Mb) tumors (as determined by an FDA-approved test) that have progressed following prior treatment and have no satisfactory alternative treatment options
- For well-differentiated grade 3 neuroendocrine tumors unresectable locally advanced/metastatic disease with favorable biology (e.g., relatively low Ki-67 [$< 55\%$], positive SSTR-based PET imaging) that has clinically significant tumor burden or evidence of disease progression with dMMR, MSI-H, or TMB-H (≥ 10 mut/Mb) as determined by an FDA-approved test that has progressed following prior treatment and has no satisfactory alternative treatment options
- For locally advanced/metastatic disease (well-differentiated grade 3 neuroendocrine tumors) with unfavorable biology (relative high Ki-67 [$\geq 55\%$], rapid growth rate, negative SSTR-based PET imaging) with dMMR, MSI-H, or TMB-H (≥ 10 mut/Mb) as determined by an FDA-approved test that has progressed following prior treatment and has no satisfactory alternative treatment options

- Adrenal gland tumors with locoregional unresectable or metastatic adrenocortical carcinoma with or without mitotane

NON-SMALL CELL LUNG CANCER (NSCLC)

Pembrolizumab (Keytruda®) for the treatment of NSCLC is considered medically necessary and, therefore, covered for the following regimens:

- As neoadjuvant systemic therapy for resectable (tumors ≥ 4 cm or node positive) disease (if candidates for immune checkpoint inhibitors)* in combination with any of the following regimens:
 - Pemetrexed and cisplatin (nonsquamous cell histology)
 - Gemcitabine and cisplatin (squamous cell histology)
- The above regimens are used for:
 - Operable clinical stage IB (T2a, N0), stage II (T1abc-2ab, N1 or T2b, N0), stage IIB (T3, N0), or stage IIIA (T3, N1) disease with no pathologic nodal disease
 - Chest wall, trachea/carina, or mediastinum; T3 invasion, N0-1; resectable T4 extension, N0-1 disease
 - Resectable stage IIIA (T4, N0-1)
 - Operable T2a-3, N0 or T1-3, N1 nodes positive, M0 findings on mediastinal biopsy
 - T1-3, N2 nodes positive**, M0 findings on mediastinal biopsy
 - Separate pulmonary nodule(s), same lobe (T3, N0-1), or ipsilateral non-primary lobe (T4, N0-1)

NCCN note: *Contraindications for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or current use of immunosuppressive agents, and some oncogenic drivers (i.e., EGFR exon 19 deletion or exon 21 L858R, ALK rearrangements) have been shown to be associated with less benefit from PD-1/PD-L1 inhibitors.

**Selected individuals with N2 disease (fit, single station non-bulky N2, requiring only lobectomy) may be considered for systemic therapy followed by surgery.

- Single-agent therapy for those with completely resected stage IIB–IIIA, high-risk stage IIA, or stage IIB (T3, N2) NSCLC that is negative for EGFR exon 19 deletion or exon 21 L858R mutations, or ALK rearrangements who received previous adjuvant chemotherapy and with no contraindications* to immune checkpoint inhibitors.

NCCN note: *Contraindications for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or current use of immunosuppressive agents, and some oncogenic drivers (i.e., EGFR exon 19 deletion or exon 21 L858R, ALK rearrangements) have been shown to be associated with less benefit from PD-1/PD-L1 inhibitors

- As single-agent adjuvant therapy for those with completely resected stage II–IIIA or stage IIIB (T3, N2) NSCLC who received previous neoadjuvant pembrolizumab plus chemotherapy
- Treatment for recurrent, advanced, or metastatic disease as first-line therapy for PD-L1 expression-positive ($\geq 1\%$) tumors that are negative for actionable molecular biomarkers* (may be KRAS G12C mutation positive) and no contraindications** to PD-1 or PD-L1 inhibitors and performance status 0-2
 - As a single agent*** (NCCN-preferred if PD-L1 $\geq 50\%$; if PD-L1 $\geq 1-49\%$) (except for locoregional recurrence or symptomatic local disease (excluding mediastinal lymph node recurrence with prior radiation therapy) with no evidence of disseminated disease)
 - In combination with pemetrexed and either carboplatin or cisplatin for nonsquamous cell histology (NCCN-preferred)
 - In combination with carboplatin and either paclitaxel or albumin-bound paclitaxel for squamous cell histology (NCCN-preferred)

NCCN note: *Complete genotyping for EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET, RET, and ERBB2 (HER2), via biopsy and/or plasma testing. If a clinically actionable marker is found, it is reasonable to start therapy based on the identified marker. Treatment is guided by available results and, if unknown, these individuals are treated as though they do not have driver oncogenes.

**Contraindications for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or current use of immunosuppressive agents, and some oncogenic drivers (i.e., EGFR exon 19 deletion or exon 21 L858R, ALK rearrangements), have been shown to be associated with less benefit from PD-1/PD-L1 inhibitors.

***When used for PD-L1 1-49%, pembrolizumab monotherapy can be considered when there are contraindications to combination chemotherapy.

- Continuation maintenance therapy for recurrent, advanced, or metastatic disease for PD-L1 expression positive ($\geq 1\%$) tumors that are negative for actionable molecular biomarkers* (may be KRAS G12C mutation positive) and no contraindications** to PD-1 or PD-L1 inhibitors and performance status 0-2, who achieve tumor response or stable disease following systemic or first-line therapy (except as a single agent for nonsquamous cell histology if PD-L1 $\geq 1-49\%$ and pembrolizumab monotherapy given

first-line; or for locoregional recurrence or symptomatic local disease (excluding mediastinal lymph node recurrence with prior radiation therapy) with no evidence of disseminated disease

- As a single agent if pembrolizumab monotherapy given first-line for nonsquamous cell histology
- In combination with pemetrexed if given first-line as part of a pembrolizumab/pemetrexed and either cisplatin or carboplatin regimen for nonsquamous cell histology
- As a single agent if pembrolizumab was given as monotherapy or as part of a pembrolizumab/carboplatin/(paclitaxel or albumin-bound paclitaxel) regimen for squamous cell histology

NCCN note: *Complete genotyping for EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET, RET, and ERBB2 (HER2), via biopsy and/or plasma testing. If a clinically actionable marker is found, it is reasonable to start therapy based on the identified marker. Treatment is guided by available results and, if unknown, these individuals are treated as though they do not have driver oncogenes

**Contraindications for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or current use of immunosuppressive agents, and some oncogenic drivers (i.e., EGFR exon 19 deletion or exon 21 L858R, ALK rearrangements) have been shown to be associated with less benefit from PD-1/PD-L1 inhibitors

- Treatment for recurrent, advanced, or metastatic disease for individuals with performance status 0-1 and no contraindications** to PD-1 or PD-L1 inhibitors in combination with (except for locoregional recurrence or symptomatic local disease (excluding mediastinal lymph node recurrence with prior radiation therapy) with no evidence of disseminated disease
 - Pemetrexed and either carboplatin or cisplatin (both NCCN-preferred) for nonsquamous cell histology
 - Carboplatin and either paclitaxel or albumin-bound paclitaxel (both NCCN-preferred) for squamous cell histology
- The above regimens are used as:
 - Initial systemic therapy for PD-L1 <1% and negative for actionable molecular biomarkers* (may be KRAS G12C mutation positive)
 - First-line therapy for EGFR exon 20 insertion mutation positive tumors

- First-line or subsequent therapy for BRAF V600E mutation positive tumors
- First-line or subsequent therapy for NTRK1/2/3 gene fusion positive tumors
- First-line or subsequent therapy for MET exon 14 skipping mutation positive tumors
- First-line or subsequent therapy for RET rearrangement positive tumors
- First-line therapy for ERBB2 (HER2) mutation positive tumors
- Subsequent therapy for EGFR exon 19 deletion or exon L858R tumors and prior erlotinib ± (ramucirumab or bevacizumab), afatinib, gefitinib, osimertinib, amivantamab-vmjw + lazertinib, or dacomitinib therapy
- Subsequent therapy for EGFR S768I, L861Q, and/or G719X mutation positive tumors and prior afatinib, osimertinib, erlotinib, gefitinib, or dacomitinib therapy
- Subsequent therapy for ALK rearrangement positive tumors and prior crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib therapy
- Subsequent therapy for ROS1 rearrangement positive tumors and prior crizotinib, entrectinib, repotrectinib, ceritinib, or lorlatinib therapy

NCCN note: *Complete genotyping for EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET, RET, and ERBB2 (HER2), via biopsy and/or plasma testing. If a clinically actionable marker is found, it is reasonable to start therapy based on the identified marker. Treatment is guided by available results and, if unknown, these individuals are treated as though they do not have driver oncogenes.

**Contraindications for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or current use of immunosuppressive agents, and some oncogenic drivers (i.e., EGFR exon 19 deletion or exon 21 L858R, ALK rearrangements) have been shown to be associated with less benefit from PD-1/PD-L1 inhibitors.

- Continuation maintenance therapy in combination with pemetrexed if given first line as part of a pembrolizumab/pemetrexed and either cisplatin or carboplatin regimen for recurrent, advanced, or metastatic disease with PD-L1 expression <1% tumors that are negative for actionable molecular biomarkers* (may be KRAS G12C mutation positive) and no contraindications** to PD-1 or PD-L1 inhibitors, and nonsquamous cell histology in those with performance status 0-2, who achieve tumor response or stable disease following initial systemic therapy (except for locoregional recurrence or symptomatic local disease (excluding mediastinal lymph node recurrence with prior radiation therapy) with no evidence of disseminated disease

NCCN note: *Complete genotyping for EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET, RET, and ERBB2 (HER2), via biopsy and/or plasma testing. If a clinically actionable marker is found, it is reasonable to start therapy based on the identified marker. Treatment is guided by available results and, if unknown, these individuals are treated as though they do not have driver oncogenes.

**Contraindications for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or current use of immunosuppressive agents, and some oncogenic drivers (i.e., EGFR exon 19 deletion or exon 21 L858R, ALK rearrangements) have been shown to be associated with less benefit from PD-1/PD-L1 inhibitors.

- Single-agent continuation maintenance therapy if given first line as part of a pembrolizumab/carboplatin/(paclitaxel or albumin-bound paclitaxel) regimen for recurrent, advanced, or metastatic disease with PD-L1 expression <1% tumors that are negative for actionable molecular biomarkers* (may be KRAS G12C mutation positive) and no contraindications** to PD-1 or PD-L1 inhibitors, and squamous cell histology, in those with performance status 0-2 who achieve tumor response or stable disease following initial systemic therapy (except for locoregional recurrence or symptomatic local disease (excluding mediastinal lymph node recurrence with prior radiation therapy) with no evidence of disseminated disease

NCCN note: *Complete genotyping for EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET, RET, and ERBB2 (HER2), via biopsy and/or plasma testing. If a clinically actionable marker is found, it is reasonable to start therapy based on the identified marker. Treatment is guided by available results and, if unknown, these individuals are treated as though they do not have driver oncogenes.

**Contraindications for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or current use of immunosuppressive agents, and some oncogenic drivers (i.e., EGFR exon 19 deletion or exon 21 L858R, ALK rearrangements) have been shown to be associated with less benefit from PD-1/PD-L1 inhibitors.

- NCCN Preferred single agent as subsequent therapy for recurrent, advanced, or metastatic disease if no contraindications* to PD-1 or PD-L1 inhibitors in those with performance status 0-2 and tumors with PD-L1 expression levels $\geq 1\%$ and no prior progression on a PD-1/PD-L1 inhibitor (except for locoregional recurrence or symptomatic local disease (excluding mediastinal lymph node recurrence with prior radiation therapy) with no evidence of disseminated disease for the following regimens:
 - In combination with pemetrexed and platinum chemotherapy, as first-line treatment of individuals with metastatic nonsquamous NSCLC, with no EGFR or ALK genomic tumor aberrations

- In combination with carboplatin and either paclitaxel or paclitaxel protein-bound, as first-line treatment of individuals with metastatic squamous NSCLC.
- As a single agent for the first-line treatment of individuals with NSCLC expressing PD-L1 [Tumor Proportion Score (TPS) $\geq 1\%$] as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations, and is:
 - Stage III where individuals are not candidates for surgical resection or definitive chemoradiation, or metastatic.
- As a single agent for the treatment of individuals with metastatic NSCLC whose tumors express PD-L1 (TPS $\geq 1\%$) as determined by an FDA-approved test, with disease progression on or after platinum-containing chemotherapy (individuals with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Keytruda)
- For the treatment of individuals with resectable (tumors ≥ 4 cm or node positive) NSCLC in combination with platinum-containing chemotherapy as neoadjuvant treatment, and then continued as a single agent as adjuvant treatment after surgery.
- As a single agent, for adjuvant treatment following resection and platinum-based chemotherapy for adult individuals with stage IB (T2a ≥ 4 cm), II, or IIIA NSCLC

NCCN note: *Contraindications for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or current use of immunosuppressive agents; some oncogenic drivers (i.e., EGFR exon 19 deletion or exon 21 L858R, ALK rearrangements) have been shown to be associated with less benefit from PD-1/PD-L1 inhibitors.

NCCN note: *if there is insufficient tissue to allow testing for all of EGFR, ALK, ROS1, BRAF, NTRK1/2/3, MET and RET, repeat biopsy and/or plasma testing should be done. If these are not feasible, treatment is guided by available results and, if unknown, these individuals are treated as though they do not have driver oncogenes.

**Contraindications for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or current use of immunosuppressive agents, or presence of an oncogene (e.g., EGFR [exon 19 deletions, p.L858R point mutation in exon 21], ALK rearrangements, RET rearrangements), which would predict lack of benefit.

***When used for squamous cell histology with PD-L1 1%-49%, pembrolizumab monotherapy can be considered in individuals with poor PS or other contraindications to combination chemotherapy.

OCCULT PRIMARY CANCERS

Pembrolizumab (Keytruda®) for the treatment of occult primary cancers is considered medically necessary and, therefore, covered as single-agent therapy in symptomatic individuals with MSI-H/dMMR tumors features:

- As a single agent in individuals with dMMR/MSI-H tumors or TMB-H [≥ 10 mut/Mb] tumors) in symptomatic individuals with PS 1-2 or asymptomatic individuals with PS 0 and aggressive disease for systemic therapy in individuals with multiple lung nodules, pleural effusion, or disseminated metastases.
- As a single agent in individuals with dMMR/MSI-H tumors or TMB-H (≥ 10 mut/Mb) tumors in symptomatic individuals with performance status (PS) 1-2 or asymptomatic individuals with PS 0 and aggressive disease for:
 - Axillary involvement in those with a prostate or post-prostatectomy if clinically indicated
 - Lung nodules or breast marker-negative pleural effusion
 - Resectable liver disease
 - Peritoneal mass or ascites with non-ovarian histology
 - Retroperitoneal mass of non-germ cell histology in selected individuals
 - Unresectable liver disease or disseminated metastases

OVARIAN CANCERS

Low-grade serous carcinoma, ovarian borderline epithelial tumors (low malignant potential) with invasive implants, grade 1 endometrioid carcinoma, endometrioid (serous), mucinous neoplasm of the ovary, clear cell carcinoma of the ovary, carcinosarcoma (malignant mixed Müllerian tumors)

Pembrolizumab (Keytruda®) for the treatment of ovarian borderline epithelial tumors (low malignant potential) with invasive implants, grade 1 endometrioid carcinoma, mucinous carcinoma, clear cell carcinoma, carcinosarcoma (malignant mixed Müllerian tumors) cancers is considered medically necessary and, therefore, covered as a single-agent therapy for persistent disease or recurrence, if MSI-H or dMMR tumors ≥ 10 mut/Mb (except [for immediate treatment of biochemical relapse](#)) for any of the following indications:

- Progression on primary, maintenance, or recurrence therapy
- Stable or persistent disease (if not on maintenance therapy) (platinum-resistant disease)
- Complete remission and relapse <6 months after completing chemotherapy (platinum-resistant disease)
- Radiographic and/or clinical relapse in individuals with previous complete remission and relapse ≥6 months after completing prior chemotherapy (platinum-sensitive disease)

Low-grade serous carcinoma

Pembrolizumab (Keytruda®) for the treatment of low-grade serous carcinoma is considered medically necessary and, therefore, covered for any of the following:

- As single-agent therapy platinum-sensitive or platinum-resistant recurrence, if MSI-H, dMMR, or TMB-H tumors ≥10 mut/Mb
- Therapy for platinum-resistant recurrence in combination with oral cyclophosphamide and bevacizumab

Grade 1 endometrioid carcinoma, endometrioid (serous), carcinosarcoma (malignant mixed Müllerian t), clear cell carcinoma of the ovary, mucinous neoplasm of the ovary

- Therapy for platinum-resistant persistent disease (except [for immediate treatment of biochemical relapse](#)) or recurrence in combination with oral cyclophosphamide and bevacizumab for one of the following:
 - As immediate treatment for serially rising CA-125 in individuals that previously received chemotherapy
 - For progression on primary, maintenance, or recurrence therapy
 - For stable or persistent disease (if not on maintenance therapy)
 - For complete remission and relapse <6 months after completing chemotherapy

Malignant germ cell tumors

- As a single agent for recurrent disease as palliative therapy only in individuals with (except for abnormal markers, definitive recurrent disease following initial complete clinical response and) MSI-H or dMMR, or TMB-H tumors ≥ 10 mut/Mb

PANCREATIC ADENOCARCINOMA

Pembrolizumab (Keytruda®) for the treatment of pancreatic adenocarcinoma is considered medically necessary and, therefore, covered as a single agent (only for MSI-H or dMMR tumors) for any of the following regimens:

- First-line therapy as single agent (if MSI-H/dMMR or TMB-H ≥ 10 mut/Mb) for:
 - Locally advanced or metastatic disease if good performance status (defined as ECOG PS 0-1, with good biliary drainage and adequate nutritional intake)
 - Locally advanced or metastatic disease if intermediate PS (ECOG 2)
 - Metastatic disease if poor PS (ECOG 3)
- Subsequent therapy as a single agent (if no prior immunotherapy and if MSI-H/dMMR or TMB-H ≥ 10 mut/Mb) for locally advanced or metastatic disease and disease progression if:
 - Good performance status (defined as ECOG PS 0-1, with good biliary drainage and adequate nutritional intake, NCCN-preferred)
 - Intermediate PS (ECOG 2)
 - Poor PS (ECOG 3, NCCN-preferred)
- Therapy as a single agent^ (if no prior immunotherapy and if MSI-H, dMMR or TMB-H ≥ 10 mut/Mb) if good performance status (ECOG PS 0-1, NCCN-preferred), intermediate PS (ECOG 2), or poor PS (ECOG 3, NCCN-preferred) for:
 - Local recurrence in the pancreatic operative bed after resection
 - Recurrent metastatic disease with or without local recurrence after resection

PENILE CANCER

Pembrolizumab (Keytruda®) for the treatment of penile cancer is considered medically necessary and, therefore, covered as a single agent

- As (NCCN preferred) as subsequent-line systemic therapy if unresectable or metastatic and one of the following:

- MSI-H or dMMR tumor that has progressed following prior treatment and no satisfactory alternative treatment options
- TMB ≥ 10 mut/Mb in individuals who have progressed on previously approved lines of therapy
- In combination with fluorouracil and either cisplatin or carboplatin followed by pembrolizumab maintenance:
 - As first-line chemotherapy for local recurrence in the inguinal region in individuals that received prior inguinal lymphadenectomy or radiotherapy
 - As first-line systemic chemotherapy for metastatic disease

PRIMARY CUTANEOUS LYMPHOMAS

Mycosis fungoides/Sézary syndrome

Pembrolizumab (Keytruda®) is considered medically necessary and, therefore, covered for the treatment of individuals with [stage III mycosis fungoides \(MF\) or Sézary syndrome \(except for refractory stage IA, for relapsed or persistent stage IB-IIA, or for relapsed stage IIB with T1-2 limited or generalized tumor lesions\)](#) as:

- Systemic therapy as a subsequent treatment for one of the following:
 - Stage IB-IIA MF that is refractory to multiple previous therapies, in combination with skin-directed therapy
 - Stage IIB MF with limited tumor lesions that is refractory to multiple previous therapies, in combination with skin-directed therapy
 - Relapsed stage IIB T3 MF with generalized tumor lesions, in combination with skin-directed therapy
 - Stage IIB MF with generalized tumor lesions that is refractory to multiple previous therapies, in combination with skin-directed therapy
 - Relapsed or persistent stage III MF in combination with skin-directed therapy
 - Stage III MF that is refractory to multiple previous therapies, in combination with skin-directed therapy
 - Relapsed or persistent stage IVA1 or IVA2 Sézary syndrome in combination with skin-directed therapy

- Limited cutaneous lesions with large cell transformation (LCT) that is refractory to multiple previous therapies, in combination with skin-directed therapy
- Relapsed or persistent generalized cutaneous or extracutaneous lesions with LCT, in combination with skin-directed therapy
- As primary systemic therapy for:
 - Stage IIB MF with generalized tumor lesions, in combination with skin-directed therapy
 - Stage III MF in combination with skin-directed therapy
 - Stage IVA1 or IVA2 Sézary syndrome in combination with skin-directed therapy
 - Generalized cutaneous or extracutaneous lesions with large cell transformation (LCT), in combination with systemic therapy
- Systemic therapy as a single agent subsequent treatment for the refractory disease to multiple previous therapies
 - Stage IIB MF with limited tumor lesions
 - Stage IIB MF with generalized tumor lesions
 - Stage III MF
 - Stage IVA1 or IVA2 Sézary syndrome
 - Stage IVA2 non-Sézary or stage IVB visceral disease (solid organ)
 - LCT with limited cutaneous lesions
 - LCT with generalized cutaneous or extracutaneous lesions

Primary cutaneous CD30+ T-cell lymphoproliferative disorders

- Therapy for primary cutaneous anaplastic large cell lymphoma (ALCL) with multifocal lesions, or cutaneous ALCL with regional node (N1) (excludes systemic ALCL), as a single agent for relapsed/refractory disease

PEDIATRIC CANCERS

Pembrolizumab (Keytruda®) for the treatment of pediatric cancers is considered medically necessary and, therefore, covered as a single agent for the treatment of the following

indications:

Pediatric aggressive mature B-cell lymphomas - primary mediastinal large B-cell lymphoma

- NCCN-preferred consolidation/additional therapy in combination with brentuximab vedotin, if PR achieved after therapy for relapsed or refractory disease

Pediatric central nervous system cancers - pediatric diffuse high-grade gliomas

- Adjuvant treatment for hypermutant tumor pediatric diffuse high-grade glioma (except diffuse midline glioma, H3 K27-altered or pontine location)
 - Following standard brain RT with or without concurrent temozolomide in individuals 3 years of age and older)
 - In individuals younger than 3 years of age
- NCCN-preferred treatment for recurrent or progressive disease for hypermutant tumor pediatric diffuse high-grade glioma (except oligodendroglioma, IDH-mutant and 1p/19q co-deleted or astrocytoma IDH-mutant [see NCCN Guidelines for Central Nervous System Cancers in Adults])

Pediatric Hodgkin lymphoma - classic Hodgkin lymphoma

- Subsequent therapy (if not previously used) as a single agent for relapsed or refractory disease as a consideration in individuals heavily pretreated (with platinum or anthracycline-based chemotherapy), or if a decrease in cardiac function observed, or who have relapsed after two or more prior lines of therapy

PRIMARY CUTANEOUS CD30+ T-CELL LYMPHOPROLIFERATIVE DISORDERS

Pembrolizumab (Keytruda®) for the treatment of primary cutaneous CD30+ t-cell lymphoproliferative disorders is considered medically necessary and, therefore, covered as a

single agent for the treatment of primary cutaneous anaplastic large cell lymphoma (ALCL) with multifocal lesions, or cutaneous ALCL with regional node (N1) (excludes systemic ALCL), for relapsed/refractory disease.

PROSTATE CANCER

Pembrolizumab (Keytruda®) for the treatment of prostate cancer is considered medically necessary and, therefore, covered as a single agent* for the treatment of the following indication:

- For castration-resistant distant metastatic (M1) disease if progression on prior docetaxel and a novel hormone therapy (for MSI-H/dMMR, or TMB ≥ 10 mut/Mb)

NCCN note: *Continue androgen deprivation therapy (ADT) to maintain castrate levels of serum testosterone (<50 ng/dL).

RECTAL CANCER

Pembrolizumab (Keytruda®) for the treatment of individuals with rectal cancer is considered medically necessary and, therefore, covered as a single agent for one of the following regimens:

- Primary treatment for unresectable metachronous metastases (dMMR/MSI-H only) and previous adjuvant FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin) within the past 12 months (NCCN preferred)
- Subsequent therapy as a single agent (NCCN preferred) for progression of advanced or metastatic disease (dMMR/MSI-H only), if no previous treatment with a checkpoint inhibitor following previous oxaliplatin-, irinotecan-, and/or fluoropyrimidine-based therapy
- Therapy as a single agent for individuals (dMMR/MSI-H only) or POLE/POLD1 mutation)
 - As neoadjuvant treatment for resectable synchronous liver only and/or lung only metastases (no previous treatment with a checkpoint inhibitor) (NCCN-preferred)
 - As initial treatment for resectable metachronous metastases and no previous immunotherapy

- Therapy for individuals (dMMR/MSI-H only), if no previous treatment with a checkpoint inhibitor (NCCN preferred):
 - As primary treatment for T3, N Any; T1-2, N1-2; T4, N Any; or locally unresectable or medically inoperable disease if resection is contraindicated following neoadjuvant or total neoadjuvant therapy
 - As primary treatment for synchronous abdominal/peritoneal metastases that are nonobstructing, or following local therapy for individuals with existing or imminent obstruction
 - As primary treatment for synchronous unresectable metastases of other sites
 - As primary treatment for unresectable isolated pelvic/anastomotic recurrence
 - As primary treatment for unresectable metachronous metastases in individuals who have not received previous adjuvant FOLFOX or CapeOX within the past 12 months, who have received previous fluorouracil/leucovorin (5-FU/LV) or capecitabine therapy, or who have not received any previous chemotherapy
 - Progression on nonintensive therapy, except if received previous fluoropyrimidine, with improvement in functional status
- Therapy as a single agent for individuals (dMMR/MSI-H] or POLE/POLD1 mutation) if candidate for immunotherapy and no prior immunotherapy received:
 - As primary treatment for synchronous abdominal/peritoneal metastases that are nonobstructing, or following local therapy for individuals with existing or imminent obstruction
 - As primary treatment for synchronous unresectable metastases
 - As primary treatment for potentially resectable or unresectable isolated pelvic/anastomotic recurrence
 - As primary treatment for unresectable metachronous metastases
- Therapy as a single agent for individuals as neoadjuvant/definitive immunotherapy (NCCN-preferred) for T3, N Any; T1-2, N1-2; T4, N Any; or locally unresectable or medically inoperable disease (dMMR/MSI-H) with no previous treatment with a checkpoint inhibitor

SMALL BOWEL ADENOCARCINOMA

Pembrolizumab (Keytruda®) for the treatment of small bowel adenocarcinoma is considered medically necessary and, therefore, covered as a single agent for one of the following:

- Therapy as primary treatment for locally unresectable or medically inoperable disease (dMMR/MSI-H or POLE/POLD1 mutation with ultrahypermutated phenotype [e.g., TMB >50 mut/Mb])
- Therapy for advanced or metastatic disease (dMMR/MSI-H) or POLE/POLD1 mutation with ultrahypermutated phenotype [e.g., TMB >50 mut/Mb), if no previous treatment with a checkpoint inhibitor, for any line of therapy

SMALL CELL LUNG CANCER

Pembrolizumab (Keytruda®) for the treatment of small cell lung cancer is considered medically necessary and, therefore, covered as a single agent for the treatment of the following indications:

- Subsequent systemic therapy if not previously treated with an immune checkpoint inhibitor and if there has been a chemotherapy-free interval of 6 months or less for individuals with performance status 0–2 for any of the following:
 - Relapse following CR or PR or stable disease with primary treatment (the use of immune checkpoint inhibitors is discouraged if there is progression on maintenance atezolizumab or durvalumab at time of relapse)
 - Primary progressive disease

SOFT TISSUE SARCOMA

Pembrolizumab (Keytruda®) for the treatment of soft tissue sarcoma is considered medically necessary and, therefore, covered as a single agent for the treatment of the following indications:

- As a palliative single-agent therapy* as subsequent lines of therapy for advanced/metastatic disease with disseminated metastases for one of the following:
 - Myxofibrosarcoma
 - UPS
 - Dedifferentiated liposarcoma
 - Cutaneous angiosarcoma
 - Undifferentiated sarcomas

NCCN note: *If atypical lipomatous tumor/well-differentiated liposarcoma (ALT/WDLPS) extremity, abdominal wall, trunk: if disease that was initially diagnosed as ALT/WDLPS shows evidence of de-differentiation, treat as other soft tissue sarcomas.

- As a palliative single-agent therapy* for the treatment of individuals with unresectable or metastatic TMB-H (≥ 10 mut/Mb) or MSI-H or dMMR tumors regardless of soft tissue sarcoma sub-type, as determined by an FDA-approved test, that have progressed following prior treatment and who have no satisfactory alternative treatment options as subsequent lines of therapy for advanced/metastatic disease with disseminated metastases.

NCCN note: *If ALT/WDLPS extremity, abdominal wall, trunk: if disease that was initially diagnosed as ALT/WDLPS shows evidence of de-differentiation, treat as other soft tissue sarcomas.

- Alveolar soft part sarcoma (ASPS) as therapy as single-agent therapy or in combination with axitinib (both NCCN-preferred)

Extremity/body wall, head/neck

- As a palliative single-agent therapy* for the treatment of individuals with unresectable or metastatic TMB-H (≥ 10 mut/Mb) or MSI-H or dMMR tumors regardless of soft tissue sarcoma subtype, as determined by an FDA-approved test, that have progressed following prior treatment and who have no satisfactory alternative treatment options as subsequent lines of therapy for advanced/metastatic disease with disseminated metastases.

NCCN note: *if ALT/WDLPS extremity, abdominal wall, trunk: if disease that was initially diagnosed as ALT/WDLPS shows evidence of de-differentiation, treat as other soft tissue sarcomas.

- As a palliative single-agent therapy* as subsequent lines of therapy for advanced/metastatic disease with disseminated metastases for one of the following:

- Myxofibrosarcoma
- UPS
- Dedifferentiated liposarcoma
- Cutaneous angiosarcoma
- Undifferentiated sarcomas

NCCN note: *If ALT/WDLPS extremity, abdominal wall, trunk: if disease that was initially diagnosed as ALT/WDLPS shows evidence of de-differentiation, treat as other soft tissue sarcomas.

Retroperitoneal/Intra-abdominal

- As a single agent* as alternative systemic therapy for unresectable or progressive disease after initial therapy for unresectable localized disease or as palliative subsequent lines of therapy for stage IV disease with disseminated metastases for one of the following:
 - Myxofibrosarcoma
 - UPS
 - Dedifferentiated liposarcoma
 - Cutaneous angiosarcoma
 - Undifferentiated sarcomas

*NCCN note: treat WDLPS (retroperitoneum, paratesticular) with or without evidence of de-differentiation as other soft tissue sarcomas.

- As a single agent for the treatment* of individuals with unresectable or metastatic TMB-H (≥ 10 mut/Mb) or MSI-H or dMMR tumors regardless of soft tissue sarcoma subtype, as determined by an FDA-approved test, that have progressed following prior treatment and who have no satisfactory alternative treatment options:

- As alternative systemic therapy for unresectable or progressive disease after initial therapy for unresectable localized disease
- As palliative subsequent lines of therapy for stage IV disease with disseminated metastases

NCCN note: *treat WDLPS (retroperitoneum, paratesticular) with or without evidence of de-differentiation as other soft tissue sarcomas

Rhabdomyosarcoma

As a single agent for advanced/metastatic pleomorphic rhabdomyosarcoma as subsequent line of therapy (including for unresectable or metastatic TMB-H (≥ 10 mut/Mb) or MSI-H or dMMR tumors, as determined by an FDA-approved test, that have progressed following prior treatment and who have no satisfactory alternative treatment options)

Alveolar soft part sarcoma

- Single-agent therapy or in combination with axitinib (both NCCN preferred) for the treatment of ASPS

Angiosarcoma

- Cutaneous angiosarcoma as a single-agent therapy

SQUAMOUS CELL SKIN CANCER

Pembrolizumab (Keytruda®) for the treatment of soft tissue sarcoma is considered medically necessary and, therefore, covered as a single agent for the treatment of squamous cell skin cancer:

- As single agent treatment (NCCN preferred) if curative radiation therapy or surgery is not feasible for disease that is:
 - Locally advanced
 - Recurrent
 - Metastatic

T-CELL LYMPHOMAS - EXTRANODAL NK/T-CELL LYMPHOMA, NASAL TYPE

Pembrolizumab (Keytruda®) for the treatment of T-cell lymphomas - extranodal NK/T lymphomas, nasal type is considered medically necessary and, therefore, covered as NCCN-preferred therapy for relapsed/refractory disease following additional therapy with an alternate combination chemotherapy regimen (asparaginase-based) not previously used, if a clinical trial is unavailable.

TESTICULAR CANCER

Pembrolizumab (Keytruda®) for the treatment of testicular cancer is considered medically necessary and, therefore, covered as single-agent :

- As third-line therapy in individuals with MSI-H/dMMR or TMB-H tumors and one of the following:
 - For seminoma
 - After prior high-dose chemotherapy for nonseminoma
 - For late relapse of nonseminoma (recurrence >2 years after completion of second-line chemotherapy)

THYMOMAS AND THYMIC CARCINOMAS

Pembrolizumab (Keytruda®) for the treatment of thymoma and thymic carcinomas is considered medically necessary and, therefore, covered for the following indications:

- As NCCN-preferred single agent for those who cannot tolerate first-line combination regimens for thymic carcinoma as preoperative systemic therapy for surgically resectable disease if R0 resection is considered uncertain
- Postoperative treatment for individuals who cannot tolerate first-line combination regimens for thymic carcinoma only after R1 or R2 resection
- First-line (NCCN preferred) therapy for individuals who cannot tolerate first-line combination regimens for:
 - Potentially resectable locally advanced disease

- Potentially resectable solitary metastasis or ipsilateral pleural metastasis
- Consideration following surgery for solitary metastasis or ipsilateral pleural metastasis
- Medically inoperable/unresectable solitary metastasis or ipsilateral pleural metastasis
- Extrathoracic metastatic disease
- Second-line (NCCN preferred) therapy as a single agent for any of the following:
 - Unresectable locally advanced disease
 - Solitary metastasis or ipsilateral pleural metastasis
 - Extrathoracic metastatic disease

THYROID CARCINOMA

Pembrolizumab (Keytruda®) is considered medically necessary and, therefore, covered for TMB-H (≥ 10 mut/Mb) tumors for progressive and/or symptomatic of the following indications:

- Anaplastic carcinoma as a single agent or in combination with lenvatinib
 - As aggressive first-line therapy for stage IVC metastatic disease
 - Second-line therapy for stage IVC metastatic disease
- Medullary carcinoma
 - Treatment for TMB-H (≥ 10 mut/Mb) tumors in
 - An unresectable locoregional disease that is symptomatic or progressing by Response Evaluation Criteria in Solid Tumors (RECIST) criteria
 - Asymptomatic recurrent or persistent distant metastases if unresectable and progressing by RECIST criteria
 - Recurrent or persistent distant metastases if symptomatic disease or progression

- Treatment for MSI-H or dMMR tumors, if progressed following prior treatment and no satisfactory alternative treatment options, in one of the following:
 - Unresectable locoregional disease that is symptomatic or progressing by RECIST criteria
 - Asymptomatic recurrent or persistent distant metastases if unresectable and progressing by RECIST criteria
 - Recurrent or persistent distant metastases if symptomatic disease or progression
- Hürthle cell carcinoma
 - Unresectable locoregional recurrent or persistent disease not amenable to radioactive iodine (RAI) therapy
 - Distant metastatic disease not amenable to RAI therapy
- Follicular carcinoma
 - Unresectable locoregional recurrent or persistent disease not amenable to RAI therapy
 - Distant metastatic disease not amenable to RAI therapy
 - For MSI-H or dMMR tumors, if progressed following prior treatment and no satisfactory alternative treatment options, consider for treatment of progressive and/or symptomatic
 - Unresectable locoregional recurrent or persistent disease not amenable to RAI therapy
 - Distant metastatic disease not amenable to RAI therapy
- Papillary carcinoma
 - Unresectable locoregional recurrent or persistent disease not amenable to RAI therapy
 - Distant metastatic disease not amenable to RAI therapy
 - For MSI-H or dMMR tumors, if progressed following prior treatment and no satisfactory alternative treatment options, consider for treatment of progressive and/or symptomatic

- Unresectable locoregional recurrent or persistent disease not amenable to RAI therapy
- Distant metastatic disease not amenable to RAI therapy
- Oncocytic carcinoma
 - For TMB-H (≥ 10 mut/Mb) tumors, consider for treatment of progressive and/or symptomatic
 - Unresectable locoregional recurrent or persistent disease not amenable to RAI therapy
 - Distant metastatic disease not amenable to RAI therapy
 - For MSI-H or dMMR tumors, if progressed following prior treatment and no satisfactory alternative treatment options, consider for treatment of progressive and/or symptomatic:
 - Unresectable locoregional recurrent or persistent disease not amenable to RAI therapy
 - Distant metastatic disease not amenable to RAI therapy

UTERINE NEOPLASMS

Pembrolizumab (Keytruda®) is considered medically necessary and, therefore, covered for one of the following indications:

Endometrial Carcinoma

- Primary treatment in combination with carboplatin and paclitaxel* and continued as a single agent for maintenance therapy[†] (NCCN-preferred regimen) for individuals with stage III–IV endometrioid adenocarcinoma
 - May be considered preoperatively for individuals presenting with abdominal/pelvic-confined disease that is suitable for primary surgery
 - With or without external beam radiation therapy (EBRT), stereotactic body radiation therapy, and/or total hysterectomy/bilateral salpingo-oophorectomy (TH/BSO) for distant metastases that are suitable for primary surgery

- With sequential EBRT and with or without brachytherapy for locoregional extrauterine disease that is not suitable for primary surgery
- For locoregional extrauterine disease or distant metastases that are not suitable for primary surgery

NCCN note: *For stage III or IVA with measurable disease post surgery or stage IVB with or without measurable disease. For individuals not meeting the eligibility criteria for NRG-GY018 carboplatin/paclitaxel + pembrolizumab should be considered for stage III-IV dMMR tumors.

†Pembrolizumab may be continued as a maintenance therapy. Refer to the original study protocol for maintenance therapy schedules.

- Adjuvant treatment in combination with carboplatin and paclitaxel* and continued as a single agent for maintenance therapy[†] (NCCN-preferred regimen) with or without EBRT and with or without vaginal brachytherapy for surgically staged individuals with stage III-IV endometrioid adenocarcinoma.

NCCN note: *For stage III or IVA with measurable disease post surgery or stage IVB with or without measurable disease. For individuals not meeting the eligibility criteria for NRG-GY018 carboplatin/paclitaxel + pembrolizumab should be considered for stage III-IV dMMR tumors.

†Pembrolizumab may be continued as a maintenance therapy. Refer to the original study protocol for maintenance therapy dosing schedules.

- First-line therapy (or second-line or subsequent therapy as clinically appropriate) in combination with carboplatin and paclitaxel* and continued as a single agent for maintenance therapy[†] (NCCN-preferred regimen) for recurrent disease (except for carcinosarcoma)
 - May be considered for isolated metastases as second-line or subsequent therapy only
 - For disseminated metastases with or without sequential palliative EBRT
 - With sequential EBRT and with or without brachytherapy for locoregional recurrence in individuals with no prior RT to site of recurrence, or previous brachytherapy only

- After surgical exploration, with sequential EBRT for locoregional recurrence in individuals with disease confined to the vagina or paravaginal soft tissue, or in pelvic, para-aortic or common iliac lymph nodes
- After surgical exploration, with or without sequential EBRT for locoregional recurrence in individuals with upper abdominal or peritoneal disease
- With or without sequential palliative EBRT or brachytherapy for locoregional recurrence in individuals who have received prior EBRT to site of recurrence

NCCN note: *For adult individuals with recurrent endometrial carcinoma with or without measurable disease.

[†]Pembrolizumab may be continued as a maintenance therapy. Refer to the original study protocol for maintenance therapy dosing schedules.

- Used in combination with carboplatin and paclitaxel and continued as a single agent for maintenance therapy[†] (NCCN-preferred regimen) for stage III–IV tumors* (except for carcinosarcoma) including serous carcinoma, clear cell carcinoma, or undifferentiated/dedifferentiated carcinoma
 - That is suitable for primary surgery as additional treatment with or without sequential EBRT and with or without vaginal brachytherapy after total hysterectomy/bilateral salpingo-oophorectomy (TH/BSO)
 - That is not suitable for primary surgery as primary treatment with or without sequential EBRT and with or without brachytherapy

NCCN note: *For stage III or IVA with measurable disease postsurgery or stage IVB with or without measurable disease. For individuals not meeting the eligibility criteria for NRG-GY018 carboplatin/paclitaxel + pembrolizumab should be considered for stage III-IV dMMR tumors.

[†]Pembrolizumab may be continued as a maintenance therapy. Refer to the original study protocol for maintenance therapy dosing schedules.

- First-line therapy after prior platinum-based therapy (including neoadjuvant and adjuvant) or second-line or subsequent therapy as clinically appropriate in combination with lenvatinib for recurrent disease that is mismatch repair proficient (pMMR)
 - For isolated metastases as second-line or subsequent therapy only
 - For disseminated metastases with or without sequential palliative EBRT

- With sequential EBRT and with or without brachytherapy for locoregional recurrence in individuals with no prior RT to site of recurrence, or previous vaginal brachytherapy only
- After surgical exploration, with sequential EBRT for locoregional recurrence in individuals with disease confined to the vagina or paravaginal soft tissue, or in pelvic or para-aortic lymph nodes
- After surgical exploration, with or without sequential EBRT for locoregional recurrence in individuals with upper abdominal or peritoneal disease
- With or without sequential palliative EBRT or brachytherapy for locoregional recurrence in individuals who have received prior EBRT to site of recurrence
- First-line therapy after prior platinum-based therapy (including neoadjuvant and adjuvant) or second-line or subsequent therapy as clinically appropriate as a single agent for recurrent unresectable or metastatic TMB-H (≥ 10 mut/Mb) tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options, or for recurrent MSI-H or dMMR tumors
 - May be considered for isolated metastases as second-line or subsequent therapy only
 - For disseminated metastases with or without sequential palliative EBRT
 - With sequential EBRT and with or without brachytherapy for locoregional recurrence in individuals with no prior RT to site of recurrence, or previous vaginal brachytherapy only
 - After surgical exploration, with sequential EBRT for locoregional recurrence in individuals with disease confined to the vagina or paravaginal soft tissue, or in pelvic or para-aortic lymph nodes
 - After surgical exploration, with or without sequential EBRT for locoregional recurrence in individuals with upper abdominal or peritoneal disease
 - With or without sequential palliative EBRT or brachytherapy for locoregional recurrence in individuals who have received prior EBRT to site of recurrence
- In combination with lenvatinib, for the treatment of individuals with advanced endometrial carcinoma that is pMMR as determined by an FDA-approved test or not MSI-H, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation
- As a single agent, for the treatment of individuals with advanced endometrial carcinoma that is MSI-H or dMMR, as determined by an FDA-approved test, who have disease

progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation

Uterine Sarcoma

- As single-agent second-line or subsequent therapy for the treatment of individuals with unresectable or metastatic TMB-H (≥ 10 mut/Mb) tumors, that have progressed following prior treatment and who have no satisfactory alternative treatment options.

TUMOR MUTATIONAL BURDEN—HIGH (TMB-H) CANCER (FDA)

Pembrolizumab (Keytruda®) is considered medically necessary and, therefore, covered for the treatment of adult and pediatric individuals with unresectable or metastatic TMB-H (≥ 10 mut/Mb) solid tumors, as determined by an FDA-approved test, that have progressed following prior treatment and who have no satisfactory alternative treatment options.

FDA note: The safety and effectiveness of pembrolizumab (Keytruda®) in pediatric individuals with TMB-H central nervous system cancers have not been established.

VAGINAL CANCER

Pembrolizumab (Keytruda®) for the treatment of vaginal cancer—squamous cell carcinoma is considered medically necessary and, therefore, covered as a single agent as:

- NCCN-preferred first-line, second-line, or subsequent therapy as clinically appropriate (if not used previously as first-line) in combination with cisplatin or carboplatin, paclitaxel, and with or without bevacizumab for PD-L1–positive tumors (CPS ≥ 1) as determined by an FDA-approved assay or a validated test performed in a CLIA-certified laboratory for:
 - Local/regional recurrence if prior intracavitary brachytherapy only, or prior EBRT with or without brachytherapy and noncentral disease
 - Stage IVB or recurrent distant metastases
- NCCN-preferred second-line or subsequent therapy as a single agent if PD-L1–positive (CPS ≥ 1) as determined by an FDA-approved assay or a validated test performed in a CLIA-certified laboratory, or if MSI-H or dMMR tumors
- for
 - Local/regional recurrence
 - Stage IVB or recurrent distant metastases
- NCCN-preferred second-line or subsequent treatment for individuals with unresectable or metastatic TMB-H (≥ 10 mut/Mb) tumors, as determined by a validated and/or FDA-

approved assay or a validated test performed in a CLIA-certified laboratory, that have progressed following prior treatment and who have no satisfactory alternative treatment options.

VULVAR CANCER–ADENOCARCINOMA, SQUAMOUS CELL CARCINOMA

Pembrolizumab (Keytruda®) for the treatment of vulvar cancer–squamous cell carcinoma is considered medically necessary and, therefore, covered as a single agent:

- As second-line or subsequent therapy for advanced or recurrent/metastatic disease as a single agent for any of the following:
 - TMB-H (≥ 10 mut/Mb) tumors, as determined by an FDA-approved assay or a validated test performed in a CLIA-certified laboratory, that have progressed following prior treatment and who have no satisfactory alternative treatment options
 - Disease progression on or after chemotherapy in individuals whose tumors express PD-L1 (CPS ≥ 1) as determined by an FDA-approved assay or a validated test performed in a CLIA-certified lab
 - oratory
 - MSI-H or dMMR tumors

EXPERIMENTAL/INVESTIGATIONAL

All other uses for pembrolizumab (Keytruda®) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

MANDATES

PENNSYLVANIA MEMBERS

In accordance with the Commonwealth of Pennsylvania's Act 6 of 2020 or Fair Access to Cancer Treatment Act, for members who are enrolled in Pennsylvania commercial products who have Stage 4, advanced metastatic cancer, refer to the Medical Policy titled "Coverage of Anticancer Prescription Oral and Injectable Drugs and Biologics and Supportive Agents" (08.01.08) for additional information regarding the applicable coverage of drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Duration of authorization: 12 months

Version Effective Date: 04/21/2025

Title: Pemetrexed (Pemfexy™)

Policy

Coverage is subject to the terms, conditions, and limitations of the member's contract.

The Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition.

INDEX OF MEDICALLY NECESSARY INDICATIONS

This policy addresses numerous medically necessary indications for the use of pemetrexed (Pemfexy) listed in order of appearance within the Policy section. Please see below for the specific medical necessity criteria. (NOTE: Experimental/Investigational section below must also be reviewed).

Type of cancer	Subtype of cancer
Central Nervous System Cancers	Leptomeningeal Metastases Primary Central Nervous System Lymphoma
Cervical Cancer	
Malignant Pleural Mesothelioma	Epithelioid, Biphasic, Sarcomatoid
Malignant Peritoneal Mesothelioma	Sarcomatoid, Epithelioid, Biphasic
Nonsquamous Non-Small Cell Lung Cancer (NSCLC) (e.g., Adenocarcinoma with Mixed Subtypes)	Large Cell Carcinoma, Locally Advanced or Metastatic
Ovarian Cancer, Fallopian Tube Cancer, Primary Peritoneal Cancers	Epithelial Ovarian Cancer, Fallopian Tube Cancer, Carcinosarcoma (Malignant Mixed Müllerian Tumors), Clear Cell Carcinoma of the Ovary, Mucinous Carcinoma of the Ovary, Grade 1 Endometrioid Carcinoma, Low-Grade Serous Carcinoma, Primary Peritoneal Cancer

MEDICALLY NECESSARY

Pemetrexed (Pemfexy) are considered medically necessary and, therefore, covered for the following conditions:

CENTRAL NERVOUS SYSTEM CANCERS

Primary Central Nervous System Lymphoma

- For the treatment of individuals as a single-agent treatment for relapsed or refractory disease, for any of the following indications:
 - Prior whole-brain radiation therapy (RT)
 - Prior high-dose methotrexate-based regimen without prior RT
 - With whole-brain RT or involved-field RT in individuals who received a prior high-dose methotrexate-based regimen, without prior RT after no response or short response duration (12 months or more) to the prior regimen
 - Prior high-dose systemic therapy with stem cell rescue
- For the treatment of individuals as a single-agent treatment for induction therapy in individuals who are unsuitable for or are intolerant to a high-dose methotrexate.

Leptomeningeal Metastases

- For the treatment of individuals with intracerebrospinal fluid (CSF) leptomeningeal metastases from non-small cell lung cancer that is EGFR mutation-positive for one of the following indications:

- As primary treatment in individuals with good risk status (KPS $\geq$ 60, no major neurologic deficits, minimal systemic disease, and reasonable systemic treatment options if needed)
- As maintenance treatment in individuals with negative CSF cytology or in clinically stable individuals with persistently positive CSF cytology

MALIGNANT PLEURAL MESOTHELIOMA (EPITHELIOID, BIPHASIC, SARCOMATOID)

- For the treatment of individuals as first-line systemic therapy in combination with bevacizumab and cisplatin followed by single-agent maintenance bevacizumab (National Comprehensive Cancer Network [NCCN] preferred regimen), for any of the following indications:
 - Unresectable clinical stage I-IIIa disease (if induction chemotherapy was not given) and tumors of epithelioid or biphasic histology
 - Clinical stage I-IIIa disease and epithelioid histology in those who have not undergone surgical exploration (if induction chemotherapy was not given)
 - Clinical stage IIIb or IV disease, tumors of sarcomatoid or biphasic histology, or medically inoperable tumors in individuals with Eastern Cooperative Oncology Group (ECOG) performance status (PS) 0-2
- For the treatment of individuals as induction therapy in combination with cisplatin (NCCN-preferred regimen) or carboplatin (in individuals not eligible for cisplatin) for medically operable clinical stage I-IIIa disease and epithelioid or biphasic histology
- For the treatment of individuals as a first-line systemic therapy in combination with cisplatin (NCCN-preferred regimen with epithelioid histology) or carboplatin (NCCN-preferred regimen in individuals not eligible for cisplatin with epithelioid histology), for any of the following indications:
 - Unresectable clinical stage I-IIIa disease and tumors of epithelioid histology after surgical exploration (if induction chemotherapy was not given)
 - Resected clinical stage I-IIIa disease and epithelioid histology in individuals not treated with induction chemotherapy
 - Clinical stage IIIb or IV disease, sarcomatoid biphasic histology or medically inoperable tumors in individuals with an ECOG PS 0-2
- For the treatment of individuals as subsequent systemic therapy as a single agent (NCCN-preferred regimen), for any of the following indications:

- If nivolumab/ipilimumab administered first-line
 - As rechallenge if good response to front-line pemetrexed-based treatment
- For the treatment of individuals in combination with bevacizumab and carboplatin (in individuals not eligible for cisplatin), for any of the following indications:
 - Unresectable clinical stage I-IIIa disease after surgical exploration (if induction chemotherapy was not given) and tumors of epithelioid
 - Clinical stage I-IIIA disease and epithelioid histology in those who have not undergone surgical exploration (if induction chemotherapy was not given)
 - Those with PS 0-2 and: clinical stage IIIB or IV disease, sarcomatoid or biphasic histology, or if medically inoperable
- For the treatment of individuals as subsequent systemic therapy (NCCN-preferred regimen), if immunotherapy was administered as first-line treatment or to be considered as a rechallenge if good response to front-line pemetrexed-based treatment, with any of the following regimens:
 - In combination with cisplatin
 - In combination with cisplatin and bevacizumab
 - In combination with carboplatin (in individuals not eligible for cisplatin)
 - In combination with carboplatin and bevacizumab (in individuals not eligible for cisplatin)
- Single-agent therapy (useful in certain circumstances) as first-line systemic therapy for
 - Unresectable clinical stage I-IIIa disease after surgical exploration (if induction chemotherapy was not given) and epithelioid histology
 - Clinical stage I-IIIA disease and epithelioid histology in those who have not undergone surgical exploration (if induction chemotherapy was not given)
 - Those with PS 0-2 and: clinical stage IIIB or IV disease, sarcomatoid or biphasic histology, or if medically inoperable
- For the treatment of individuals in combination with cisplatin (NCCN-preferred regimen for epithelioid histology), or carboplatin (for individuals not eligible for cisplatin NCCN-preferred regimen for epithelioid histology), or as a single agent as first-line systemic therapy, for any of the following indications:

- Adjuvant treatment of diffuse malignant peritoneal mesothelioma (MPeM) with unicavitary, epithelioid histology that is medically operable and complete cytoreduction achievable, following cytoreductive surgery (CRS) + hyperthermic intraperitoneal chemotherapy (HIPEC), if surgical/pathologic high-risk features** and no neoadjuvant therapy given
- Diffuse MPeM with unicavitary, epithelioid histology that is medically inoperable and/or complete cytoreduction not achievable (including high-risk features**) and an ECOG PS 0-2
- Diffuse MPeM with biphasic/sarcomatoid histology or bicavitary disease and an ECOG PS 0-2
- Recurrence of diffuse MPeM with unicavitary, epithelioid histology after prior CRS + HIPEC, if no previous adjuvant systemic therapy given and an ECOG PS 0-2
- Recurrence of biphasic/sarcomatoid (PeM) after prior CRS ± HIPEC for an ECOG PS 0-2
- For the treatment of individuals in combination with bevacizumab and cisplatin (NCCN-preferred regimen for epithelioid histology) as first-line systemic therapy for any of the following indications:
 - As adjuvant treatment of peritoneal mesothelioma (PeM) with unicavitary, epithelioid histology that is medically operable and complete cytoreduction achievable, following CRS + HIPEC, if surgical/pathologic high-risk features** and no neoadjuvant therapy given
 - MPeM with unicavitary, epithelioid histology that is medically inoperable and/or complete cytoreduction not achievable (including high-risk features**) and an ECOG PS 0-2
 - Unresectable diffuse MPeM with biphasic/sarcomatoid histology or bicavitary disease and ECOG PS 0-2
 - ECOG PS 0-2 and: recurrence of PeM with unicavitary, epithelioid histology after prior CRS + HIPEC if no previous adjuvant systemic therapy given
 - ECOG PS 0-2 and: recurrence of PeM with biphasic/sarcomatoid histology after prior CRS + HIPEC
- For the treatment of individuals not eligible for cisplatin in combination with bevacizumab and carboplatin (NCCN-preferred regimen for epithelioid histology) as first-line systemic therapy for any of the following indications:

- Adjuvant treatment of PeM with unicavitary, epithelioid histology that is medically operable and complete cytoreduction achievable, following CRS + HIPEC, if surgical/pathologic high-risk features** and no neoadjuvant therapy given
- MPeM with unicavitary, epithelioid histology that is medically inoperable and/or complete cytoreduction not achievable (including high-risk features**) and an ECOG PS 0-2
- Unresectable diffuse MPeM with biphasic/sarcomatoid histology or bicavitary disease and ECOG PS 0-2
- Unresectable recurrence of diffuse MPeM with unicavitary, epithelioid histology after prior CRS + HIPEC, if no previous adjuvant systemic therapy given and an ECOG PS 0-2
- ECOG PS 0-2 and: recurrence of PeM with biphasic/sarcomatoid histology after prior CRS + HIPEC
- For the treatment of individuals for subsequent systemic therapy as a single agent (preferred) for an ECOG PS 0-2, for any of the following indications:
 - If nivolumab/ipilimumab administered first-line
 - As rechallenge if good response to front-line pemetrexed-based treatment
- For the treatment of individuals for subsequent systemic therapy (NCCN-preferred regimen), if immunotherapy was administered as first-line treatment or to be considered as a rechallenge if good response to front-line pemetrexed-based treatment and an ECOG PS 0-2, with any of the following regimens:
 - In combination with cisplatin
 - In combination with cisplatin and bevacizumab
 - In combination with carboplatin (in individuals not eligible for cisplatin)
 - In combination with carboplatin and bevacizumab (in individuals not eligible for cisplatin)

NCCN notes: *May also be used for pericardial mesothelioma and tunica vaginalis testis mesothelioma.

****High-risk features include Ki-67 >9%, nodal metastasis, high tumor burden (Peritoneal Cancer Index [PCI] >17), completeness of cytoreduction (CC) score >1, biphasic disease, or bicavitary disease.**

NONSQUAMOUS NON-SMALL CELL LUNG CANCER (NSCLC) (e.g., ADENOCARCINOMA WITH MIXED SUBTYPES), LARGE CELL CARCINOMA

Pemetrexed (Pemfexy) are indicated for the treatment of individuals with nonsquamous NSCLC for the following indications:

Preoperative Therapy

- For the treatment of individuals as preoperative concurrent chemoradiation (NCCN-preferred regimen) in combination with carboplatin or cisplatin, for any of the following indications:
 - Superior sulcus tumors (T3 invasion, N0-1)
 - Chest wall, trachea/carina, or mediastinum; T3 invasion, N0-1; resectable T4 extension, N0-1 disease
 - Resectable stage IIIA (T4, N0-1) disease

Induction Therapy

- As induction systemic therapy as an alternative for those likely to receive adjuvant chemotherapy for nonsquamous cell histology, in combination with cisplatin (preferred) or carboplatin (useful in certain circumstances, for those who are not candidates for cisplatin-based therapy) if not a candidate for immune checkpoint inhibitors as neoadjuvant therapy for:
 - Operable clinical stage IB (peripheral T2a, N0), stage I (central T1abc-2a, N0), stage II (T1abc-2ab, N1 or T2b, N0), stage IIB (T3, N0), or stage IIIA (T3, N1) disease with no pathologic nodal disease
 - Chest wall, trachea/carina, or mediastinum; T3 invasion, N0-1; resectable T4 extension, N0-1 disease
 - Resectable stage IIIA (T4, N0-1) disease

- Operable T2a-3, N0 or T1-3, N1 nodes positive, M0 findings on mediastinal biopsy
- T1-3, N2 nodes positive*, M0 findings on mediastinal biopsy
- Separate pulmonary nodule(s), same lobe (T3, N0-1), or ipsilateral non-primary lobe (T4, N0-1)

NCCN note: *Selected individuals with N2 disease (fit, single station non-bulky N2, requiring only lobectomy) may be considered for systemic therapy followed by surgery.

- As induction systemic therapy as an alternative for those likely to receive adjuvant chemotherapy in combination with cisplatin or carboplatin (for those who are not candidates for cisplatin-based therapy) and nivolumab* for nonsquamous cell histology as induction systemic therapy for resectable (tumors ≥ 4 cm or node positive) disease as an alternative for those likely to receive adjuvant chemotherapy (if candidates for immune checkpoint inhibitors)** as neoadjuvant therapy for:
 - Operable clinical stage IB (T2a, N0), stage II (T1abc-2ab, N1 or T2b, N0), stage IIB (T3, N0), or stage IIIA (T3, N1) disease with no pathologic nodal disease
 - Chest wall, trachea/carina, or mediastinum; T3 invasion, N0-1; resectable T4 extension, N0-1 disease
 - Resectable stage IIIA (T4, N0-1)
 - Operable T2a-3, N0 or T1-3, N1 nodes positive, M0 findings on mediastinal biopsy
 - T1-3, N2 nodes positive***, M0 findings on mediastinal biopsy
 - Separate pulmonary nodule(s), same lobe (T3, N0-1), or ipsilateral non-primary lobe (T4, N0-1)

NCCN note: *Clinical trials for neoadjuvant nivolumab + chemotherapy excluded individuals harboring EGFR and ALK rearrangements. Thus, exclusion of these biomarkers, at minimum, is recommended prior to consideration for neoadjuvant nivolumab + chemotherapy.

**Contraindications for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or current use of immunosuppressive agents, and some oncogenic drivers (i.e., EGFR exon 19 deletion or exon 21 L858R, ALK rearrangements) have been shown to be associated with less benefit from PD-1/PD-L1 inhibitors.

***Selected individuals with N2 disease (fit, single station non-bulky N2, requiring only lobectomy) may be considered for systemic therapy followed by surgery.

- As induction systemic therapy as an alternative for those likely to receive adjuvant chemotherapy in combination with cisplatin and pembrolizumab for nonsquamous cell histology for resectable (tumors ≥ 4 cm or node positive) disease (if candidates for immune checkpoint inhibitors)* as neoadjuvant therapy for:
 - Operable clinical stage IB (T2a, N0), stage II (T1abc-2ab, N1 or T2b, N0), stage IIB (T3, N0), or stage IIIA (T3, N1) disease with no pathologic nodal disease
 - Chest wall, trachea/carina, or mediastinum; T3 invasion, N0-1; resectable T4 extension, N0-1 disease
 - Resectable stage IIIA (T4, N0-1)
 - Operable T2a-3, N0 or T1-3, N1 nodes positive, M0 findings on mediastinal biopsy
 - T1-3, N2 nodes positive**, M0 findings on mediastinal biopsy
 - Separate pulmonary nodule(s), same lobe (T3, N0-1), or ipsilateral nonprimary lobe (T4, N0-1)

NCCN note: *Contraindications for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or current use of immunosuppressive agents, and some oncogenic drivers (i.e., EGFR exon 19 deletion or exon 21 L858R, ALK rearrangements) have been shown to be associated with less benefit from PD-1/PD-L1 inhibitors.

**Selected individuals with N2 disease (fit, single station non-bulky N2, requiring only lobectomy) may be considered for systemic therapy followed by surgery.

Initial Treatment

- For the treatment of individuals as initial treatment, for any of the following regimens:
 - In combination with pembrolizumab and platinum chemotherapy for metastatic disease with no EGFR or ALK genomic tumor aberrations

- In combination with cisplatin for locally advanced or metastatic disease
- As a single agent for the maintenance treatment of individuals with locally advanced or metastatic, nonsquamous NSCLC whose disease has not progressed after four cycles of platinum-based first-line chemotherapy.
- As a single agent for the treatment of individuals with recurrent, metastatic nonsquamous, NSCLC after prior chemotherapy.
- For the treatment of individuals as initial (NCCN-preferred regimen) definitive concurrent chemoradiation (in combination with carboplatin or cisplatin for any of the following indications:
 - Medically inoperable high surgical risk as determined by thoracic surgeon, and those who decline surgery after thoracic consultation for T1-3, N1 nodes positive, M0 disease on mediastinal biopsy
 - Unresectable superior sulcus tumors (T4 extension, N0-1)
 - Unresectable stage IIIA (T4, N0-1)
 - T1-T3, N2 nodes positive, M0 disease on mediastinal biopsy
 - Stage IIIB (T1-2, N3) and stage IIIC (T3, N3)
 - Contralateral or ipsilateral mediastinal node-positive stage IIIB (T4, N2) and stage IIIC (T4, N3)
 - Stage IVA, M1b (T1-3, N1-2 or T4, N0-2) disease and limited non-brain progression confirmed, if definitive therapy for the thoracic disease is feasible (NCCN preferred for T1-3, N1)

NCCN note: *If there is insufficient tissue to allow testing for all of EGFR, ALK, ROS1, BRAF, NTRK1/2/3, MET, and RET, repeat biopsy and/or plasma testing should be done. If these are not feasible, treatment is guided by available results and, if unknown, these individuals are treated as though they do not have driver oncogenes.

**Contraindications for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or current use of immunosuppressive agents, or presence of an oncogene (e.g., EGFR [exon 19 deletions, p.L858R point mutation in exon 21], ALK rearrangements, RET rearrangements), which would predict lack of benefit.

Treatment for Recurrent, Advanced, or Metastatic Disease

- For the treatment of individuals as first-line therapy (except for locoregional recurrence or symptomatic local disease [excluding mediastinal lymph node recurrence with prior RT] with no evidence of disseminated disease, for one of the following:
 - As first-line therapy for EGFR exon 19 deletion or exon 21 L858R recurrent, advanced, or metastatic disease in combination with osimertinib and cisplatin or carboplatin.
 - NCCN preferred first-line therapy for EGFR exon 20 insertion mutation positive recurrent, advanced, or metastatic disease in combination with amivantamab-vmjw and carboplatin.
- For the treatment of individuals as first-line therapy for PD-L1 expression–positive ($\geq 1\%$) tumors that are negative for actionable molecular biomarkers* (may be KRAS G12C mutation positive) and no contraindications** to PD-1 or PD-L1 inhibitors, and an ECOG PS 0-2, except for locoregional recurrence or symptomatic local disease (excluding mediastinal lymph node recurrence with prior RT) with no evidence of disseminated disease or for PD-L1 $\geq 50\%$ in combination with tremelimumab-actl, durvalumab, and either carboplatin or cisplatin for any of the following regimens:
 - In combination with pembrolizumab and either carboplatin or cisplatin (NCCN-preferred regimen)
 - In combination with nivolumab, ipilimumab, and either carboplatin or cisplatin
 - in combination with cemiplimab-rwlc and either carboplatin or cisplatin (preferred)
 - in combination with tremelimumab-actl, durvalumab, and either carboplatin or cisplatin
- For the treatment of individuals with recurrent, advanced, or metastatic disease in combination with one of the following regimens and lines of therapy, except for locoregional recurrence or symptomatic local disease (excluding mediastinal lymph node recurrence with prior RT) with no evidence of disseminated disease for any of the following regimens and lines of therapy:
 - In combination with one of the following regimens:
 - Cisplatin or carboplatin and pembrolizumab (NCCN preferred)

- Nivolumab, ipilimumab, and either carboplatin or cisplatin
 - Cemiplimab-rwlc and either carboplatin or cisplatin (NCCN preferred)
 - Tremelimumab-actl, durvalumab, and either carboplatin or cisplatin
- For any of the following lines of therapy:
 - Initial systemic therapy for PD-L1 <1% and negative for actionable molecular biomarkers* (may be KRAS G12C mutation positive)
 - First-line therapy for EGFR exon 20 mutation–positive tumors
 - First-line therapy for KRAS G12C mutation–positive tumors
 - First-line or subsequent therapy for BRAF V600E-mutation–positive tumors
 - First-line or subsequent therapy for NTRK1/2/3 gene fusion–positive tumors
 - First-line or subsequent therapy for MET exon 14 skipping mutation–positive tumors
 - First-line or subsequent therapy for RET rearrangement–positive tumors
 - First-line therapy for ERBB2 (HER2) mutation–positive tumors
 - Subsequent therapy for EGFR mutation–positive (e.g., exon 19 deletion or exon 21 L858R) tumors and prior erlotinib ± (ramucirumab or bevacizumab), afatinib, gefitinib, osimertinib, or dacomitinib therapy
 - Subsequent therapy for ALK rearrangement–positive tumors and prior crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib therapy
 - Subsequent therapy for EGFR S768I, L861Q, and/or G719X mutation–positive tumors and prior afatinib, osimertinib, erlotinib, gefitinib, or dacomitinib therapy
 - Subsequent therapy for ROS1 rearrangement–positive tumors and prior crizotinib, entrectinib, or ceritinib therapy
 - Treatment for recurrent, advanced, or metastatic disease of nonsquamous cell histology except for locoregional recurrence or symptomatic local disease (excluding mediastinal lymph node recurrence with prior RT) with no evidence of disseminated disease

- In combination with cisplatin for PS 0-1 (useful in certain circumstances if contraindications** to PD-1 or PD-L1 inhibitors)
- In combination with carboplatin for PS 0-2 (useful in certain circumstances if contraindications** to PD-1 or PD-L1 inhibitors for PS 0-1 or preferred for PS 2)
- As a single agent for PS 2 (useful in certain circumstances)
 - The above regimens are used as:
 - Initial systemic therapy for PD-L1 expression positive ($\geq 1\%$) and negative for actionable molecular biomarkers* (may be KRAS G12C mutation positive) with contraindications to PD-1 or PD-L1 inhibitors
 - Initial systemic therapy for PD-L1 $< 1\%$ and negative for actionable molecular biomarkers* (may be KRAS G12C mutation positive)
 - First-line therapy for EGFR exon 20 mutation–positive tumors
 - First-line or subsequent therapy for BRAF V600E mutation–positive tumors
 - First-line (useful in certain circumstances) or subsequent therapy for NTRK1/2/3 gene fusion–positive tumors
 - First-line (useful in certain circumstances) or subsequent therapy for MET exon 14 skipping mutation–positive tumors
 - First-line or subsequent therapy for RET rearrangement–positive tumors
 - First-line therapy for ERBB2 (HER2) mutation–positive tumors
 - Subsequent therapy for EGFR exon 19 deletion or exon 21 L858R tumors and prior erlotinib $\pm$ (ramucirumab or bevacizumab), afatinib, gefitinib, osimertinib, or dacomitinib therapy
 - Subsequent therapy for EGFR S768I, L861Q, and/or G719X mutation–positive tumors and prior afatinib, osimertinib, erlotinib, gefitinib, or dacomitinib therapy
 - Subsequent therapy for ALK rearrangement–positive tumors and prior crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib therapy
 - Subsequent therapy for ROS1 rearrangement–positive tumors and prior crizotinib, entrectinib, repotrectinib, or ceritinib therapy

- Subsequent therapy for PD-L1 expression–positive ($\geq 1\%$) tumors and negative for actionable molecular biomarkers* after prior PD-1/PD-L1 inhibitor but no prior platinum-containing chemotherapy
- For the treatment of individuals with recurrent, advanced, or metastatic disease, with an ECOG PS 0-1 and no history of recent hemoptysis, except for locoregional recurrence or symptomatic local disease (excluding mediastinal lymph node recurrence with prior RT) with no evidence of disseminated disease, in combination with one of the following regimens and lines of therapy:
 - In combination with one of the following regimens:
 - Bevacizumab and cisplatin (if contraindications** to PD-1 or PD-L1 inhibitors)
 - Bevacizumab and carboplatin (if contraindications** to PD-1 or PD-L1 inhibitors)
 - For any of the following lines of therapy:
 - Initial systemic therapy for PD-L1 $< 1\%$ and negative for actionable molecular biomarkers* (may be KRAS G12C mutation positive) with contraindications to PD-1 or PD-L1 inhibitors
 - Initial systemic therapy for PD-L1 $< 1\%$ and negative for actionable molecular biomarkers* (may be KRAS G12C mutation positive)
 - First-line therapy for EGFR exon 20 mutation–positive tumors
 - First-line or subsequent therapy for BRAF V600E mutation–positive tumors
 - First-line or subsequent therapy for NTRK1/2/3 gene fusion–positive tumors
 - First-line or subsequent therapy for MET exon 14 skipping mutation–positive tumors
 - First-line or subsequent therapy for RET rearrangement–positive tumors

- First-line therapy for ERBB2 (HER2) mutation–positive tumors
 - Subsequent therapy for EGFR mutation–positive (e.g., exon 19 deletion or exon 21 L858R) tumors and prior erlotinib ± (ramucirumab or bevacizumab), afatinib, gefitinib, osimertinib, or dacomitinib therapy
 - Subsequent therapy for EGFR S768I, L861Q, and/or G719X mutation–positive tumors and prior afatinib, osimertinib, erlotinib, gefitinib, or dacomitinib therapy
 - Subsequent therapy for ALK rearrangement–positive tumors and prior crizotinib, ceritinib, alectinib, brigatinib, or lorlatinib therapy
 - Subsequent therapy for ROS1 rearrangement–positive tumors and prior crizotinib, entrectinib, repotrectinib or ceritinib therapy
 - Subsequent therapy for PD-L1 expression–positive ($\geq 1\%$) tumors and negative for actionable molecular biomarkers* after prior PD-1/PD-L1 inhibitor but no prior platinum-containing chemotherapy
- For the treatment of individuals with recurrent, advanced, or metastatic disease, with an ECOG PS 0-2 and who achieve tumor response or stable disease following initial systemic therapy, except for locoregional recurrence or symptomatic local disease (excluding mediastinal lymph node recurrence with prior RT) with no evidence of disseminated disease, or for PD-L1 $\geq 50\%$ in combination with durvalumab, for any of the following lines of therapy:
 - As a single agent for continuation maintenance therapy
 - In combination with bevacizumab for continuation maintenance therapy if bevacizumab previously used with a first-line pemetrexed/platinum chemotherapy regimen
 - In combination with pembrolizumab for continuation maintenance therapy if previously used first-line as part of a pembrolizumab/pemetrexed and either cisplatin or carboplatin regimen
 - In combination with cemiplimab-rwlc for continuation maintenance therapy if previously used as first-line as part of cemiplimab/pemetrexed and either cisplatin or carboplatin

- In combination with durvalumab for continuation maintenance therapy if previously used as first-line as part of tremelimumab-actl/durvalumab/pemetrexed and either cisplatin or carboplatin
- As a single agent for switch maintenance
- For the treatment of individuals as a single agent (if not already given) as subsequent systemic therapy for recurrent, advanced, or metastatic disease in individuals with an ECOG PS 0-2 and tumors, except for progression after subsequent systemic therapy and for locoregional recurrence or symptomatic local disease, except for locoregional recurrence or symptomatic local disease (excluding mediastinal lymph node recurrence with prior RT) with no evidence of disseminated disease.
- Continuation maintenance therapy in combination with pembrolizumab for recurrent, advanced, or metastatic disease for PD-L1 expression–positive ($\geq 1\%$) or PD-L1 expression $< 1\%$ tumors that are negative for actionable molecular biomarkers* (may be KRAS G12C mutation positive) and no contraindications** to PD-1 or PD-L1 inhibitors in individuals with PS 0-2 who achieve a response or stable disease following first-line therapy with pembrolizumab/pemetrexed and either cisplatin or carboplatin for nonsquamous cell histology (except for locoregional recurrence or symptomatic local disease (excluding mediastinal lymph node recurrence with prior RT) with no evidence of disseminated disease.

NCCN note: *Complete genotyping for EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET, RET, and ERBB2 (HER2), via biopsy and/or plasma testing. If a clinically actionable marker is found, it is reasonable to start therapy based on the identified marker. Treatment is guided by available results and, if unknown, these individuals are treated as though they do not have driver oncogenes.

**Contraindications for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or current use of immunosuppressive agents, or presence of an oncogene (e.g., EGFR [exon 19 deletions, p.L858R point mutation in exon 21], ALK rearrangements, RET rearrangements), which would predict lack of benefit.

- Preferred subsequent therapy for EGFR exon 19 deletion or exon 21 L858R or EGFR S768I, L861Q, and/or G719X mutation–positive recurrent, advanced, or metastatic disease (nonsquamous) in combination with amivantamab-vmjw and carboplatin following disease progression on osimertinib for symptomatic systemic disease with

multiple lesions except for locoregional recurrence or symptomatic local disease (excluding mediastinal lymph node recurrence with prior RT) with no evidence of disseminated disease.

- Single agent (if not already given) as subsequent systemic therapy for recurrent, advanced, or metastatic disease in those with PS 0-2 and tumors of nonsquamous cell histology except for progression after subsequent systemic therapy and for locoregional recurrence or symptomatic local disease (excluding mediastinal lymph node recurrence with prior RT) with no evidence of disseminated disease

Concurrent Chemoradiation Therapy

- For the treatment of individuals in combination with carboplatin or cisplatin (with or without an additional four cycles of pemetrexed after concurrent chemoradiation if given with cisplatin) if radiation not previously given for the treatment of locoregional recurrence or symptomatic local disease, for one of the following indications:
 - Mediastinal lymph nodes
 - Superior vena cava (SVC) obstruction with or without an SVC stent

Sequential Chemoradiation Therapy in Combination with Cisplatin (NCCN preferred) or Carboplatin

- For the treatment of individuals as adjuvant therapy for those who are not candidates for cisplatin-based therapy), for any of the following indications:
 - Margin-positive, R1 stage IIB (T1abc-2a, N1; T3, N0; T2b, N1)
 - Margin-negative, stage IIIA (T1-2, N2) and stage IIIB (T3, N2)
 - Margin-positive, R1 stage IIIA (T1-2, N2; T3, N1) and stage IIIB (T3, N2)
 - Margin-positive, R1 disease in the chest wall, trachea/carina, or mediastinum; T3 invasion or resectable T4 extension, N0-1 tumors following initial treatment with surgery
 - Margin-positive, R1 stage IIIA (T4, N0-1) disease following initial treatment with surgery
 - Margin-negative, separate pulmonary nodule(s) in the same lobe (T3) or ipsilateral non-primary lobe (T4), N2

- Margin-positive, R1 separate pulmonary nodule(s) in the same lobe (T3) or ipsilateral non-primary lobe (T4), N2

Adjuvant Concurrent Chemoradiation Therapy in Combination with Carboplatin or Cisplatin

- As NCCN-preferred adjuvant concurrent chemoradiation therapy in combination with carboplatin or cisplatin for any of the following indications:
 - Margin-positive stage IIB (T1abc-2a, N1; T3, N0; T2b, N1)
 - Margin-positive stage IIIA (T1-2, N2; T3, N1) and stage IIIB (T3, N2)
 - Margin-positive disease in the chest wall, trachea/carina, or mediastinum; T3 invasion or T4 extension, N0-1 tumors following initial treatment with surgery
 - Margin-positive stage IIIA (T4, N0-1) disease following initial treatment with surgery
 - Margin-positive separate pulmonary nodule(s) in the same lobe (T3) or ipsilateral nonprimary lobe (T4), N2

Adjuvant Chemotherapy in Combination with Cisplatin (NCCN-preferred regimen) or Carboplatin (for individuals who are not candidates for cisplatin)

- For the treatment of individuals who are not candidates for cisplatin-based therapy, for any of the following indications:
 - Following definitive RT in medically inoperable high-risk* stage as determined by thoracic surgeon, and those who decline surgery after thoracic surgical consultation for high-risk* stage II (T1abc- 2ab, N1; T2b, N0), with no nodal disease
 - High-risk, margin-negative stage IIA (T2b, N0)
 - Margin-positive stage IIA (T2b, N0)
 - Margin-positive stage IIA (T2b, N0)
 - Stage IIB (T1abc-2a, N1; T3, N0; T2b, N1)
 - Margin-negative stage IIIA (T1-2, N2; T3, N1) and stage IIIB (T3, N2)
 - Resectable superior sulcus tumors (T3 invasion or T4 extension, N0-1)
 - For resected chest wall, trachea/carina, or mediastinum; T3 invasion or resectable T4 extension, N0-1 tumors or stage IIIA (T4, N0-1) disease for resected T2b-3, N0^* or T1-3, N1 nodes positive, M0 disease on mediastinal biopsy

- For T1-3, N2 nodes positive, M0 on mediastinal biopsy following surgery
- For T1-T3, N2 nodes positive, M0 disease on mediastinal biopsy with local progression after induction systemic therapy
- Following definitive RT in medically inoperable, high surgical risk as determined by thoracic surgeon, and those who decline surgery after thoracic surgical consultation for high-risk* stage II (T2b-3, N0) disease on mediastinal biopsy
- For separate pulmonary nodule(s) in the same lobe (T3) or ipsilateral non-primary lobe (T4), N0-1
- For margin-negative separate pulmonary nodule(s) in the same lobe (T3) or ipsilateral non-primary lobe (T4), N2

NCCN note: *Examples of high-risk features may include poorly differentiated tumors (including lung neuroendocrine tumors [excluding well-differentiated neuroendocrine tumors]), vascular invasion, wedge resection, visceral pleural involvement, and unknown lymph node status (Nx). These factors independently may not be an indication and may be considered when determining treatment with adjuvant chemotherapy.

^* For stage IIA (T2b, N0) and negative margins, adjuvant chemotherapy is recommended for high-risk features.

OVARIAN CANCER, FALLOPIAN TUBE CANCER, PRIMARY PERITONEAL CANCER

Epithelial Ovarian Cancer, Fallopian Tube Cancer, Clear Cell Carcinoma of the Ovary, Mucinous Carcinoma of the Ovary, Grade 1 Endometrioid Carcinoma, Primary Peritoneal Cancer Carcinoma (Malignant Mixed Müllerian Tumors)

- For the treatment of individuals as a single-agent therapy for clinical relapse of a persistent disease or recurrence for platinum-resistant and platinum-sensitive disease, except for immediate treatment of biochemical relapse, for any of the following indications:
 - As immediate treatment for serially rising CA-125 in individuals who previously received chemotherapy
 - For progression on primary, maintenance, or recurrence therapy (platinum-resistant disease)
 - For stable or persistent disease (if not on maintenance therapy) (platinum-resistant disease)

- For complete remission and relapse less than 6 months after completing chemotherapy (platinum-resistant disease)
- For radiographic and/or clinical relapse in individuals with previous complete remission and relapse after 6 or more months after completing prior chemotherapy (platinum-sensitive disease)

Low-Grade Serous Carcinoma

- For the treatment of individuals with a single-agent therapy of platinum-sensitive or platinum-resistant recurrence.

CERVICAL CANCER

- As second-line or subsequent therapy as a single agent for the treatment of individuals with one of the following indications:
 - Local/regional recurrence
 - Stage IVB or recurrence with distant metastases

THYMIC CARCINOMA AND THYMOMA

- For the treatment of individuals as a first-line therapy as a single agent who cannot tolerate first-line combination regimens as preoperative systemic therapy for surgically resectable disease if R0 resection is considered uncertain
- For the treatment of individuals as second-line therapy as a single agent, for any of the following indications:
 - Unresectable locally advanced disease
 - Solitary metastasis or ipsilateral pleural metastasis
 - Extrathoracic metastatic disease
- For the treatment of individuals as postoperative treatment as a single agent for individuals who cannot tolerate first-line combination regimens, for any of the following indications:
 - Thymic carcinoma after R1 or R2 resection

- Thymoma after R2 resection
- For the treatment of individuals as first-line therapy for recurrent, advanced, or metastatic disease as a single agent for those who cannot tolerate first-line combination regimens for:
 - Potentially resectable locally advanced disease
 - Potentially resectable solitary metastasis or ipsilateral pleural metastasis
 - Consideration following surgery for solitary metastasis or ipsilateral pleural metastasis
 - Medically inoperable/unresectable solitary metastasis or ipsilateral pleural metastasis
 - Extrathoracic metastatic disease

EXPERIMENTAL/INVESTIGATIONAL

All other uses of pemetrexed (Pemfexy) are considered experimental/investigational and, therefore, are not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

MANDATES

PENNSYLVANIA MEMBERS

In accordance with the Commonwealth of Pennsylvania's Act 6 of 2020 or Fair Access to Cancer Treatment Act, for members who are enrolled in Pennsylvania commercial products who have stage 4, advanced metastatic cancer, refer to the Medical Policy titled "Coverage of Anticancer Prescription Oral and Injectable Drugs and Biologics and Supportive Agents" (08.01.08) for additional information regarding the applicable coverage of drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Duration of authorization: 12 months

Version Effective Date: 10/01/2024

Attachment A: [Pemetrexed \(Pemfexy™\)](#)

Description: ICD-10 CODES AND NARRATIVES

Policy Attachment

Attachment to Policy # 08.00.87n

Attachment: A

Policy #: 08.00.87n

Description: ICD-10 CODES AND NARRATIVES

Title: Pemetrexed (Pemfexy™)

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

ICD-10 CODES AND NARRATIVES

C33 Malignant neoplasm of trachea
C34.01 Malignant neoplasm of right main bronchus
C34.02 Malignant neoplasm of left main bronchus
C34.11 Malignant neoplasm of upper lobe, right bronchus or lung
C34.12 Malignant neoplasm of upper lobe, left bronchus or lung
C34.2 Malignant neoplasm of middle lobe, bronchus or lung
C34.31 Malignant neoplasm of lower lobe, right bronchus or lung
C34.32 Malignant neoplasm of lower lobe, left bronchus or lung
C34.81 Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82 Malignant neoplasm of overlapping sites of left bronchus and lung
C34.91 Malignant neoplasm of unspecified part of right bronchus or lung
C34.92 Malignant neoplasm of unspecified part of left bronchus or lung
C37 Malignant neoplasm of thymus
C38.4 Malignant neoplasm of pleura
C45.0 Mesothelioma of pleura
C45.1 Mesothelioma of peritoneum
C45.2 Mesothelioma of pericardium
C45.7 Mesothelioma of other sites
C45.9 Mesothelioma, unspecified
C48.1 Malignant neoplasm of specified parts of peritoneum
C48.2 Malignant neoplasm of peritoneum, unspecified
C48.8 Malignant neoplasm of overlapping sites of retroperitoneum and peritoneum

C53.0 Malignant neoplasm of endocervix

C53.1 Malignant neoplasm of exocervix

C53.8 Malignant neoplasm of overlapping sites of cervix uteri

C53.9 Malignant neoplasm of cervix uteri, unspecified
C56.1 Malignant neoplasm of right ovary
C56.2 Malignant neoplasm of left ovary
C56.3 Malignant neoplasm of bilateral ovaries
C57.01 Malignant neoplasm of right fallopian tube
C57.02 Malignant neoplasm of left fallopian tube
C57.11 Malignant neoplasm of right broad ligament
C57.12 Malignant neoplasm of left broad ligament
C57.21 Malignant neoplasm of right round ligament
C57.22 Malignant neoplasm of left round ligament
C57.3 Malignant neoplasm of parametrium
C57.4 Malignant neoplasm of uterine adnexa, unspecified
C57.7 Malignant neoplasm of other specified female genital organs

C57.8 Malignant neoplasm of overlapping sites of female genital organs
C57.9 Malignant neoplasm of female genital organ, unspecified

C79.32 Secondary malignant neoplasm of cerebral meninges
C83.30 Diffuse large B-cell lymphoma, unspecified site
C83.31 Diffuse large B-cell lymphoma, lymph nodes of head, face, and neck

C83.390 Primary central nervous system lymphoma
C83.398 Diffuse large B-cell lymphoma of other extranodal and solid organ sites

C83.3A Diffuse large B-cell lymphoma, in remission

C83.5A Lymphoblastic (diffuse) lymphoma, in remission

C83.7A Burkitt lymphoma, in remission

C83.8A Other non-follicular lymphoma, in remission

C83.9A Non-follicular (diffuse) lymphoma, unspecified, in remission
C83.80 Other non-follicular lymphoma, unspecified site
C83.81 Other non-follicular lymphoma, lymph nodes of head, face, and neck
C83.89 Other non-follicular lymphoma, extranodal and solid organ sites
C85.89 Other specified types of non-Hodgkin lymphoma, extranodal and solid organ sites
C85.99 Non-Hodgkin lymphoma, unspecified, extranodal and solid organ sites

Version Effective Date: 10/01/2024

Title: Personalized Vaccines (e.g., Provenge®)

MEDICALLY NECESSARY

Sipuleucel-T (Provenge) therapy, limited to three complete doses, is considered medically necessary, and, therefore covered for asymptomatic or minimally symptomatic metastatic castration-resistant (hormone-refractory) prostate cancer (CRPC) when all of the following criteria are met:

- A castrate level of testosterone (less than 50 ng/dL) *
- An Eastern Cooperative Oncology Group (ECOG) performance status of zero or one
- A life expectancy of greater than six months
- No hepatic metastases
- One of the following:
 - No prior docetaxel use and no prior novel hormone therapy
 - Prior docetaxel use and no prior novel hormone therapy
 - Prior novel hormone therapy and no prior docetaxel use

* Continue androgen deprivation therapy (ADT) to maintain castrate levels of serum testosterone < 50 ng/dL

MANDATES

PENNSYLVANIA MEMBERS

In accordance with the Commonwealth of Pennsylvania's >Act 6 of 2020< or >Fair Access to Cancer Treatment Act<, for members who are enrolled in Pennsylvania commercial products who have Stage 4, advanced metastatic cancer, refer to the Medical Policy titled "Coverage of Anticancer Prescription Oral and Injectable Drugs and Biologics and Supportive agents" (08.01.08) for additional information regarding the applicable coverage of drugs and biologics.

EXPERIMENTAL/INVESTIGATIONAL

All other uses for sipuleucel-T (Provenge) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

All other personalized vaccines are considered experimental/investigational and, therefore, not covered because there are no other personalized vaccines approved by the US Food and Drug

Administration (FDA).

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Duration of authorization: 12 months

Version Effective Date: 05/28/2025

Title: Pertuzumab (Perjeta®)

MEDICALLY NECESSARY

Pertuzumab (Perjeta®) is considered medically necessary and, therefore, covered for the indication(s) identified below in individuals who meet the applicable criteria, and whose tumors have human epidermal growth factor receptor 2 (HER2) protein overexpression verified as a positive result by one of the US Food and Drug Administration (FDA)–approved diagnostic tests for the following:

BREAST CANCER

Early Breast Cancer (EBC)

- For the neoadjuvant treatment of individuals with HER2-positive, locally advanced, inflammatory, or early stage breast cancer (either >2 cm in diameter or node-positive) as part of a complete treatment regimen for EBC in combination with trastuzumab and chemotherapy
- For the adjuvant treatment of individuals with HER2-positive EBC at high risk of recurrence in combination with trastuzumab and chemotherapy

Inflammatory Breast cancer

- As adjuvant systemic therapy** for individuals who had a response to preoperative systemic therapy, followed by surgery, and need to complete planned chemotherapy, for node-positive HER2-positive tumors:
 - In combination with trastuzumab and paclitaxel following AC (doxorubicin and cyclophosphamide) (dose-dense or every 3 weeks) regimen (both useful in certain circumstances)*
 - As a component of TCHP (docetaxel, carboplatin, trastuzumab, and pertuzumab) regimen (preferred regimen)
 - In combination with paclitaxel, carboplatin, and trastuzumab
 - In combination with trastuzumab and docetaxel following AC regimen*
 - In combination with paclitaxel and trastuzumab

- As preoperative systemic therapy for HER2-positive disease
 - In combination with trastuzumab and paclitaxel following AC (doxorubicin and cyclophosphamide) (dose-dense or every 3 weeks) regimen (both useful in certain circumstances)*
 - As a component of TCHP (docetaxel, carboplatin, trastuzumab, and pertuzumab) regimen (preferred regimen)
 - In combination with paclitaxel, carboplatin, and trastuzumab
 - In combination with trastuzumab and docetaxel following AC regimen*
 - In combination with paclitaxel and trastuzumab (useful in certain circumstances)
- For individuals with no response to preoperative systemic therapy, or recurrent unresectable (local or regional) or stage IV (M1) HER2-positive disease that is either hormone receptor-negative or hormone receptor-positive
 - As National Comprehensive Cancer Network (NCCN)-preferred first-line therapy in combination with trastuzumab with either docetaxel or paclitaxel
 - In combination with trastuzumab with or without cytotoxic therapy (e.g., vinorelbine or taxane) for one line of therapy in individuals previously treated with chemotherapy and trastuzumab in the absence of pertuzumab

Invasive Breast Cancer

- As preoperative systemic therapy for individuals with HER2-positive tumors and locally advanced c≥T2 or cN+ and M0 disease (NCCN preferred), or cT1c, cN0 disease
 - As a component of TCHP (docetaxel, carboplatin, trastuzumab, and pertuzumab) regimen (NCCN-preferred regimen)
 - In combination with paclitaxel, carboplatin, and trastuzumab

- In combination with trastuzumab and paclitaxel following AC (doxorubicin and cyclophosphamide) (dose-dense or every 3 weeks) regimen (both useful in certain circumstances)*
- In combination with trastuzumab and docetaxel following AC regimen*
- In combination with paclitaxel and trastuzumab
- As adjuvant systemic therapy** for (pT1-3 and pN0 or pN+ tumors) individuals with node-positive HER2-positive tumors
 - In combination with paclitaxel, carboplatin and trastuzumab
 - In combination with trastuzumab and paclitaxel following AC (doxorubicin and cyclophosphamide) (dose-dense or every 3 weeks) regimen (both useful in certain circumstances)*
 - As a component of TCHP (docetaxel, carboplatin, trastuzumab, and pertuzumab) regimen (NCCN-preferred regimen)
 - In combination with trastuzumab and docetaxel following AC regimen*
 - In combination with paclitaxel and trastuzumab
- As adjuvant systemic therapy for individuals with HER2-positive tumors and locally advanced disease following completion of planned chemotherapy and following mastectomy or breast-conserving surgery (BCS) with surgical axillary staging, with trastuzumab as NCCN-preferred regimen if:
 - ypT0N0 or pCR (especially if node positive at initial staging)
 - ypT1-4N0 (if ado-trastuzumab discontinued for toxicity) (especially if node positive at initial staging)

- ypN≥1 (if ado-trastuzumab discontinued for toxicity) (especially if node positive at initial staging)
- For recurrent unresectable (local or regional) or stage IV (M1) HER2-positive disease that is either hormone receptor-negative or hormone receptor-positive
 - As NCCN preferred first-line therapy in combination with trastuzumab with either docetaxel or paclitaxel
 - In combination with trastuzumab with or without cytotoxic therapy (e.g., vinorelbine or taxane) for one line of therapy in individuals previously treated with chemotherapy and trastuzumab in the absence of pertuzumab

*It is acceptable to change the administration sequence to taxane (with or without HER2-targeted therapy) followed by AC.

**If no residual disease after preoperative therapy, complete up to 1 year of HER2-targeted therapy with trastuzumab with or without pertuzumab after completing planned chemotherapy regimen course. If residual disease is present after preoperative therapy and ado-trastuzumab emtansine is discontinued for toxicity, then trastuzumab with or without pertuzumab to complete 1 year of therapy can be used. (NCCN-preferred regimen).

Metastatic Breast Cancer (MBC)

- For the treatment of individuals with HER2-positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease in combination with trastuzumab and docetaxel.

CENTRAL NERVOUS SYSTEM CANCERS

Limited Brain Metastases with HER2-positive breast cancer

- In combination with high-dose trastuzumab
 - As initial treatment in individuals with small asymptomatic brain metastases
 - As treatment for recurrent brain metastases
 - Treatment of relapsed disease with either stable systemic disease or reasonable systemic treatment options

Extensive Brain Metastases with HER2-positive Breast Cancer

- In combination with high-dose trastuzumab
 - As primary treatment in individuals with small asymptomatic brain metastases
 - As treatment for recurrent disease with stable systemic disease or reasonable systemic treatment options

COLON CANCER

Colon Cancer

- Initial treatment in combination with trastuzumab in individuals (HER2-amplified and RAS and BRAF wild-type) (proficient mismatch repair/microsatellite-stable [pMMR/MSS]) for individuals with unresectable metachronous metastases and previous FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin) within the past 12 months
- Second-line and subsequent therapy (biomarker-directed) in combination with trastuzumab for progression of advanced or metastatic disease (HER2-amplified and RAS and BRAF wild-type) pMMR/MSS or ineligible for or progressed on checkpoint inhibitor immunotherapy for deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] or polymerase epsilon/delta [POLE/POLD1] mutation) not previously treated with HER2 inhibitor

Appendiceal adenocarcinoma

- Initial systemic therapy for advanced or metastatic disease (pMMR/MSS) or ineligible for or progressed on checkpoint inhibitor immunotherapy for dMMR/MSI-H or POLE/POLD1 mutation (HER2-amplified and RAS and BRAF wild-type) in combination with trastuzumab if intensive therapy not recommended and no previous treatment with a HER2 inhibitor
- Second-line and subsequent therapy (biomarker-directed) in combination with trastuzumab for progression of advanced or metastatic disease (pMMR/MSS) or ineligible for or progressed on checkpoint inhibitor immunotherapy for dMMR/MSI-H or POLE/POLD1 mutation (HER2-amplified and RAS and BRAF wild-type) not previously treated with HER2 inhibitor

HEAD AND NECK

- As systemic therapy for HER2-positive recurrent disease in combination with trastuzumab, for one of the following:

- Treatment of individuals with a performance status (PS) of 0–3 with distant metastases
- Treatment of individuals with unresectable locoregional recurrence or second primary with prior radiation therapy

BILIARY TRACT CANCERS

Biliary Tract Cancers: Extrahepatic Cholangiocarcinoma/Gallbladder Cancer/Intrahepatic Cholangiocarcinoma

- As subsequent treatment in combination with trastuzumab for progression on or after systemic treatment for unresectable or resected gross residual (R2) disease, or metastatic disease that is HER2-positive

RECTAL CANCER

- Therapy in combination with trastuzumab in individuals (HER2-amplified and RAS and BRAF wild-type)(pMMR/MSS) or ineligible for or progressed on checkpoint inhibitor immunotherapy for dMMR/MSI-H or POLE/POLD1 mutation if intensive therapy not recommended and no previous treatment with a HER2 inhibitor
 - As primary treatment for synchronous abdominal/peritoneal metastases that are nonobstructing, or following local therapy for individuals with existing or imminent obstruction
 - As primary treatment for synchronous unresectable metastases of other sites
 - As primary treatment for unresectable isolated pelvic/anastomotic recurrence
 - As initial treatment for unresectable metachronous metastases in individuals who have not received previous FOLFOX or CapeOX within the past 12 months, who have received previous fluorouracil/leucovorin (5-FU/LV) or capecitabine therapy, or who have not received any previous chemotherapy
- Primary treatment in combination with trastuzumab for T3, N Any; T1-2, N1-2; T4, N Any; or locally unresectable or medically inoperable disease (HER2-amplified and RAS and BRAF wild-type) if resection is contraindicated following total neoadjuvant therapy (pMMR/MSS or ineligible for or progressed on checkpoint inhibitor immunotherapy for dMMR/MSI-H or POLE/POLD1 mutation) or dMMR/MSI-H if intensive therapy not recommended
- Initial treatment in combination with trastuzumab for individuals (HER2-amplified and RAS and BRAF wild-type) with unresectable metachronous metastases (pMMR/MSS) and

previous FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin) within the past 12 months

- Second-line and subsequent therapy (biomarker-directed therapy) in combination with trastuzumab, if not previously given, for progression of advanced or metastatic disease (HER2-amplified and RAS and BRAF wild-type) (pMMR/MSS or ineligible for or progressed on checkpoint inhibitor immunotherapy for dMMR/MSI-H or POLE/POLD1 mutation) not previously treated with HER2 inhibitor

EXPERIMENTAL/INVESTIGATIONAL

All other uses of pertuzumab (Perjeta®) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

NOT MEDICALLY NECESSARY

When FDA-approved diagnostic tests do not reveal HER2 protein overexpression, pertuzumab (Perjeta®) is considered not medically necessary and, therefore, not covered because the available published peer-reviewed literature does not support its use in the treatment of those diseases.

MANDATES

PENNSYLVANIA MEMBERS

In accordance with the Commonwealth of Pennsylvania's Act 6 of 2020 or Fair Access to Cancer Treatment Act, for members who are enrolled in Pennsylvania commercial products who have Stage 4, advanced metastatic cancer, refer to the Medical Policy titled "Coverage of Anticancer Prescription Oral and Injectable Drugs and Biologics and Supportive Agents" (08.01.08) for additional information regarding the applicable coverage of drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include but are not limited to: records from the professional provider's

office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Duration of authorization: 12 months

Version Effective Date: 04/08/2024

Attachment A: [Pertuzumab \(Perjeta®\)](#)

Description: ICD-10-CM Codes and Narratives

Policy Attachment

Attachment to Policy # 08.01.07j

Attachment: A

Policy #: 08.01.07j

Description: ICD-10-CM Codes and Narratives

Title: Pertuzumab (Perjeta®)

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

ICD-10-CM CODES AND NARRATIVES

C06.9 Malignant neoplasm of mouth, unspecified

C07 Malignant neoplasm of parotid gland

C08.0 Malignant neoplasm of submandibular gland

C08.1 Malignant neoplasm of sublingual gland

C08.9 Malignant neoplasm of major salivary gland, unspecified

C18.0 Malignant neoplasm of cecum

C18.1 Malignant neoplasm of appendix

C18.2 Malignant neoplasm of ascending colon

C18.3 Malignant neoplasm of hepatic flexure

C18.4 Malignant neoplasm of transverse colon

C18.5 Malignant neoplasm of splenic flexure

C18.6 Malignant neoplasm of descending colon

C18.7 Malignant neoplasm of sigmoid colon

C18.8 Malignant neoplasm of overlapping sites of colon

C18.9 Malignant neoplasm of colon, unspecified

C19 Malignant neoplasm of rectosigmoid junction

C20 Malignant neoplasm of rectum

C21.8 Malignant neoplasm of overlapping sites of rectum, anus and anal canal

C22.1 Intrahepatic bile duct carcinoma

C23 Malignant neoplasm of gallbladder

C24.0 Malignant neoplasm of extrahepatic bile duct

C24.8 Malignant neoplasm of overlapping sites of biliary tract

C24.9 Malignant neoplasm of biliary tract, unspecified

C50.011 Malignant neoplasm of nipple and areola, right female breast

C50.012 Malignant neoplasm of nipple and areola, left female breast

C50.019 Malignant neoplasm of nipple and areola, unspecified female breast

C50.021 Malignant neoplasm of nipple and areola, right male breast

C50.022 Malignant neoplasm of nipple and areola, left male breast

C50.029 Malignant neoplasm of nipple and areola, unspecified male breast

C50.111 Malignant neoplasm of central portion of right female breast

C50.112 Malignant neoplasm of central portion of left female breast

C50.119 Malignant neoplasm of central portion of unspecified female breast

C50.121 Malignant neoplasm of central portion of right male breast

C50.122 Malignant neoplasm of central portion of left male breast

C50.129 Malignant neoplasm of central portion of unspecified male breast

C50.211 Malignant neoplasm of upper-inner quadrant of right female breast

C50.212 Malignant neoplasm of upper-inner quadrant of left female breast

C50.219 Malignant neoplasm of upper-inner quadrant of unspecified female breast

C50.221 Malignant neoplasm of upper-inner quadrant of right male breast

C50.222 Malignant neoplasm of upper-inner quadrant of left male breast

C50.229 Malignant neoplasm of upper-inner quadrant of unspecified male breast

C50.311 Malignant neoplasm of lower-inner quadrant of right female breast

C50.312 Malignant neoplasm of lower-inner quadrant of left female breast

C50.319 Malignant neoplasm of lower-inner quadrant of unspecified female breast

C50.321 Malignant neoplasm of lower-inner quadrant of right male breast

C50.322 Malignant neoplasm of lower-inner quadrant of left male breast

C50.329 Malignant neoplasm of lower-inner quadrant of unspecified male breast

C50.411 Malignant neoplasm of upper-outer quadrant of right female breast

C50.412 Malignant neoplasm of upper-outer quadrant of left female breast

C50.419 Malignant neoplasm of upper-outer quadrant of unspecified female breast

C50.421 Malignant neoplasm of upper-outer quadrant of right male breast

C50.422 Malignant neoplasm of upper-outer quadrant of left male breast

C50.429 Malignant neoplasm of upper-outer quadrant of unspecified male breast

C50.511 Malignant neoplasm of lower-outer quadrant of right female breast

C50.512 Malignant neoplasm of lower-outer quadrant of left female breast

C50.519 Malignant neoplasm of lower-outer quadrant of unspecified female breast

C50.521 Malignant neoplasm of lower-outer quadrant of right male breast

C50.522 Malignant neoplasm of lower-outer quadrant of left male breast

C50.529 Malignant neoplasm of lower-outer quadrant of unspecified male breast

C50.611 Malignant neoplasm of axillary tail of right female breast

C50.612 Malignant neoplasm of axillary tail of left female breast

C50.619 Malignant neoplasm of axillary tail of unspecified female breast

C50.621 Malignant neoplasm of axillary tail of right male breast

C50.622 Malignant neoplasm of axillary tail of left male breast

C50.629 Malignant neoplasm of axillary tail of unspecified male breast

C50.811 Malignant neoplasm of overlapping sites of right female breast

C50.812 Malignant neoplasm of overlapping sites of left female breast

C50.819 Malignant neoplasm of overlapping sites of unspecified female breast

C50.821 Malignant neoplasm of overlapping sites of right male breast

C50.822 Malignant neoplasm of overlapping sites of left male breast

C50.829 Malignant neoplasm of overlapping sites of unspecified male breast

C50.911 Malignant neoplasm of unspecified site of right female breast

C50.912 Malignant neoplasm of unspecified site of left female breast

C50.919 Malignant neoplasm of unspecified site of unspecified female breast

C50.921 Malignant neoplasm of unspecified site of right male breast

C50.922 Malignant neoplasm of unspecified site of left male breast

C50.929 Malignant neoplasm of unspecified site of unspecified male breast

C78.5 Secondary malignant neoplasm of large intestine and rectum

C78.6 Secondary malignant neoplasm of retroperitoneum and peritoneum

C79.31 Secondary malignant neoplasm of brain

C79.81 Secondary malignant neoplasm of breast

Version Effective Date: 04/08/2024

Title: Pertuzumab, Trastuzumab, and Hyaluronidase-zzxf (Phesgo®)

MEDICALLY NECESSARY

Pertuzumab, trastuzumab, and hyaluronidase-zzxf (Phesgo), administered subcutaneously by a healthcare professional, is considered medically necessary and, therefore, covered when any of the following criteria are met:

- Use in combination with chemotherapy in individuals with a left ventricular ejection fraction (LVEF) greater than 55 percent for either of the following:
 - Neoadjuvant treatment of individuals with Human Epidermal growth Receptor 2 (HER2)-positive, locally advanced, inflammatory, or early-stage breast cancer (either greater than 2 cm in diameter or node positive) as part of a complete treatment regimen for early breast cancer
 - Adjuvant treatment of individuals with HER2-positive early breast cancer at high risk of recurrence
- Use in combination with docetaxel for treatment of individuals with HER2-positive metastatic breast cancer (MBC), with a LVEF greater than 50 percent, who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease
- Use as a substitute for the combination of intravenous pertuzumab and intravenous trastuzumab when given as part of systemic therapy for either invasive breast cancer (i.e., lobular, mixed, metaplastic, ductal/NST, or micropapillary histology) or inflammatory breast cancer in individuals with a LVEF greater than 50 percent

Pertuzumab, trastuzumab, and hyaluronidase-zzxf (Phesgo) is contraindicated in individuals with known hypersensitivity to pertuzumab, or trastuzumab, or hyaluronidase, or to any of its excipients.

HER2 PROTEIN OVEREXPRESSION TESTING

Coverage of pertuzumab, trastuzumab, and hyaluronidase-zzxf (Phesgo) requires that HER2 protein overexpression is verified as a positive result, and is considered medically necessary and, therefore, covered by one of the following Food and Drug Administration (FDA)-approved

diagnostic tests:

- Immunohistochemical (IHC) assay with a result of 3+
- Fluorescence in situ hybridization (FISH) test (HER2 gene/chromosome 17 ratio greater than 2.0)
- Single probe in situ hybridization (ISH) test with average HER2 copy number of 6.0 signals/cell or greater
- Dual probe ISH test HER2/CEP17 (chromosome enumeration probe 17) ratio 2.0 or greater or HER2/CEP17 ratio less than 2.0 AND average HER2 copy number of 6.0 signals/cell or greater

Confirmatory tests should be performed for borderline results by using the same specimen with an alternative test or by using a new specimen with the same or alternative test as follows:

- If IHC assay has a result of 2+
- If FISH test has a HER2 gene/chromosome 17 ratio of 1.8-2.0
- If single probe ISH assay has an average HER2 copy number result of 4.0 to less than 6.0 signals/cell
- If dual probe ISH assay has a HER2/CEP17 ratio less than 2.0 and an average HER2 copy number result of 4.0 to less than 6.0 signals/cell

NOT MEDICALLY NECESSARY

When FDA-approved diagnostic tests do not reveal HER2 protein overexpression, pertuzumab, trastuzumab, and hyaluronidase-zzxf (Phesgo) are considered not medically necessary and, therefore, not covered because the available published peer-reviewed literature does not support their use in the treatment of those diseases.

EXPERIMENTAL INVESTIGATIONAL

All other uses for pertuzumab, trastuzumab, and hyaluronidase-zzxf (Phesgo) are considered experimental/investigational and, therefore, not covered because their safety and/or effectiveness cannot be established by review of the available published peer-reviewed literature.

MANDATES

PENNSYLVANIA MEMBERS

In accordance with the Commonwealth of Pennsylvania's >Act 6 of 2020< or >Fair Access to Cancer Treatment Act<, for members who are enrolled in Pennsylvania commercial products who have Stage 4, advanced metastatic cancer, refer to the Medical Policy titled "Coverage of Anticancer Prescription Oral and Injectable Drugs and Biologics and Supportive agents" (08.01.08) for additional information regarding the applicable coverage of drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the service.

Duration of authorization: 12 months

Version Effective Date: 04/03/2024

Title: Photodynamic Therapy (PDT) Using Levulan® Kerastick® or Ameluz® (Aminolevulinic Acid HCl [ALA])

MEDICALLY NECESSARY:

Photodynamic therapy (PDT) using Levulan Kerastick with the BLU-U Blue Light Photodynamic Therapy Illuminator is considered medically necessary and, therefore, covered for any of the following indications:

- Field cancerization/confluent epidermal dysplasia
 - Treatment of non-hyperkeratotic actinic keratoses of the face, scalp, or upper extremities
 - Treatment of squamous cell carcinoma in situ (Bowen's disease) in individuals only when surgery AND radiation therapy are contraindicated
- Treatment of superficial basal cell carcinoma in individuals only when surgery AND radiation therapy are contraindicated

PDT using Ameluz with BF RhodoLED lamp is considered medically necessary and, therefore, covered for any of the following indications:

- Field cancerization/confluent epidermal dysplasia
 - Treatment of non-hyperkeratotic actinic keratoses of the face, scalp, or upper extremities
 - Treatment of squamous cell carcinoma in situ (Bowen's disease) in individuals only when surgery AND radiation therapy are contraindicated
- Treatment of superficial basal cell carcinoma in individuals only when surgery AND radiation therapy are contraindicated

Duration of authorization: 12 months

Version Effective Date: 06/12/2024

Title: Polatuzumab vedotin-piiq (Polivy®)

MEDICALLY NECESSARY

Polatuzumab vedotin-piiq (Polivy®) is considered medically necessary and, therefore, covered for a maximum of six cycles in adult individuals for **any** of the following indications:

DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL)

For individuals with DLBCL for **any** of the following:

- First-line therapy for stage II with extensive mesenteric disease or stage III-IV disease as a component of Pola-R-CHP (polatuzumab vedotin-piiq [Polivy], rituximab, cyclophosphamide, doxorubicin, prednisone) regimen for individuals with an International Prognostic Index (IPI) score of 2 or greater (National Comprehensive Cancer Network [NCCN] preferred)
- Used as a single agent or in combination with bendamustine and/or rituximab as second-line and subsequent therapy in individuals who are noncandidates for hematopoietic stem cell transplantation (HSCT) for **any** of the following (NCCN preferred):
 - Relapsed or refractory disease greater than 12 months after completion of first-line therapy
 - Primary refractory disease (partial response, no response, or progression) or relapsed disease less than 12 months after completion of first-line therapy in noncandidates for chimeric antigen receptor (CAR) T-cell therapy
 - Alternative systemic therapy (if not previously given) for relapsed/refractory disease in noncandidates for CAR T-cell therapy
- Used with or without bendamustine and with or without rituximab (consider/add bendamustine only after leukapheresis) as clinically indicated as a bridging option until CAR T-cell product is available for individuals with intention to proceed to CAR T-cell therapy who have primary refractory disease or relapsed disease less than 12 months after completion of first-line therapy

HIGH-GRADE B-CELL LYMPHOMAS

For individuals with high-grade B-cell lymphoma for **either** of the following:

- Used as a single agent or in combination with bendamustine and/or rituximab as second-line and subsequent therapy in noncandidates for HSCT in **any** of the following:
 - Relapsed or refractory disease greater than 12 months after completion of first-line therapy
 - Primary refractory disease (partial response, no response, or progression) or relapsed disease less than 12 months after completion of first-line therapy in noncandidates for CAR T-cell therapy
 - Alternative systemic therapy (if not previously given) for relapsed/refractory disease in noncandidates for CAR T-cell therapy
- Used with or without bendamustine and with or without rituximab (consider/add bendamustine only after leukapheresis) as clinically indicated as a bridging option until CAR T-cell product is available for individuals with intention to proceed to CAR T-cell therapy who have primary refractory disease or relapsed disease less than 12 months after completion of first-line therapy

FOLLICULAR LYMPHOMA (FL) (grade 1-2)

Used as a single agent or in combination with bendamustine and/or rituximab as second-line and subsequent therapy (if not previously given) for no response, relapsed, or progressive disease in individuals with

indications for treatment (e.g., symptoms attributable to the FL, threatened end-organ function, cytopenia secondary to FL, bulky disease [single mass > 7 cm or three or more masses >3 cm], splenomegaly, steady progression over at least 6 months).

HISTOLOGIC TRANSFORMATION OF INDOLENT LYMPHOMAS TO DIFFUSE LARGE B-CELL LYMPHOMA

Used as a single agent or in combination with bendamustine and/or rituximab for treatment of histologic transformation of marginal zone lymphoma or FL without translocations of MYC and BCL2 and/or BCL6 disease to DLBCL in individuals who have received an anthracycline-based regimen (e.g., doxorubicin, epirubicin, daunorubicin) in noncandidates for transplant as either of the following (NCCN preferred):

- As additional therapy for partial response, no response, or progressive disease following chemoimmunotherapy
- For individuals who have received multiple prior therapies for indolent or transformed disease

ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS)/HUMAN IMMUNODEFICIENCY VIRUS (HIV)-RELATED B-CELL LYMPHOMA

For individuals with AIDS/HIV-related B-cell lymphoma as **either** of the following:

- Used as a single agent or in combination with bendamustine and/or rituximab as second-line and subsequent therapy for relapse of AIDS/HIV-related DLBCL, primary effusion lymphoma, and human herpesvirus (HHV)-8-positive DLBCL, not otherwise specified (NOS) or without rituximab for relapse of AIDS/HIV-related plasmablastic lymphoma in noncandidates for HSCT for **any** of the following:
 - Relapsed or refractory disease greater than 12 months after completion of first-line therapy
 - Primary refractory disease (partial response, no response, or progression) or relapsed disease less than 12 months after completion of first-line therapy in noncandidates for CAR T-cell therapy
 - Alternative systemic therapy (if not previously given) for relapsed/refractory disease in noncandidates for CAR T-cell therapy
- Used as a single agent or in combination with bendamustine and/or rituximab (consider/add bendamustine only after leukapheresis) as clinically indicated as a bridging option until CAR T-cell product is available for individuals with intention to proceed to CAR T-cell therapy who have primary refractory disease or relapsed disease less than 12 months after completion of first-line therapy

POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDERS (PTLD)

For individuals with PTLD as **either** of the following:

- Used as a single agent or with bendamustine and/or rituximab second-line and subsequent therapy for individuals with monomorphic PTLD (B-cell type) who are noncandidates for HSCT for **any** of the following:
 - Relapsed or refractory disease greater than 12 months after completion of initial treatment with chemoimmunotherapy
 - Primary refractory disease (partial response, no response, or progression) or relapsed disease less than 12 months after completion of initial treatment with chemoimmunotherapy in noncandidates for CAR T-cell therapy
 - Alternative systemic therapy (if not previously given) for relapsed/refractory disease in noncandidates for CAR T-cell therapy
- Used as clinically indicated as a single agent or in combination with bendamustine and/or rituximab as a bridging option (consider/add bendamustine only after leukapheresis) until CAR T-cell product is available for individuals with intention to proceed to CAR T-cell therapy who have primary refractory disease or relapsed disease less than 12 months after completion of initial treatment with chemoimmunotherapy

EXPERIMENTAL/INVESTIGATIONAL

All other uses for polatuzumab vedotin-piiq (Polivy) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy titled "Off-label Coverage for Prescription Drugs and Biologics" (08.00.15f).

MANDATE

PENNSYLVANIA MEMBERS

In accordance with the Commonwealth of Pennsylvania's Act 6 of 2020 or Fair Access to Cancer Treatment Act, for members who are enrolled in Pennsylvania commercial products who have Stage 4, advanced metastatic cancer, refer to the medical policy titled "Coverage of Anticancer Prescription Oral and Injectable Drugs and Biologics and Supportive Agents" (08.01.08) for additional information regarding the applicable coverage of drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the service.

Duration of authorization: 12 months

Version Effective Date: 10/30/2024

Title: Pozelimab-bbfg (Veopoz TM)

MEDICALLY NECESSARY

INITIAL THERAPY

Pozelimab-bbfg (Veopoz™) is considered medically necessary and, therefore, covered for the treatment of individuals one year of age and older with cluster of differentiation (CD)55-deficient protein-losing enteropathy (PLE), also known as CHAPLE (complement hyperactivation, angiopathic thrombosis and protein-losing enteropathy) disease, when **all** of the following are met:

- Presence of laboratory-confirmed genotype of biallelic CD55 loss-of-function mutation
- Presence of at least **one** of the following symptoms, attributable to CHAPLE disease, within the last six months (unless the individual is currently being treated with eculizumab [Soliris®] therapy with the willingness by the professional provider to discontinue the treatment before initiating treatment with pozelimab-bbfg [Veopoz]):
 - Hypoalbuminemia (serum albumin concentration of 3.2 g/dL or less)
 - Facial edema
 - Peripheral edema
 - Diarrhea
 - Abdominal pain
 - Thromboembolic event(s)
- Completion or update of meningococcal vaccination (in serogroups A, C, W and Y, and serogroup B) at least two weeks prior to the planned start of pozelimab-bbfg (Veopoz) therapy unless the risks of delaying therapy outweigh the risks of developing meningococcal infection (follow the most current Advisory Committee on Immunization Practices [ACIP] recommendations for meningococcal vaccination)
- Pozelimab-bbfg (Veopoz) is ordered by, or in consultation with, a professional provider who has the expertise to treat CHAPLE disease (e.g., Gastroenterology, Hematology, Immunology, rare genetic hematologic disease specialist)
- The individual will not be concurrently treated with any other complement inhibitors
- The individual does not have unresolved *Neisseria meningitidis* infection at the start of treatment with pozelimab-bbfg (Veopoz)

CONTINUATION THERAPY

Continuation of pozelimab-bbfg (Veopoz) will be considered to be medically necessary when all of the following are met:

- Hypoalbuminemia has improved or resolved from baseline levels
- Symptoms have improved or resolved from baseline levels

EXPERIMENTAL/INVESTIGATIONAL

All other uses of pozelimab-bbfg (Veopoz) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the service.

Duration of authorization: 12 months

Version Effective Date: 05/28/2025

Title: Radioimmunotherapy with Ibritumomab Tiuxetan (Zevalin®) (Independence Administrators)

MEDICALLY NECESSARY

A single course of radioimmunotherapy with ibritumomab tiuxetan (Zevalin®) is considered medically necessary and, therefore, covered for the following non-Hodgkin's lymphoma (NHL)--related indications:

FOLLICULAR LYMPHOMA

- In the treatment of individuals with relapsed or refractory, CD20-positive, low-grade or follicular, B-cell NHL, including individuals with rituximab-refractory follicular NHL
- In the treatment of individuals with previously untreated CD20-positive, B-cell follicular NHL who achieve a partial or complete response to first-line chemotherapy
- In the initial treatment of low grade, CD20-positive, B-cell follicular NHL in individuals unable to tolerate standard chemotherapy (e.g., elderly or infirm individuals)
- In the treatment of histologic transformation of follicular lymphoma (grade 1-2) to diffuse large B-cell lymphoma (DLBCL) in individuals who have received:
 - Minimal or no chemotherapy prior to histologic transformation to DLBCL and have partial response, no response, or progressive disease after chemoimmunotherapy, or
 - Multiple prior therapies including two or more lines of chemoimmunotherapy for indolent or transformed disease

MARGINAL ZONE LYMPHOMA

- As a subsequent therapy for histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma (DLBCL) in individuals who have received:
 - Minimal or no chemotherapy prior to histologic transformation to DLBCL and have partial response, no response, or progressive disease after chemoimmunotherapy, or
 - Multiple prior therapies including two or more lines of chemoimmunotherapy for indolent or transformed disease

PRIMARY CUTANEOUS DIFFUSE LARGE B-CELL LYMPHOMA

- As a second-line or subsequent therapy for relapsed or refractory primary cutaneous diffuse large B-cell lymphoma (DLBCL), leg type

EXPERIMENTAL/INVESTIGATIONAL

The use of ibritumomab tiuxetan (Zevalin®) beyond a single course of treatment is considered experimental/investigational and, therefore, not covered because the safety and/or effectiveness of this regimen cannot be established by review of the available published literature.

All other uses of ibritumomab tiuxetan (Zevalin®) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the service.

Duration of authorization: 12 months

Version Effective Date: 10/01/2024

Attachment A: [Radioimmunotherapy with Ibritumomab Tiuxetan \(Zevalin®\) \(Independence Administrators\)](#)

Description: ICD-10 Codes

Policy Attachment

Attachment to Policy # 08.00.08k

Attachment: A

Policy #: 08.00.08k

Description: ICD-10 Codes

Title: Radioimmunotherapy with Ibritumomab Tiuxetan (Zevalin®) (Independence Administrators)

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

C82.00 Follicular lymphoma grade I, unspecified site

C82.01 Follicular lymphoma grade I, lymph nodes of head, face, and neck

C82.02 Follicular lymphoma grade I, intrathoracic lymph nodes

C82.03 Follicular lymphoma grade I, intra-abdominal lymph nodes

C82.04 Follicular lymphoma grade I, lymph nodes of axilla and upper limb

C82.05 Follicular lymphoma grade I, lymph nodes of inguinal region and lower limb

C82.06 Follicular lymphoma grade I, intrapelvic lymph nodes

C82.07 Follicular lymphoma grade I, spleen

C82.08 Follicular lymphoma grade I, lymph nodes of multiple sites

C82.09 Follicular lymphoma grade I, extranodal and solid organ sites

C82.10 Follicular lymphoma grade II, unspecified site

C82.11 Follicular lymphoma grade II, lymph nodes of head, face, and neck

C82.12 Follicular lymphoma grade II, intrathoracic lymph nodes

C82.13 Follicular lymphoma grade II, intra-abdominal lymph nodes

C82.14 Follicular lymphoma grade II, lymph nodes of axilla and upper limb

C82.15 Follicular lymphoma grade II, lymph nodes of inguinal region and lower limb

C82.16 Follicular lymphoma grade II, intrapelvic lymph nodes

C82.17 Follicular lymphoma grade II, spleen

C82.18 Follicular lymphoma grade II, lymph nodes of multiple sites

C82.19 Follicular lymphoma grade II, extranodal and solid organ sites

C82.20 Follicular lymphoma grade III, unspecified, unspecified site

C82.21 Follicular lymphoma grade III, unspecified, lymph nodes of head, face, and neck

C82.22 Follicular lymphoma grade III, unspecified, intrathoracic lymph nodes

C82.23 Follicular lymphoma grade III, unspecified, intra-abdominal lymph nodes

C82.24 Follicular lymphoma grade III, unspecified, lymph nodes of axilla and upper limb

C82.25 Follicular lymphoma grade III, unspecified, lymph nodes of inguinal region and lower limb

C82.26 Follicular lymphoma grade III, unspecified, intrapelvic lymph nodes

C82.27 Follicular lymphoma grade III, unspecified, spleen

C82.28 Follicular lymphoma grade III, unspecified, lymph nodes of multiple sites

C82.29 Follicular lymphoma grade III, unspecified, extranodal and solid organ sites

C82.30 Follicular lymphoma grade IIIa, unspecified site

C82.31 Follicular lymphoma grade IIIa, lymph nodes of head, face, and neck

C82.32 Follicular lymphoma grade IIIa, intrathoracic lymph nodes

C82.33 Follicular lymphoma grade IIIa, intra-abdominal lymph nodes

C82.34 Follicular lymphoma grade IIIa, lymph nodes of axilla and upper limb

C82.35 Follicular lymphoma grade IIIa, lymph nodes of inguinal region and lower limb

C82.36 Follicular lymphoma grade IIIa, intrapelvic lymph nodes

C82.37 Follicular lymphoma grade IIIa, spleen

C82.38 Follicular lymphoma grade IIIa, lymph nodes of multiple sites

C82.39 Follicular lymphoma grade IIIa, extranodal and solid organ sites

C82.40 Follicular lymphoma grade IIIb, unspecified site

C82.41 Follicular lymphoma grade IIIb, lymph nodes of head, face, and neck

C82.42 Follicular lymphoma grade IIIb, intrathoracic lymph nodes

C82.43 Follicular lymphoma grade IIIb, intra-abdominal lymph nodes

C82.44 Follicular lymphoma grade IIIb, lymph nodes of axilla and upper limb

C82.45 Follicular lymphoma grade IIIb, lymph nodes of inguinal region and lower limb

C82.46 Follicular lymphoma grade IIIb, intrapelvic lymph nodes

C82.47 Follicular lymphoma grade IIIb, spleen

C82.48 Follicular lymphoma grade IIIb, lymph nodes of multiple sites

C82.49 Follicular lymphoma grade IIIb, extranodal and solid organ sites

C82.50 Diffuse follicle center lymphoma, unspecified site

C82.51 Diffuse follicle center lymphoma, lymph nodes of head, face, and neck

C82.52 Diffuse follicle center lymphoma, intrathoracic lymph nodes

C82.53 Diffuse follicle center lymphoma, intra-abdominal lymph nodes

C82.54 Diffuse follicle center lymphoma, lymph nodes of axilla and upper limb

C82.55 Diffuse follicle center lymphoma, lymph nodes of inguinal region and lower limb

C82.56 Diffuse follicle center lymphoma, intrapelvic lymph nodes

C82.57 Diffuse follicle center lymphoma, spleen

C82.58 Diffuse follicle center lymphoma, lymph nodes of multiple sites

C82.59 Diffuse follicle center lymphoma, extranodal and solid organ sites

C82.60 Cutaneous follicle center lymphoma, unspecified site

C82.61 Cutaneous follicle center lymphoma, lymph nodes of head, face, and neck

C82.62 Cutaneous follicle center lymphoma, intrathoracic lymph nodes

C82.63 Cutaneous follicle center lymphoma, intra-abdominal lymph nodes

C82.64 Cutaneous follicle center lymphoma, lymph nodes of axilla and upper limb

C82.65 Cutaneous follicle center lymphoma, lymph nodes of inguinal region and lower limb

C82.66 Cutaneous follicle center lymphoma, intrapelvic lymph nodes

C82.67 Cutaneous follicle center lymphoma, spleen

C82.68 Cutaneous follicle center lymphoma, lymph nodes of multiple sites

C82.69 Cutaneous follicle center lymphoma, extranodal and solid organ sites

C82.80 Other types of follicular lymphoma, unspecified site

C82.81 Other types of follicular lymphoma, lymph nodes of head, face, and neck

C82.82 Other types of follicular lymphoma, intrathoracic lymph nodes

C82.83 Other types of follicular lymphoma, intra-abdominal lymph nodes

C82.84 Other types of follicular lymphoma, lymph nodes of axilla and upper limb

C82.85 Other types of follicular lymphoma, lymph nodes of inguinal region and lower limb

C82.86 Other types of follicular lymphoma, intrapelvic lymph nodes

C82.87 Other types of follicular lymphoma, spleen

C82.88 Other types of follicular lymphoma, lymph nodes of multiple sites

C82.89 Other types of follicular lymphoma, extranodal and solid organ sites

C82.90 Follicular lymphoma, unspecified, unspecified site

C82.91 Follicular lymphoma, unspecified, lymph nodes of head, face, and neck

C82.92 Follicular lymphoma, unspecified, intrathoracic lymph nodes

C82.93 Follicular lymphoma, unspecified, intra-abdominal lymph nodes

C82.94 Follicular lymphoma, unspecified, lymph nodes of axilla and upper limb

C82.95 Follicular lymphoma, unspecified, lymph nodes of inguinal region and lower limb

C82.96 Follicular lymphoma, unspecified, intrapelvic lymph nodes

C82.97 Follicular lymphoma, unspecified, spleen

C82.98 Follicular lymphoma, unspecified, lymph nodes of multiple sites

C82.99 Follicular lymphoma, unspecified, extranodal and solid organ sites

C83.30 Diffuse large B-cell lymphoma, unspecified site

C83.31 Diffuse large B-cell lymphoma, lymph nodes of head, face, and neck

C83.32 Diffuse large B-cell lymphoma, intrathoracic lymph nodes

C83.33 Diffuse large B-cell lymphoma, intra-abdominal lymph nodes

C83.34 Diffuse large B-cell lymphoma, lymph nodes of axilla and upper limb

C83.35 Diffuse large B-cell lymphoma, lymph nodes of inguinal region and lower limb

C83.36 Diffuse large B-cell lymphoma, intrapelvic lymph nodes

C83.37 Diffuse large B-cell lymphoma, spleen

C83.38 Diffuse large B-cell lymphoma, lymph nodes of multiple sites

C83.390 Primary central nervous system lymphoma

C83.398 Diffuse large B-cell lymphoma of other extranodal and solid organ sites

C83.3A Diffuse large B-cell lymphoma, in remission

C83.5A Lymphoblastic (diffuse) lymphoma, in remission

C83.7A Burkitt lymphoma, in remission

C83.8A Other non-follicular lymphoma, in remission

C83.9A Non-follicular (diffuse) lymphoma, unspecified, in remission

C88.40 Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue [MALT-lymphoma] not having achieved remission

Z85.72 Personal history of non-Hodgkin lymphomas

Version Effective Date: 10/01/2024

Title: Radium Ra 223 dichloride (Xofigo®) Injection (Independence Administrators)

MEDICALLY NECESSARY

Radium Ra 223 dichloride (Xofigo®) injection is considered medically necessary and, therefore, covered for a maximum of six injections for the treatment of castration resistant prostate cancer (also known as hormone resistant prostate cancer) when all of the following criteria are met:

- The individual has castration (hormone) resistant prostate cancer, as defined by:
 - A serum testosterone level of less than < 50 ng/dL and either
- 1. Sequential rise of prostate specific antigen (PSA) levels or
- 2. Worsening of existing bone metastases or development of new bone metastases on a bone scan performed within the past 60 days despite androgen-deprivation treatment
 - Documented failure of available hormonal therapies. The individual may be kept on their ablative hormonal treatment to maintain castrate levels of serum testosterone.
- The individual has symptomatic skeletal (bone) metastases
- The individual has no evidence of visceral metastases or bulky regional lymph nodes > 3 cm on imaging performed within the past 30 days

EXPERIMENTAL/INVESTIGATIONAL

All other uses for radium Ra 223 dichloride (Xofigo®) injection, including the use of more than six injections, are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

BILLING REQUIREMENTS

Inclusion of a code in this policy does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

If there is no specific HCPCS code available for the drug administered, then the drug must be reported with the most appropriate unlisted code along with the corresponding National Drug Code (NDC).

Duration of authorization: 12 months

Version Effective Date: 06/11/2025

Title: Ramucirumab (Cyramza®)

MEDICALLY NECESSARY

COLON AND RECTAL CANCERS

Ramucirumab (Cyramza) is considered medically necessary and, therefore, covered for adult individuals with colon and/or rectal cancer and **one** of the following:

- In combination with FOLFIRI (folinic acid, 5-fluorouracil [5FU], irinotecan) regimen for the treatment of metastatic colorectal cancer (mCRC) with disease progression on or after prior therapy with bevacizumab, oxaliplatin, and a fluoropyrimidine.
- Primary treatment, in combination with irinotecan or FOLFIRI regimen, for unresectable metachronous metastases (proficient mismatch repair/microsatellite-stable [pMMR/MSS]) in individuals previously treated with adjuvant FOLFOX (folinic acid, 5FU, oxaliplatin) regimen or CapeOX (capecitabine and oxaliplatin) regimen within the past 12 months.
- Second-line and subsequent therapy for progression of advanced or metastatic (pMMR/MSS) disease (including appendiceal adenocarcinoma) or ineligible for or progressed on checkpoint inhibitor immunotherapy for deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] or polymerase epsilon/delta [POLE/POLD1] mutation) in combination with irinotecan or with FOLFIRI regimen in individuals not previously treated with irinotecan-based therapy or not previously treated with oxaliplatin or irinotecan.

ESOPHAGEAL AND ESOPHAGOGASTRIC JUNCTION CANCERS

Ramucirumab (Cyramza) is considered medically necessary and, therefore, covered for adult individuals with esophageal or esophagogastric junction cancer and **one** of the following:

- As a single agent, or in combination with paclitaxel, for the treatment of advanced or metastatic gastric or gastroesophageal junction adenocarcinoma with disease progression on or after prior fluoropyrimidine- or platinum-containing chemotherapy
- Palliative therapy for individuals who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic adenocarcinoma and Karnofsky performance score (PS) of 60 percent or greater or Eastern Cooperative Oncology Group (ECOG) PS of 2 or less as second-line or subsequent therapy in **one** of the following regimens:
 - In combination with paclitaxel (National Comprehensive Cancer Network [NCCN] preferred)

- In combination with irinotecan with or without 5FU
- As a single agent

GASTRIC CANCERS

Ramucirumab (Cyramza) is considered medically necessary and, therefore, covered for adult individuals with gastric cancer and **one** of the following:

- As a single agent, or in combination with paclitaxel, for the treatment of advanced or metastatic gastric or gastroesophageal junction adenocarcinoma with disease progression on or after prior fluoropyrimidine- or platinum-containing chemotherapy
- Palliative therapy for locoregional disease for individuals who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease (including peritoneal and positive cytology) and Karnofsky PS of 60 percent or greater or ECOG PS of 2 or less as second-line or subsequent therapy in one of the following regimens:
 - In combination with paclitaxel (NCCN preferred)
 - With irinotecan with or without 5FU
 - As a single agent

HEPATOCELLULAR CARCINOMA (HCC)

Ramucirumab (Cyramza) is considered medically necessary and, therefore, covered for adult individuals with HCC as subsequent treatment as a single agent for progressive disease in individuals with alpha-fetoprotein (AFP*) of 400 ng/mL or greater, and Child-Pugh Class A only and who meet **one** of the following criteria:

- Unresectable disease and not a transplant candidate
- Have liver-confined disease
- Metastatic/extrahepatic disease and not a candidate for transplant, resection or locoregional therapy
- For the treatment of individuals with HCC who have been treated with sorafenib (Nexavar)

*Alpha-fetoprotein (AFP) is an oncofetal protein produced by HCC.

MESOTHELIOMA: PLEURAL

Ramucirumab (Cyramza) is considered medically necessary and, therefore, covered for adult

individuals with pleural mesothelioma (may also be used for pericardial mesothelioma and tunica vaginalis testis mesothelioma) as subsequent systemic therapy in combination with gemcitabine.

NON-SMALL CELL LUNG CANCER (NSCLC)

Ramucirumab (Cyramza) is considered medically necessary and, therefore, covered for adult individuals with non-small cell lung cancer (NSCLC) and **one** of the following:

- For the treatment of individuals with metastatic NSCLC in combination with docetaxel who have disease progression on or after platinum-based chemotherapy
 - Individuals with epidermal growth factor receptor (EGFR) or anaplastic lymphoma kinase (ALK) genomic tumor aberrations should have disease progression on a US Food and Drug Administration (FDA)-approved therapy (e.g., erlotinib [Tarceva], crizotinib [Xalkori]) for the aberration prior to receiving ramucirumab (Cyramza).
- As subsequent therapy for the first progression after initial systemic therapy (excluding locoregional recurrence or symptomatic local disease but including mediastinal lymph node recurrence with prior radiation therapy) in combination with docetaxel (if not previously given) for recurrent, advanced, or metastatic NSCLC when the individual has ECOG PS 0 to 2
- For first-line treatment of individuals with metastatic NSCLC with EGFR exon 19 deletions or exon 21 (L858R) mutations in combination with erlotinib (Tarceva)
- In combination with erlotinib (Tarceva) for EGFR exon 19 deletion or exon 21 L858R mutation-positive recurrent, advanced, or metastatic NSCLC disease (excluding locoregional recurrence or symptomatic local disease but including mediastinal lymph node recurrence with prior radiation therapy) for either of the following:
 - As first-line therapy
 - Continuation of therapy following disease progression on combination of erlotinib (Tarceva) and ramucirumab (Cyramza) for asymptomatic disease, symptomatic brain lesions, or symptomatic systemic limited progression (if T790M negative)

EXPERIMENTAL/INVESTIGATIONAL

All other uses for ramucirumab (Cyramza) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

MANDATES

PENNSYLVANIA MEMBERS

In accordance with the Commonwealth of Pennsylvania's Act 6 of 2020 or Fair Access to Cancer Treatment Act, for members who are enrolled in Pennsylvania commercial products who have Stage 4, advanced metastatic cancer, refer to the Medical Policy titled "Coverage of Anticancer Prescription Oral and Injectable Drugs and Biologics and Supportive Agents" (08.01.08) for additional information regarding the applicable coverage of drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Duration of authorization: 12 months

Version Effective Date: 07/15/2024

Title: Repository Corticotropin Injection (Acthar® Gel, Purified Cortrophin[™] Gel)

MEDICALLY NECESSARY

WEST SYNDROME

Repository corticotropin injection (Acthar Gel) for West syndrome (infantile spasms) is considered medically necessary and, therefore, covered for a period of 12 months when both of the following criteria are met:

- The individual is diagnosed with West syndrome (infantile spasms)
- The individual is 2 years of age or younger

In accordance with the US Food and Drug Administration (FDA)-approved prescribing information labeling, repository corticotropin injection (Acthar Gel) dosing for the treatment of West syndrome (infantile spasms) is as follows:

- Dosage should be given via intramuscular injections of 75 U/m² twice daily
- Dosing should be tapered after 2 weeks and eventually discontinued over a 2-week period to avoid adrenal insufficiency
- Tapering schedule: 30 U/m² in the morning for 3 days, 15 U/m² in the morning for 3 days, 10 U/m² in the morning for 3 days, then 10 U/m² every other morning for 6 days

NOT MEDICALLY NECESSARY

MULTIPLE SCLEROSIS

The Company's products contain a definition of medical necessity that includes a requirement that a service not be more costly than an alternative service that is at least as likely to produce equivalent therapeutic or diagnostic results for the treatment of that individual's illness. Repository corticotropin injection (Acthar Gel, Purified Cortrophin Gel) is considered not medically necessary and, therefore, not covered for the treatment of acute exacerbations of multiple sclerosis because it is more costly than an alternative service that is at least as likely to produce equivalent therapeutic results for that individual's illness.

OTHER INDICATIONS

Coverage for repository corticotropin injection (Acthar Gel, Purified Cortrophin Gel) for the treatment of additional indications on the prescribing label may depend on the Company's applicable health benefit plan definition of medical necessity. The Company's products contain definitions of medical necessity that include a requirement that a service be covered in accordance with generally accepted standards of medical practice.

Generally accepted standards of medical practice means standards that are based on all of the following:

- Credible scientific evidence, published in peer-reviewed medical literature that is generally recognized by the relevant medical community
- Physician specialty society recommendations
- Views of physicians practicing in relevant clinical areas
- Other relevant factors

Because repository corticotropin injection (Acthar Gel, Purified Cortrophin Gel) for the treatment of conditions other than West syndrome is not based on generally accepted standards of medical practice and does not meet the requirement that a service not be more costly than an alternative service that is at least as likely to produce equivalent therapeutic or diagnostic results to the treatment of that individual's illness, repository corticotropin injection (Acthar Gel, Purified Cortrophin Gel) is considered not medically necessary for additional indications under those benefit plans. Some examples of indications that are considered not medically necessary and, therefore, not covered are:

- Rheumatic disorders: psoriatic arthritis, rheumatoid arthritis, juvenile rheumatoid arthritis, ankylosing spondylitis,

acute gouty arthritis (Purified Cortrophin Gel)

- Collagen disease: systemic lupus erythematosus, systemic dermatomyositis (polymyositis)
- Dermatologic disease: severe erythema multiforme, Stevens-Johnson syndrome, severe psoriasis (Purified Cortrophin Gel)
- Allergic states: serum sickness, atopic dermatitis (Purified Cortrophin Gel)
- Ophthalmic diseases: keratitis, iritis, iridocyclitis, diffuse posterior uveitis, choroiditis, optic neuritis, chorioretinitis, anterior segment inflammation, allergic conjunctivitis (Purified Cortrophin Gel)
- Respiratory: symptomatic sarcoidosis
- To induce a diuresis or a remission of proteinuria in the nephrotic syndrome without uremia of the idiopathic type or that due to lupus erythematosus
- Corticosteroid-responsive conditions
- Diagnostic testing for adrenocortical function

OFF-LABEL INDICATIONS

Repository corticotropin injection (Acthar Gel, Purified Cortrophin Gel) is considered not medically necessary and, therefore, not covered for any indications supported as an off-label indication, by the Company's medical policy on off-label coverage for prescription drugs and biologics due to the lack of supporting evidence of effectiveness and safety through controlled clinical studies or clinical practice guidelines.

EXPERIMENTAL/INVESTIGATIONAL

All other uses for repository corticotropin injection (Acthar Gel, Purified Cortrophin Gel) are considered experimental/investigational and, therefore, not covered because the indication is not supported as an accepted off-label use, as defined in the Company medical policy on Off-label Coverage for Prescription Drugs and Biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Duration of authorization: 12 months

Version Effective Date: 07/24/2024

Title: Retifanlimab-dlwr (Zynyz®)

MEDICALLY NECESSARY

ANAL CARCINOMA

Retifanlimab-dlwr (Zynyz®) is considered medically necessary and, therefore, covered as an intravenous infusion for the treatment of individuals 18 years of age or older with metastatic squamous carcinoma of the anal canal as second-line and subsequent therapy as a single agent if no prior immunotherapy received (National Comprehensive Cancer Network [NCCN] preferred).

MERKEL CELL CARCINOMA

Retifanlimab-dlwr (Zynyz) is considered medically necessary and, therefore, covered as an intravenous infusion for the treatment of individuals 18 years of age or older with metastatic or recurrent locally advanced Merkel cell carcinoma (MCC) when BOTH of the following criteria are met:

- Diagnosis of MCC with distant metastatic disease or recurrent advanced locoregional disease not amenable to surgery or radiation
- No prior systemic therapy for MCC including chemotherapy and prior programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1)-directed therapy
- As single-agent treatment for **ONE** of the following:
 - For primary clinical N0 locally advanced disease if curative surgery and curative radiation therapy (RT) are not feasible, or for progression on neoadjuvant nivolumab
 - For recurrent N0 locally advanced disease if curative surgery and curative RT are not feasible (NCCN preferred)
 - For recurrent N+ regional disease if curative surgery and curative RT are not feasible (NCCN preferred)
 - For M1 disseminated disease (NCCN preferred)
- No known central nervous system (CNS) metastases and/or carcinomatous meningitis

EXPERIMENTAL/INVESTIGATIONAL

All other uses of retifanlimab-dlwr (Zynyz) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the medical policy on off-label coverage for prescription drugs and biologics.

MANDATES

PENNSYLVANIA MEMBERS

In accordance with the Commonwealth of Pennsylvania's Act 6 of 2020 or Fair Access to Cancer Treatment Act, for members who are enrolled in Pennsylvania commercial products who have Stage 4, advanced metastatic cancer, refer to the Medical Policy titled "Coverage of Anticancer Prescription Oral and Injectable Drugs and Biologics and Supportive agents" (08.01.08) for additional information regarding the applicable coverage of drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Duration of authorization: 12 months

Version Effective Date: 09/09/2024

Title: Risankizumab-rzaa (Skyrizi®) for Intravenous Use

MEDICALLY NECESSARY

ULCERATIVE COLITIS

Risankizumab-rzaa (Skyrizi) for intravenous use is considered medically necessary and, therefore, covered for moderately to severely active ulcerative colitis when all of the following criteria, including dosing and frequency, are met:

- The individual is 18 years of age or older
- There is documentation of inadequate response, contraindication, or intolerance to conventional (nonadvanced) and/or advanced therapies of at least one of the following:
 - Corticosteroids (e.g., budesonide, prednisone, hydrocortisone, methylprednisolone)
 - Biologic therapy (e.g., infliximab [Remicade]), adalimumab [Humira], golimumab [Simponi Aria], vedolizumab [Entyvio])
 - Immunomodulators (e.g., azathioprine, 6-mercaptopurine, methotrexate)
 - JAK Inhibitors (e.g., tofacitinib [Xeljanz], Upadacitinib [Rinvoq])
 - S1P receptor modulators (e.g., ozanimod [Zeposia])
- Prescribed by or in consultation with a gastroenterologist
- No concurrent use with any other biologic therapy (i.e., tumor necrosis factor antagonists)
- Dosing and frequency: induction dosage is 1200 mg administered by intravenous infusion at Week 0, Week 4, and Week 8. The recommended maintenance dosage is 180 mg or 360 mg administered by subcutaneous injection at Week 12, and every 8 weeks thereafter.

CROHN'S DISEASE

Risankizumab-rzaa (Skyrizi) for intravenous use is considered medically necessary and, therefore, covered for moderately to severely active Crohn's disease when all of the following criteria, including dosing and frequency, are met:

- The individual is 18 years of age or older
- There is documentation of failure, contraindication, or intolerance to a trial of at least one of the following:

- Corticosteroids (e.g., budesonide [Entocort EC], prednisone, hydrocortisone, methylprednisolone)
- Immunomodulators (e.g., azathioprine, 6-mercaptopurine, methotrexate)
- Biologic therapy (e.g., certolizumab [Cimzia], adalimumab [Humira], infliximab [Remicade]), ustekinumab (Stelara), vedolizumab [Entyvio])
- Prescribed by or in consultation with a gastroenterologist
- No concurrent use with any other biologic therapy (i.e., tumor necrosis factor antagonists)
- Dosing and frequency: 600 mg administered by intravenous infusion at Weeks 0, 4, and 8. (Maintenance doses are administered by subcutaneous injection.)

EXPERIMENTAL/INVESTIGATIONAL

All other uses for risankizumab-rzaa (Skyrizi) for intravenous use are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

DOSING AND FREQUENCY REQUIREMENTS

The Company reserves the right to modify the Dosing and Frequency Requirements listed in this policy to ensure consistency with the most recently published recommendations for the use of risankizumab-rzaa (Skyrizi). Changes to these guidelines are based on a consensus of information obtained from resources such as, but not limited to, the US Food and Drug Administration (FDA); Company-recognized authoritative pharmacology compendia; or published peer-reviewed clinical research. The professional provider must supply supporting documentation (i.e., published peer-reviewed literature) to request coverage for an amount of risankizumab-rzaa (Skyrizi) outside of the Dosing and Frequency Requirements listed in this policy. For a list of Company-recognized pharmacology compendia, view our policy on off-label coverage for prescription drugs and biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of this drug. If the member's dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider must submit those changes to the Company for a new approval based on those changes as part of the

utilization management activities. The Company reserves the right to conduct postpayment review and audit procedures for any claims submitted for risankizumab-rzaa (Skyrizi).

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the service.

When coverage of risankizumab-rzaa (Skyrizi) is requested outside of the Dosing and Frequency Requirements listed in this policy, the prescribing professional provider must supply documentation (i.e., published peer-reviewed literature) to the Company that supports this request.

Duration of authorization: 12 months

Version Effective Date: 10/21/2024

Title: Rituximab (Rituxan®) Infusion and Related Biosimilars, and Rituximab/Hyaluronidase Human for Subcutaneous Injection (Rituxan Hycela®)

MEDICALLY NECESSARY

RITUXIMAB AND RELATED BIOSIMILARS

- Antineutrophil cytoplasmic antibodies (ANCA)–associated vasculitides (granulomatosis with polyangiitis, microscopic polyangiitis [MPA], eosinophilic granulomatosis with polyangiitis [EGPA] [formerly Churg-Strauss syndrome], pauci-immune glomerulonephritis)
- Anemia, autoimmune hemolytic (AIHA)
- Castleman disease (CD), multicentric and unicentric
- Central nervous system cancers
- Hematopoietic cell transplantation

- Idiopathic membranous nephropathy
- Immunoglobulin G4 (IgG4)–related disease

- Toxicities related to immune checkpoint inhibitors
- Leukemia, mature B-cell acute leukemia (B-AL)
- Leukemia, acute lymphoblastic (ALL)
- Lupus nephritis
- Lymphoma, Hodgkin
- Lymphoma, non-Hodgkin (NHL)
 - High-grade B-cell lymphomas (HGBLs)
 - HIV-related B-cell lymphoma
 - Burkitt lymphoma
 - Burkitt-like lymphoma
 - Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)
 - Diffuse large B-cell lymphoma
 - Extranodal marginal zone lymphoma of the stomach
 - Follicular lymphoma
 - Hairy cell leukemia
 - Histiocytic neoplasms (Rosai-Dorfman disease)
 - Histologic transformation of indolent lymphomas to diffuse large B-cell lymphoma
 - Mantle cell lymphoma
 - Nodal marginal zone lymphoma
 - Nongastric mucosa-associated lymphoid tissue (MALT) lymphoma (noncutaneous)
 - Pediatric aggressive mature B-cell lymphomas (age 6 months and older)
 - Burkitt lymphoma and diffuse large B-cell lymphoma

- Primary mediastinal large B-cell lymphoma
 - Posttransplantation lymphoproliferative disorder (PTLD)
 - Primary cutaneous B-cell lymphoma
 - Splenic marginal zone lymphoma
 - Multiple sclerosis, relapsing-remitting
 - Myasthenia gravis
 - Nephrotic syndrome, including minimal change disease, in pediatric individuals
 - Neuromyelitis optica (NMO)
 - Pemphigoid diseases
 - Pemphigus diseases (i.e., pemphigus vulgaris, pemphigus foliaceus, and paraneoplastic pemphigus)
 - Pure red cell aplasia
 - Rheumatoid arthritis, active
 - Scleroderma
 - Sjögren syndrome, primary
 - Systemic lupus erythematosus (SLE)
 - Thrombocytopenic purpura, immune or idiopathic (ITP)
 - Thrombocytopenic purpura, thrombotic (TTP)
 - Transplantation, prophylaxis
 - Transplantation, antibody-mediated rejection (AMR)
 - Waldenström macroglobulinemia/lymphoplasmacytic lymphoma
- RITUXIMAB AND HYALURONIDASE HUMAN (RITUXAN HYCELA)
- Castleman disease (CD)
 - Lymphoma, Hodgkin
 - Lymphoma, non-Hodgkin (NHL)
 - Chronic lymphocytic leukemia (CLL)
 - Diffuse large B-cell lymphoma (DLBCL)
 - Follicular lymphoma
 - Gastric MALT lymphoma
 - Hairy cell leukemia
 - HGBLs
 - Histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma
 - Mantle cell lymphoma
 - Nodal marginal zone lymphoma
 - Nongastric MALT lymphoma (noncutaneous)
 - Posttransplantation lymphoproliferative disorder (PTLD)
 - Primary cutaneous B-cell lymphomas
 - Splenic marginal zone lymphoma
 - Waldenström macroglobulinemia/lymphoplasmacytic lymphoma

CHEMOTHERAPY REGIMEN ABBREVIATIONS USED THROUGHOUT THE POLICY:

- **ABVD** (doxorubicin, bleomycin, vinblastine, dacarbazine)
- **BR** (bendamustine and rituximab)
- **CaRD** (carfilzomib, rituximab, dexamethasone)
- **CEOP** (cyclophosphamide, etoposide, vincristine, and prednisone)
- **COP** (cyclophosphamide, vincristine, prednisone)
- **COPADM** (cyclophosphamide, vincristine, prednisone, doxorubicin, methotrexate, and intrathecal therapy with methotrexate and hydrocortisone)
- **CVAD** (cyclophosphamide, vincristine, doxorubicin, and dexamethasone)
- **CVbP** (cyclophosphamide, vinblastine, prednisolone)
- **CVP** (cyclophosphamide, vincristine, and prednisone)
- **CYM** (cytarabine, methotrexate, and intrathecal therapy with methotrexate, cytarabine, and hydrocortisone)
- **DA-EPOCH** (etoposide, prednisolone, vincristine, cyclophosphamide, and doxorubicin)
- **DA-EPOCH-R** (rituximab, etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin)
- **DHA** (dexamethasone and cytarabine) + platinum (carboplatin, cisplatin, or oxaliplatin)
- **DHAP** (dexamethasone, cytarabine, and cisplatin or carboplatin)
- **Dose-adjusted EPOCH** (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin)
- **ESHAP** (etoposide, methylprednisolone, cytarabine, and cisplatin)
- **FCR** (fludarabine, cyclophosphamide, and rituximab)
- **GDP** (gemcitabine, dexamethasone, and cisplatin)
- **GemOx** (gemcitabine, oxaliplatin)
- **GMALL** (idarubicin, dexamethasone, vincristine, cyclophosphamide, cytarabine)
- **HDAC** (high-dose cytarabine)
- **Hyper-CVAD** (cyclophosphamide, vincristine, doxorubicin, and dexamethasone)
- **ICE** (ifosfamide, carboplatin, and etoposide)
- **IGEV** (ifosfamide, gemcitabine, and vinorelbine)
- **IVAC** (ifosfamide, cytarabine, etoposide, and intrathecal methotrexate)
- **MINE** (mesna, ifosfamide, mitoxantrone, and etoposide)
- **Modified CODOX-M** (cyclophosphamide, doxorubicin, and vincristine, with intrathecal methotrexate and cytarabine followed by high-dose systemic methotrexate)
- **MOpAD** (methotrexate, vincristine, pegaspargase, dexamethasone)
- **OFAR** (oxaliplatin, fludarabine, cytarabine, and rituximab)
- **Pola-R-CHP** (polatuzumab vedotin-piiq, rituximab, cyclophosphamide, doxorubicin, and prednisone)
- **RCDOP** (rituximab, cyclophosphamide, liposomal doxorubicin, vincristine, and prednisone)
- **RCEPP** (rituximab, cyclophosphamide, etoposide, prednisone, and procarbazine)
- **RCEOP** (rituximab, cyclophosphamide, etoposide, vincristine, and prednisone) regimen
- **RGCVP** (rituximab, gemcitabine, cyclophosphamide, vincristine, and prednisolone)
- **RCHOP** (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone)

- **R-CODOX-M** (rituximab, cyclophosphamide, vincristine, and doxorubicin with methotrexate)
- **R-COPADM** (cyclophosphamide, vincristine, prednisone, doxorubicin, methotrexate, and intrathecal therapy with methotrexate and hydrocortisone)
- **RCVP** (rituximab, cyclophosphamide, vincristine, and prednisone)
- **R-CYVE** (cytarabine, etoposide and intrathecal therapy with methotrexate and hydrocortisone)
- **RDHA** (rituximab, dexamethasone, and cytarabine) + platinum (carboplatin, cisplatin, or oxaliplatin)
- **R-EPOCH** (rituximab, etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin)
- **RGDP** (rituximab, gemcitabine, dexamethasone, cisplatin)
- **R-HyperCVAD** (rituximab, cyclophosphamide, vincristine, doxorubicin, and dexamethasone alternating with high-dose methotrexate and cytarabine)
- **RICE** (rituximab, ifosfamide, carboplatin, and etoposide)
- **R-IVAC** (rituximab, ifosfamide, cytarabine, etoposide)
- **R-MPV** (rituximab, methotrexate, procarbazine, and vincristine)
- **VR-CAP** (bortezomib, rituximab, cyclophosphamide, doxorubicin, and prednisone)

MEDICALLY NECESSARY

COMPANY-DESIGNATED PREFERRED PRODUCTS

Although there are many rituximab products on the market (e.g., rituximab [Rituxan], rituximab-abbs [Truxima], rituximab-arrx [Riabni], rituximab-pvvr [Ruxience]), there is no reliable evidence of the superiority of any one product of rituximab compared with other products. The Company has designated the following rituximab biosimilar products as its preferred products: rituximab-pvvr (Ruxience) and rituximab-abbs (Truxima).

These products are less costly and at least as likely to produce equivalent therapeutic results as the nonpreferred products, which include, but are not limited to, rituximab (Rituxan), rituximab-arrx (Riabni), and any other nonpreferred rituximab biosimilars.

According to the US Food and Drug Administration (FDA), “a biosimilar is a biological product that has no clinically meaningful differences from the existing FDA-approved reference product. All biosimilar products meet the FDA’s rigorous standards for approval for the indications described in the product labeling. Once a biosimilar has been approved by the FDA, the safety and effectiveness of these products have been established, just as they have been for the reference product.” Coverage of a biosimilar product as an alternate to a reference product is not considered a form of step therapy by the Company.

NONPREFERRED PRODUCTS

Use of the nonpreferred rituximab products that include but are not limited to rituximab (Rituxan), rituximab-arrx (Riabni), or any other nonpreferred biosimilars is considered medically necessary and, therefore, covered only for individuals who are currently receiving or have

previously received a nonpreferred product for the specified rituximab indication.

If the individual has not previously received rituximab (Rituxan), rituximab-arxx (Riabni), or any other nonpreferred biosimilar to treat the specified indication, these nonpreferred products are eligible for coverage when the individual has contraindication(s) or intolerance(s) to the Company-designated preferred products (e.g., as documented per the FDA labeling).

RITUXIMAB AND RELATED BIOSIMILARS

Rituximab infusion and related biosimilars are considered medically necessary and, therefore, covered for the following indications when the requirements listed in the sections above (COMPANY-DESIGNATED PREFERRED PRODUCTS and NONPREFERRED PRODUCTS) are met:

- **Antineutrophil cytoplasmic antibodies (ANCA)–associated vasculitides (granulomatosis with polyangiitis, microscopic polyangiitis [MPA], eosinophilic granulomatosis with polyangiitis [EGPA] [formerly Churg-Strauss syndrome], pauci-immune glomerulonephritis)**
 - In adult and pediatric individuals 2 years of age and older, in combination with glucocorticoids
- **Anemia, autoimmune hemolytic (AIHA)**
 - For refractory autoimmune hemolytic anemia
- **Castleman disease (CD), multicentric**
 - Active multicentric CD with no organ failure with or without prednisone for individuals who are human immunodeficiency virus (HIV)–negative and human herpesvirus-8 (HHV-8)–negative, in one of the following regimens:
 - As primary treatment
 - As alternate treatment for relapsed disease
 - If no response to alternate primary treatment
 - Active multicentric CD with no organ failure with or without liposomal doxorubicin and/or prednisone for individuals who are HHV-8–positive, in one of the following regimens:
 - As preferred primary treatment
 - As alternate treatment for relapsed disease
 - If no response to alternate primary treatment
 - Active multicentric CD with or without prednisone for individuals with no organ failure who have disease progression ≥6 months following completion of rituximab
 - Primary treatment for multicentric CD for individuals with fulminant HHV-8 with or without organ failure in combination with:
 - CHOP
 - CVAD
 - CVP
 - Liposomal doxorubicin
 - As a single agent if individual is not a candidate for combination therapy

- Refractory or progressive multicentric CD in combination with liposomal doxorubicin or with CHOP, CVAD, or regimen:
 - As initial treatment
 - If no response to initial treatment for refractory or progressive disease
- Subsequent therapy for multicentric CD that has progressed following treatment of relapsed/refractory or progressive disease in combination with:
 - Bortezomib
 - Lenalidomide
 - Thalidomide
- **Castleman Disease (CD), unicentric**
 - Unicentric CD with or without prednisone and/or cyclophosphamide for one of the following conditions:
 - For surgically unresectable disease
 - For symptomatic disease following incomplete resection
 - As second-line therapy for relapsed or refractory disease
- **Central nervous system cancers**
 - For leptomeningeal metastases
 - Intra-cerebrospinal fluid (CSF) treatment for leptomeningeal metastases from lymphoma by intrathecal administration
 - As primary treatment in individuals with good risk status (Karnofsky Performance Status [KPS] ≥60, no major neurologic deficits, minimal systemic disease, and reasonable systemic treatment options if needed)
 - As maintenance therapy for individuals with negative CSF cytology or for clinically stable individuals with persistently positive CSF cytology
 - For primary central nervous system lymphoma
 - Induction therapy as a single agent if individual is unsuitable for or intolerant to high-dose methotrexate
 - Induction therapy in combination with one of the following regimens:
 - As a component of R-MPV (National Comprehensive Cancer Network [NCCN] preferred)
 - High-dose methotrexate (NCCN preferred)
 - High-dose methotrexate and temozolomide (NCCN preferred)
 - High-dose methotrexate, cytarabine, and thiopeta
 - Temozolomide (if individual is unsuitable for or intolerant to high-dose methotrexate)
 - Lenalidomide (if individual is unsuitable for or intolerant to high-dose methotrexate)
 - Treatment as a single agent or in combination with either temozolomide or lenalidomide, or as a component of rituximab, methotrexate, carmustine, etoposide, and prednisone (R-MBVP) regimen for relapsed or refractory disease

- In individuals who received prior whole-brain radiation therapy (RT)
 - In individuals who received a prior high-dose methotrexate-based regimen without prior RT
 - In combination with whole-brain RT or involved field RT in individuals who received a prior high-dose methotrexate-based regimen without prior RT after no response or short response duration (<12 months) to prior regimen
 - In individuals who received prior high-dose chemotherapy with stem cell rescue
- Treatment in combination with high-dose methotrexate with or without ibrutinib for relapsed or refractory disease for one of the following:
 - In individuals who received prior whole-brain RT
 - Individuals who received a prior high-dose methotrexate-based regimen without prior RT and a previous long response duration (≥ 12 months)
 - In individuals who received a prior high-dose methotrexate-based regimen without prior RT and a previous short response duration (<12 months) to prior regimen if clinically indicated
- Intra-CSF therapy if CSF positive or spinal magnetic resonance imaging (MRI) positive
 - As part of induction therapy
 - As treatment alone or in combination with systemic therapy for relapsed or refractory disease in individuals with prior whole-brain RT
- Treatment with autologous stem cell reinfusion (if the recurrent disease goes into complete remission with reinduction systemic therapy) for relapsed or refractory disease in eligible individuals who received prior whole-brain RT as a component of high-dose cytarabine + rituximab + thiotepa followed by thiotepa + rituximab + carmustine
- Consolidation therapy (monthly maintenance) therapy as continuation of induction regimen in individuals with complete response or complete response unconfirmed (CRu) to induction therapy
 - As a single agent
 - In combination with high-dose methotrexate
- **Hematopoietic cell transplantation**
 - For chronic graft-versus-host disease (GVHD) as additional therapy in conjunction with systemic corticosteroids following no response (steroid-refractory disease) to first-line therapy options
 - Conditioning for allogeneic transplant as part of a nonmyeloablative regimen in combination with cyclophosphamide and fludarabine
- **Idiopathic membranous nephropathy, resistant to at least one of the following conventional therapies:**

- Conventional nonimmunosuppressive therapies (e.g, angiotensin-converting enzyme [ACE] inhibitor, angiotensin 2 receptor blocker [ARB])
- Immunosuppressive therapies (e.g., cyclophosphamide, cyclosporine, chlorambucil, corticosteroids, mycophenolate mofetil)
- **Immunoglobulin G4 (IgG4)–related disease, refractory to corticosteroids**
- **Toxicities related to immune checkpoint inhibitors (e.g., ipilimumab [Yervoy], nivolumab [Opdivo], pembrolizumab [Keytruda])**
 - As additional therapy for moderate grade 2 (G2), severe (G3), or life-threatening (G4) immunotherapy-related bullous dermatitis
 - Moderate or severe steroid-refractory myalgias or myositis (**proximal muscle weakness, neck flexor weakness, with or without myalgias**) for **significant dysphagia, life-threatening situations, or** steroid-refractory myositis
 - As additional therapy for severe (G3 to G4) myasthenia gravis in individuals refractory to plasmapheresis or intravenous immune globulin (IVIG)
 - For encephalitis in individuals positive for autoimmune encephalopathy antibody, or who have had limited or no improvement after 7 to 14 days on pulse-dose methylprednisolone with or without IVIG
- **Leukemia, mature B-cell acute leukemia (B-AL)**
 - Pediatric individuals, aged 6 months and older with previously untreated, advanced stage, CD20-positive disease, in combination with chemotherapy
- **Leukemia, acute lymphoblastic (ALL) in combination with one of the following:**
 - Tyrosine kinase inhibitor (TKI) for adolescents and young adults (AYA) and adults aged less than 65 years without substantial comorbidities with Philadelphia chromosome–positive B-ALL, during frontline therapy or relapsed/refractory (R/R) therapy if not previously given
 - GRAALL-2005 regimen for induction, salvage re-induction, consolidation, late intensification, or maintenance for AYA and adults aged less than 60 years without substantial comorbidities with Philadelphia chromosome–negative B-ALL during frontline therapy or as a consideration if in late relapse (>3 years from initial diagnosis) if regimen used in frontline
 - Linker four-drug regimen (daunorubicin, vincristine, prednisone, pegaspargase) for AYA and adults aged less than 60 years without substantial comorbidities with Philadelphia chromosome–negative B-ALL during frontline therapy or as a consideration if in late relapse (>3 years from initial diagnosis) if regimen used in frontline
 - Hyper-CVAD regimen: (hyperfractionated cyclophosphamide, mesna, vincristine, doxorubicin, dexamethasone, IT methotrexate, IT cytarabine alternating with high-dose methotrexate, leucovorin, methylprednisolone, cytarabine, IT methotrexate, IT cytarabine); with (for minimal residual disease negative) or without blinatumomab as consolidation, for AYA and adults aged less than 65 years without substantial comorbidities with Philadelphia chromosome–negative B-ALL during frontline therapy or as a consideration if in late relapse (>3 years from initial diagnosis) if regimen used in frontline

- MOpAD regimen during R/R therapy as a consideration for Philadelphia chromosome–positive B-ALL if refractory to TKIs or during R/R therapy for Philadelphia chromosome–negative B-ALL
 - GMALL regimen (idarubicin, dexamethasone, vincristine, cyclophosphamide, cytarabine) for adults aged 65 years or more, or adults with substantial comorbidities with Philadelphia chromosome–negative B-ALL during frontline therapy, refractory therapy, or as a consideration if in late relapse (>3 years from initial diagnosis) if regimen used in frontline
 - ECOG1910 regimen (NCCN-preferred in frontline for adults aged <65 years without substantial comorbidities): induction phase 1 (daunorubicin, vincristine, prednisone, pegaspargase); and induction phase 2 (cyclophosphamide, cytarabine, mercaptopurine); + blinatumomab as consolidation (for minimal residual disease negative) for AYA and adults less than 65 years without substantial comorbidities with Philadelphia chromosome–negative B-ALL during frontline therapy or as a consideration if in late relapse (>3 years from initial diagnosis) if regimen used in frontline
- **Lupus nephritis refractory to corticosteroids and other immunosuppressive therapies (e.g., cyclophosphamide, mycophenolate, hydroxychloroquine, azathioprine, cyclosporine)**
 - **Lymphoma, Hodgkin**
 - For nodular lymphocyte-predominant Hodgkin lymphoma (age ≥18 years)
 - Primary treatment with involved site RT (ISRT) for stage IB or IIB disease, or stage IA (bulky) or IIA (bulky or noncontiguous) disease, or with or without ISRT for stage III-IV disease (based on clinical judgement), in combination with one of the following regimens:
 - ABVD
 - RCHOP
 - CVbP (cyclophosphamide, vinblastine, prednisolone)
 - Primary treatment for palliation as a single agent for:
 - stage IA (bulky) or IIA (bulky or noncontiguous) disease
 - stage IB or IIB disease
 - stage III to IV disease (based on clinical judgement)
 - Second-line or subsequent treatment (if not previously used) for refractory, relapsed, or progressive disease
 - As a single agent
 - In combination with one of the following regimens:
 1. DHAP
 2. ICE
 3. IGEV regimen
 4. Bendamustine
 5. ABVD

6. RCHOP

7. CVbP

- Maintenance therapy for individuals treated with second-line systemic therapy with rituximab alone for refractory, relapsed, or progressive disease

- **Lymphoma, Hodgkin (Pediatric)**

- Nodular lymphocyte-predominant Hodgkin lymphoma: primary treatment for stage IA or IIA (incomplete resection and nonbulky disease) as a component of CVbP regimen with rituximab (NCCN-preferred)

- **Lymphoma, non-Hodgkin (NHL)**

- **High-grade B-cell lymphomas**

- Second-line and subsequent therapy with rituximab in individuals with intention to proceed to transplantation when they meet both of the following criteria:
 - One of the following conditions:
 - Relapsed disease >12 months after completion of first-line therapy
 - Primary refractory disease (partial response, no response, or progression) or relapsed disease <12 months after completion of first-line therapy on noncandidates for chimeric antigen receptor (CAR) T-cell therapy
 - Alternative systemic therapy (if not previously used) for relapsed/refractory disease in noncandidates for CAR T-cell therapy
 - As a component of one of the following regimens:
 - DHA (dexamethasone and cytarabine) + platinum (carboplatin, cisplatin, or oxaliplatin)
 - GDP (gemcitabine, dexamethasone, cisplatin)
 - Gemcitabine, dexamethasone, and carboplatin
 - ICE
 - ESHAP
 - GemOx (gemcitabine, oxaliplatin)
 - MINE
- Second-line and subsequent therapy with rituximab in noncandidates for transplant when they meet both of the following criteria:
 - One of the following conditions:
 - Relapsed disease >12 months after completion of first-line therapy
 - Primary refractory disease (partial response, no response, or progression) or relapsed disease <12 months after completion of first-line therapy on noncandidates for CAR T-cell therapy

- Alternative systemic therapy (if not previously used) for relapsed/refractory disease in noncandidates for CAR T-cell therapy
 - As a component of one of the following regimens:
 - Polatuzumab vedotin-piiq with or without bendamustine
 - As a single agent
 - In combination with lenalidomide (nongerminal center diffuse large B-cell lymphoma), or bendamustine
 - Dose-adjusted EPOCH regimen
 - CEOP
 - GDP
 - GemOx
 - Gemcitabine, dexamethasone, carboplatin
 - Used as clinically indicated as a bridging option until CAR T-cell product is available, in individuals with primary refractory disease or relapsed disease <12 months after completion of first-line therapy
 - As a component of one of the following:
 - DHA + platinum (carboplatin, cisplatin, or oxaliplatin)
 - Polatuzumab vedotin-piiq with or without bendamustine (consider/add bendamustine only after leukopheresis)
 - GDP
 - Gemcitabine, dexamethasone, carboplatin
 - GemOx
 - ICE
- **HIV-related B-cell lymphoma**
 - NCCN-preferred therapy in combination with growth factor support as first-line therapy for HIV-related Burkitt lymphoma as a component of one of the following:
 - DA-EPOCH-R
 - Modified CODOX-M regimen alternating with IVAC regimen
 - First-line therapy for HIV-related Burkitt lymphoma, in combination with growth factor support, as a component of R-HyperCVAD regimen
 - First-line therapy, in combination with growth factor support, for CD20+ HIV-related diffuse large B-cell lymphoma, primary effusion lymphoma, and HHV8-positive diffuse large B-cell lymphoma not otherwise specified (NOS) as a component of:
 - R-EPOCH (rituximab, etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin) regimen (NCCN-preferred regimen)
 - Second-line and subsequent therapy for HIV-related diffuse large B-cell lymphoma, primary effusion lymphoma, and HHV8-positive diffuse large B-cell lymphoma NOS in individuals with intention to proceed to transplantation when they meet both of the following criteria:

- One of the following conditions:
 - Relapsed disease >12 months after completion of first-line therapy
 - Primary refractory disease (partial response, no response, or progression) or relapsed disease <12 months after completion of first-line therapy on noncandidates for CAR T-cell therapy
 - Alternative systemic therapy (if not previously used) for relapsed/refractory disease in noncandidates for CAR T-cell therapy
- As a component of one of the following regimens:
 - DHA (dexamethasone and cytarabine) + platinum (carboplatin, cisplatin, or oxaliplatin) regimen
 - ESHAP
 - GD
 - Gemcitabine, dexamethasone, carboplatin
 - GemOx
 - ICE
 - MINE
- Second-line and subsequent therapy for HIV-related diffuse large B-cell lymphoma, primary effusion lymphoma, and HHV8-positive diffuse large B-cell lymphoma NOS in noncandidates for transplantation when they meet both of the following criteria:
 - One of the following conditions:
 - Relapsed disease >12 months after completion of first-line therapy
 - Primary refractory disease (partial response, no response, or progression) or relapsed disease <12 months after completion of first-line therapy on noncandidates for CAR T-cell therapy
 - Alternative systemic therapy (if not previously used) for relapsed/refractory disease in noncandidates for CAR T-cell therapy
 - As a component of one of the following regimens:
 - Polatuzumab vedotin-piiq with or without bendamustine
 - As a single agent
 - In combination with lenalidomide (nongerminal center diffuse large B-cell lymphoma), or bendamustine
 - Dose-adjusted EPOCH (if not previously given)
 - CEOP
 - GDP
 - Gemcitabine, dexamethasone, carboplatin
 - GemOx

- Used as clinically indicated as a bridging option until CAR T-cell product is available for individuals with primary refractory disease or relapsed disease <12 months after completion of first-line therapy as a component of one of the following:
 - DHA (dexamethasone and cytarabine) + platinum (carboplatin, cisplatin, or oxaliplatin) regimen
 - Polatuzumab vedotin-piiq with or without bendamustine (consider/add bendamustine only after leukapheresis)
 - GDP regimen
 - Gemcitabine, dexamethasone, and carboplatin regimen
 - GemOx regimen
 - ICE regimen
- Second-line therapy for relapse of HIV-related Burkitt lymphoma as a component of:
 - Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin) regimen with rituximab (if not previously given as first-line therapy)
 - RICE (rituximab, ifosfamide, carboplatin, and etoposide) regimen (in combination with intrathecal methotrexate if not previously given)
 - R-IVAC (rituximab, ifosfamide, cytarabine, etoposide) regimen (in combination with intrathecal methotrexate if not previously given)
 - RGDP (rituximab, gemcitabine, dexamethasone, cisplatin) regimen
 - High-dose cytarabine + rituximab regimen
- **Burkitt lymphoma**
 - Pediatric individuals, aged 6 months or greater with previously untreated, advanced stage, CD20-positive disease, in combination with chemotherapy.
 - Induction therapy for low-risk disease in individuals less than 60 years of age as a component of one of the following NCCN-preferred regimens:
 - CODOX-M (cyclophosphamide, doxorubicin, and vincristine, with intrathecal methotrexate and cytarabine followed by high-dose systemic methotrexate) regimen (original or modified) with rituximab
 - Dose-adjusted EPOCH regimen with rituximab and intrathecal methotrexate
 - HyperCVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone) alternating with high-dose methotrexate and cytarabine regimen with rituximab (regimen includes intrathecal therapy)
 - Induction therapy for high-risk disease in individuals less than 60 years of age, as a component of one of the following NCCN-preferred regimens

(Note: high-risk individuals presenting with symptomatic central nervous system [CNS] disease should be started with the portion of the systemic therapy that contains CNS-penetrating drugs)

- CODOX-M regimen (original or modified) alternating with IVAC (ifosfamide, cytarabine, etoposide, and intrathecal methotrexate) regimen with rituximab
 - HyperCVAD alternating with high-dose methotrexate and cytarabine regimen with rituximab (regimen includes intrathecal therapy)
 - Induction therapy for high-risk disease in individuals less than 60 years of age, as a component of dose-adjusted EPOCH regimen with rituximab and intrathecal methotrexate (for high-risk individuals with baseline CNS disease who are not able to tolerate aggressive treatments)
 - Induction therapy (NCCN-preferred) for low-risk and high-risk disease in individuals 60 years of age or older, as a component of dose-adjusted EPOCH regimen with rituximab and intrathecal methotrexate (Note: for high-risk individuals presenting with symptomatic CNS disease, the management of the CNS disease should be addressed with the initial regimen)
 - Second-line therapy for relapse of Burkitt lymphoma greater than 6 to 18 months following appropriate first-line therapy, or for individuals with partial response to second-line therapy as additional second-line therapy (if not previously given) for relapse or refractory disease as a component of one of the following:
 - Dose-adjusted EPOCH regimen with rituximab and intrathecal methotrexate
 - ICE regimen with rituximab, and with intrathecal methotrexate if not previously given
 - R-IVAC regimen with intrathecal methotrexate if not previously given
 - RGDP regimen
 - HDAC with rituximab regimen
- **Burkitt-like lymphoma (BLL)**
 - Pediatric individuals, aged 6 months and older with previously untreated, advanced stage, CD20-positive disease, in combination with chemotherapy
 - **Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)**
 - First-line therapy
 - FCR for individuals with previously untreated CD20-positive CLL
 - As a component of FCR regimen for individuals with immunoglobulin heavy-chain variable-region (IGHV)-mutated CLL in individuals aged less than 65 years without significant comorbidities who have indications for treatment[†]

- In combination with bendamustine as first-line therapy for CLL/SLL without del(17p)/TP53 mutation in individuals who are not frail and have indications for treatment (consider when Bruton Tyrosine Kinase inhibitor [BTKi] and venetoclax are not available or contraindicated or rapid disease de-bulking is needed)
- Therapy for relapsed or refractory CLL
 - As a component of FCR for individuals with previously treated CD20-positive CLL
- Therapy for relapsed or refractory CLL with del(17p)/TP53 in individuals who have indications for retreatment[†]
 - In combination with venetoclax (Venclexta) as second- or third-line therapy (NCCN-preferred regimen)
 - In combination with alemtuzumab (Campath), lenalidomide, idelalisib (Zydelig), or high-dose methylprednisolone, after prior therapy with BTKi- and venetoclax-based regimens
- First-line therapy in combination with high-dose methylprednisolone for CLL/SLL with del(17p)/TP53 mutation in individuals who have indications for treatment (consider when BTKi and venetoclax are not available or contraindicated or rapid disease de-bulking is needed)
- Initial therapy for histologic (Richter) transformation to diffuse large B-cell lymphoma (clonally related or unknown clonal status) as a component of one of the following regimens:
 - RCHOP
 - Dose-adjusted EPOCH with rituximab regimen
 - HyperCVAD with rituximab regimen alternating with high-dose methotrexate and cytarabine with rituximab regimen
 - OFAR (oxaliplatin, fludarabine, cytarabine, and rituximab) regimen
 - Venetoclax + RCHOP regimen
- Second-line or third-line therapy in combination with venetoclax for CLL/SLL without del(17p)/TP53 mutation (NCCN-preferred regimen) in individuals with indications for treatment and one of the following:
 - Intolerance to first-line therapy with a BTKi with or without anti-CD20 monoclonal antibody (mAb)
 - Intolerance to first-line therapy with a BTKi with or without anti-CD20 mAb and following second-line therapy with an alternative BTKi
 - Disease relapse after first-line therapy with fixed-duration treatment (chemoimmunotherapy or immunotherapy) in individuals with indications for treatment
 - Disease progression while on first-line therapy with a BTKi with or without anti-CD20 mAb

- Disease progression or intolerance while on first-line therapy with fixed-duration treatment with chemoimmunotherapy or immunotherapy and following second-line therapy with a BTKi
- In combination with venetoclax (if previously used) for CLL/SLL with or without del(17p)/TP53 as treatment for relapse after a period of remission in individuals with indications for treatment
- Subsequent therapy for relapsed or refractory CLL/SLL without del(17p)/TP53 mutation after prior therapy with BTKi- and venetoclax-based regimens in individuals who have indications for treatment
 - As a component of FCR regimen, in individuals aged less than 65 years of age without significant comorbidities
 - In combination with bendamustine in individuals aged less than 65 years without significant comorbidities and who are not frail
 - in combination with high-dose methylprednisolone (HDMP), in individuals aged less than 65 years without significant comorbidities
- Subsequent therapy in combination with idelalisib or lenalidomide for relapsed or refractory CLL/SLL without del(17p)/TP53 mutation after prior therapy with BTKi- and venetoclax-based regimens in individuals who have indications for treatment

[†]Indications for treatment/retreatment: eligible for clinical trial, significant disease-related symptoms (fatigue [severe], drenching night sweats, unintentional weight loss [$\geq 10\%$ in previous 6 months], fever without infection), threatened end-organ function, progressive, symptomatic, or bulky disease (spleen > 6 cm below costal margin, lymph nodes > 10 cm), progressive anemia, progressive thrombocytopenia, steroid-refractory autoimmune cytopenias.

○ **Diffuse large B-cell lymphoma**

- Pediatric individuals, aged 6 months and older with previously untreated, advanced stage, CD20-positive disease, in combination with chemotherapy
- First-line therapy for* stage I-II (excluding stage II with extensive mesenteric disease) as a component of:
 - RCHOP
 - Pola-R-CHP (polatuzumab vedotin-piiq, rituximab, cyclophosphamide, doxorubicin, and prednisone) regimen for stage modified International Prognostic Index (smIPI) > 1
- First-line therapy for* stage II with extensive mesenteric disease or stage III-IV disease as a component of:
 - RCHOP (NCCN-preferred)
 - Pola-R-CHP regimen for IPI ≥ 2 (NCCN-preferred)
 - Dose-adjusted EPOCH regimen with rituximab

- First-line therapy for stage I-IV disease in individuals with poor left ventricular function as a component of one of the following regimens:
 - RCDOP (rituximab, cyclophosphamide, liposomal doxorubicin, vincristine, and prednisone) regimen
 - Dose-adjusted EPOCH regimen with rituximab
 - RCEOP (rituximab, cyclophosphamide, etoposide, vincristine, and prednisone) regimen
 - RGCVP (rituximab, gemcitabine, cyclophosphamide, vincristine, and prednisolone)
- First-line therapy for stage I-IV disease in very frail individuals and individuals aged more than 80 years with comorbidities as a component of one of the following regimens:
 - RCDOP
 - R-mini-CHOP
 - RGCVP
- First-line therapy for gray zone lymphoma as a component of one of the following:
 - RCHOP (NCCN-preferred)
 - Dose-adjusted EPOCH regimen with rituximab
- First-line therapy for gray zone lymphoma in individuals with poor left ventricular function as a component of one of the following regimens:
 - RCDOP
 - Dose-adjusted EPOCH regimen with rituximab
 - RCEOP regimen with rituximab
 - RGCVP
- First-line therapy for gray zone lymphoma in very frail individuals and individuals aged more than 80 years with comorbidities as a component of one of the following regimens:
 - RCDOP
 - R-mini-CHOP
 - RGCVP
- Second-line or subsequent therapy for relapsed or refractory disease in individuals with intention to proceed to transplant, when they meet both of the following criteria:
 - One of the following conditions:
 - Relapsed disease more than 12 months after completion of first-line therapy
 - Primary refractory disease (partial response, no response, or progression) or relapsed disease less than 12 months after completion of first-line therapy in noncandidates for CAR T-cell therapy

- Alternative systemic therapy (if not previously used) for relapsed/refractory disease in noncandidates for CAR T-cell therapy
 - As a component of one of the following regimens:
 - DHA (dexamethasone and cytarabine) + platinum (carboplatin, cisplatin, or oxaliplatin) regimen (NCCN-preferred)
 - GDP (NCCN-preferred)
 - Gemcitabine, dexamethasone, and carboplatin regimen (NCCN-preferred)
 - ICE (NCCN-preferred)
 - ESHAP
 - GemOX (gemcitabine and oxaliplatin)
 - MINE
- First-line treatment of primary mediastinal large B-cell lymphoma as a component of one of the following regimens:
 - RCHOP
 - Dose-adjusted EPOCH
- First-line therapy for extracutaneous primary cutaneous diffuse large B-cell lymphoma, leg type
 - As a component of one of the following regimens:
 1. Dose-adjusted EPOCH with rituximab
 2. RCHOP
 3. Pola-R-CHP regimen for IPI ≥ 2
 - Individuals with poor left ventricular function as a component of one of the following regimens:
 1. RCDOP regimen
 2. Dose-adjusted EPOCH regimen with rituximab
 3. RCEOP regimen
 4. RGCVP
 - For very frail individuals and individuals aged more than 80 years with comorbidities as a component of one of the following regimens:
 1. RCDOP regimen
 2. R-mini-CHOP
 3. RGCVP
- Primary cutaneous diffuse large B-cell lymphoma, leg type, as a component of RCHOP for one of the following:
 - First-line therapy with ISRT
 - Second-line therapy (if not previously received) for solitary regional, T1-2 disease
 - First-line therapy for generalized cutaneous disease (skin only) T3

- Primary cutaneous diffuse large B-cell lymphoma, leg type in individuals with poor left ventricular function, when they meet both of the following criteria:
 - One of the following conditions:
 - First-line therapy with ISRT
 - Second-line therapy (if not previously received) for solitary regional, T1-2 disease
 - First-line therapy for generalized cutaneous disease (skin only) T3
 - As a component of one of the following regimens:
 - RCDOP
 - Dose-adjusted EPOCH regimen with rituximab
 - RCEOP regimen with rituximab
 - RGCVP
- Primary cutaneous diffuse large B-cell lymphoma, leg type in very frail individuals and individuals aged older than 80 years with comorbidities, when they meet both of the following criteria:
 - One of the following conditions:
 - First-line therapy with ISRT
 - Second-line therapy (if not previously received) for solitary regional, T1-2 disease
 - First-line therapy for generalized cutaneous disease (skin only) T3
 - As a component of one of the following regimens:
 - RCDOP
 - R-mini-CHOP
 - RGCVP
- Second-line and subsequent therapy with rituximab in noncandidates for transplant, when they meet both of the following criteria:
 - One of the following conditions:
 - Relapsed disease more than 12 months after completion of first-line therapy
 - Primary refractory disease (partial response, no response, or progression) or relapsed disease less than 12 months after completion of first-line therapy on noncandidates for CAR T-cell therapy
 - Alternative systemic therapy (if not previously used) for relapsed/refractory disease in noncandidates for CAR T-cell therapy
 - As a component of one of the following regimens:
 - Polatuzumab vedotin-piiq (with or without bendamustine) (NCCN-preferred)
 - As a single agent

- In combination with lenalidomide (nongerminal center diffuse large B-cell lymphoma) (regimens useful in certain circumstances outlined in NCCN guidelines)
 - Dose-adjusted EPOCH
 - CEO
 - GD
 - Gemcitabine, dexamethasone, carboplatin
 - GemOx
- Used as clinically indicated as a bridging option until CAR T-cell product is available for individuals with primary refractory disease or relapsed disease less than 12 months after completion of first-line therapy as a component of one of the following:
 - DHA (dexamethasone and cytarabine) + platinum (carboplatin, cisplatin, or oxaliplatin) regimen
 - Polatuzumab vedotin-piiq with or without bendamustine (consider/add bendamustine only after leukapheresis)
 - GDP regimen
 - Gemcitabine, dexamethasone, and carboplatin regime
 - GemOx regimen
 - ICE regimen
- **Extranodal Marginal Zone Lymphoma of the Stomach**
 - Initial therapy (if irradiation is contraindicated) as a single agent for individuals with stage I₁, or I₂, or stage II₁ disease in individuals who are *Helicobacter pylori* (H. pylori)–positive and t(11;18) positive or who are H. pylori–negative
 - As a single agent in individuals with indications for treatment** as:
 - First-line therapy for stage II_E, or II₂, or stage IV disease (distant nodal, advanced stage)
 - Second-line or subsequent therapy for relapsed, refractory, or progressive disease
 - As a single agent in individuals with indications for treatment** stage I₁, or I₂, or stage II₁ disease as:
 - Additional therapy for H. pylori–positive disease if repeat endoscopy shows no response or recurrence after antibiotic therapy and ISRT
 - Additional therapy after ISRT alone for disease that is lymphoma positive after restaging with endoscopy
 - As additional therapy for recurrence for disease that is lymphoma positive after previous antibiotic therapy and locoregional ISRT
 - Second-line or subsequent therapy for relapsed, refractory, or progressive disease if longer duration of remission
 - As a single agent (NCCN-preferred) or in combination with chlorambucil or cyclophosphamide in elderly or infirm individuals with indications for

treatment** where tolerability of combination chemotherapy is a concern as:

- First-line therapy for stage II_E, or II₂, or stage IV (distant nodal, advanced stage) disease
- Second-line or subsequent therapy for relapsed, refractory, or progressive disease
- As a single agent (NCCN-preferred) or in combination with chlorambucil or cyclophosphamide in older or infirm individuals with indications for treatment** when tolerability of combination chemoimmunotherapy is a concern and stage I₁, or I₂, or stage II₁ disease as:
 - Additional therapy for *H. pylori*-positive disease if repeat endoscopy shows no response or recurrence after antibiotic therapy and ISRT
 - Additional therapy after ISRT or rituximab alone for disease that is lymphoma positive after restaging with endoscopy
 - As additional therapy for recurrence for disease that is lymphoma positive after previous antibiotic therapy and locoregional ISRT
 - Second-line or subsequent therapy for relapsed, refractory, or progressive disease
- Individuals with indications for treatment** as a NCCN-preferred component of RCHOP, RCVP, or in combination with bendamustine
 - As first-line therapy for stage II_E, or II₂, or stage IV disease (distant nodal, advanced stage)
 - As additional therapy for stage I₁, or I₂, or stage II₁ *H. pylori*-positive disease if repeat endoscopy shows no response or recurrence after antibiotic therapy and ISRT
 - As additional therapy after ISRT or rituximab alone for stage I₁, or I₂, or stage II₁ disease that is lymphoma positive after restaging with endoscopy
 - As additional therapy for recurrence for stage I₁, or I₂, or stage II₁ disease that is lymphoma positive after previous antibiotic therapy and locoregional ISRT
- Second-line or subsequent therapy (NCCN-preferred) for relapsed, refractory, or progressive disease in individuals with the indications for treatment** in one of the following regimens:
 - Bendamustine with rituximab (if bendamustine not previously used)
 - RCHOP
 - RCVP
 - Lenalidomide with rituximab, including for the elderly or infirm when tolerability of combination therapy is a concern

**Indications for treatment of gastric MALT lymphoma are as follows: candidate for clinical trial, symptoms, gastrointestinal bleeding, threatened end-organ function, clinically

significant bulky disease, steady or rapid progression,

- **Follicular lymphoma, Classic**

- First-line therapy for stage I, contiguous stage II, noncontiguous stage II disease, or for individuals with indications for treatment* with stage III or IV disease (NCCN-preferred for high tumor burden)
 - As a component of RCHOP or RCVP regimen
 - In combination with bendamustine or lenalidomide
- First-line therapy for stage I, contiguous stage II, noncontiguous stage II disease, or for individuals with indications for treatment* with stage III or IV disease, as a single agent (NCCN-preferred for low tumor burden)
- Elderly or infirm individuals, as a single agent (NCCN-preferred), when tolerability of combination chemotherapy is a concern as:
 - First-line therapy for stage I, contiguous stage II, noncontiguous stage II disease, or for individuals with indications for treatment* with stage III or IV disease
 - Second-line and subsequent therapy (if not previously given) for no response, relapsed, or progressive disease individuals with indications for treatment*
- Elderly or infirm individuals with indications for treatment* in combination with cyclophosphamide as:
 - First-line therapy for stage I, contiguous stage II, noncontiguous stage II disease, or for individuals with indications for treatment* with stage III or IV disease
 - Second-line and subsequent therapy (if not previously given) for no response, relapsed, or progressive disease individuals with indications for treatment*
- Elderly or infirm individuals with indications for treatment* in combination with chlorambucil as first-line therapy for stage I, contiguous stage II, noncontiguous stage II disease, or for individuals with indications for treatment* with stage III or IV disease
- First-line therapy for stage I, II pediatric-type follicular lymphoma in adults with extensive local disease who are not candidates for excision or ISRT, as a component RCHOP regimen
- Second-line or subsequent therapy (if not previously given) for no response, relapsed, or progressive disease in individuals with the indications for treatment* in one of the following regimens:
 - As a single agent (NCCN-preferred in older or infirm)
 - Bendamustine with rituximab (NCCN-preferred)
 - RCHOP (NCCN-preferred)

- RCVP (NCCN-preferred)
- Lenalidomide with rituximab (NCCN-preferred)
- Maintenance therapy
 - First-line extended therapy in individuals with the indications for treatment* if initially treated with single-agent rituximab
 - NCCN-preferred as first-line extended dosing for individuals initially presenting with high tumor burden (stage III,IV) who achieve a complete or partial response following treatment with RCHOP regimen or RCVP regimen
 - NCCN-preferred second-line extended dosing

*Indications for treatment of follicular lymphoma are as follows: candidate for clinical trial, symptoms, threatened end-organ function, clinically significant or progressive cytopenia secondary to lymphoma, clinically significant bulky disease, steady or rapid progression.

○ **Hairy cell leukemia**

- In combination with cladribine in individuals with the indication for treatment*** for initial therapy (NCCN preferred)
- In combination with cladribine in individuals with the indication for treatment*** for relapse at 2 or more years if pentostatin was used as initial therapy (NCCN preferred)
- In combination with pentostatin in individuals with the indication for treatment*** for relapse at 2 or more years if cladribine was used as initial therapy (NCCN preferred)
- In combination with cladribine in individuals with the indication for treatment*** for less than complete response or relapse within 2 years of complete response if pentostatin was used as initial therapy
- In combination with pentostatin in individuals with the indication for treatment*** for less than complete response or relapse within 2 years of complete response if cladribine was used as initial therapy
- In combination with vemurafenib in individuals with the indication for treatment*** for progression after therapy for relapsed/refractory disease (NCCN preferred)
- In combination with vemurafenib in individuals with the indication for treatment*** for less than complete response or relapse within 2 years of complete response if cladribine or pentostatin was used as initial therapy (NCCN preferred)
- In combination with vemurafenib in individuals with the indication for treatment*** as initial therapy (consider for individuals unable to receive purine analogues, including frail or those with active infection)
- In combination with cladribine or pentostatin in individuals with the indication for treatment*** as retreatment for relapse 2 years or greater following initial treatment (NCCN preferred)

- In combination with venetoclax in individuals with the indication for treatment*** for progression after therapy for relapsed/refractory disease (for individuals with disease resistant to BRAF inhibitor therapy)
- As a single agent in individuals with the indication for treatment*** for individuals who are unable to receive purine analogues for one of the following:
 - Less than complete response or relapse within 2 years following initial treatment
 - Relapse 2 or more years following initial treatment

***Indications for treatment of hairy cell leukemia are as follows: systemic symptoms with physical discomfort due to splenomegaly or hepatomegaly, unexplained weight loss (>10% within prior 6 months), excessive fatigue, cytopenias (hemoglobin <11 g/dL, platelets <100,000/ μ L, absolute neutrophil count [ANC] <1000/ μ L), progressive lymphocytosis or lymphadenopathy.

- **Histiocytic neoplasms (Rosai-Dorfman disease)**
 - First-line or subsequent therapy, irrespective of mutation, for IgG4-related, nodal and immune-cytopenia diseases, as a single agent, for:
 - Symptomatic unresectable (bulky/site of disease) unifocal disease
 - Symptomatic multifocal disease
 - Relapsed/refractory disease
- **Histologic transformation of indolent lymphomas to diffuse large B-cell lymphoma**
 - Histologic transformation of follicular or marginal zone lymphoma to diffuse large B-cell lymphoma or HGBL with MYC and BCL6 and without BCL2 rearrangements after minimal or no prior therapy as a component of:
 - RCHOP
 - Dose-adjusted EPOCH
 - Pola-R-CHP regimen for IPI ≥ 2
 - Histologic transformation of follicular or marginal zone lymphoma to diffuse large B-cell lymphoma or HGBL with MYC and BCL6 and without BCL2 rearrangements after minimal or no prior therapy in those with poor left ventricular function, as a component of:
 - RCDOP regimen
 - Dose-adjusted EPOCH regimen with rituximab
 - RCEOP regimen with rituximab
 - RGCVP
 - Histologic transformation of follicular or marginal zone lymphoma to diffuse large B-cell lymphoma or HGBL with MYC and BCL6 and without BCL2 rearrangements after minimal or no prior therapy in those very frail and/or aged more than 80 years with comorbidities, as a component of:
 - RCDOP
 - R-mini-CHOP regimen
 - RGCVP

- Partial response, no response, progressive, or relapsed disease following chemoimmunotherapy for histologic transformation of follicular or marginal zone lymphoma after minimal or no prior therapy, as additional therapy
- Histologic transformation of follicular or marginal zone lymphoma after multiple lines of prior therapies including two or more chemoimmunotherapy regimens for indolent or transformed disease
- NCCN-preferred without regard to transplant if not previously given as a component of RCHOP regimen (Note: If partial response and proceeding to transplant, consider additional systemic therapy not previously given with or without involved site RT to induce complete response prior to transplant)
- NCCN-preferred in individuals with intention to proceed to transplant if previously treated with an anthracycline-based regimen as a component of one of the following:
 - RDHA regimen
 - GDP with rituximab regimen
 - Gemcitabine, dexamethasone, and carboplatin with rituximab regimen
 - ICE with rituximab regimen
- NCCN-preferred in noncandidates for transplant if previously treated with anthracycline-based regimen as a component of polatuzumab vedotin-piiq with or without bendamustine and with rituximab
- Used in noncandidates for transplant as a component of one of the following:
 - CEOP with rituximab regimen
 - GDP with rituximab regimen
 - Gemcitabine, dexamethasone, and carboplatin with rituximab regimen
 - GemOX with rituximab regimen
- Induction therapy for HGBLs with MYC and BCL2 with or without BCL6 rearrangements and HGBL, not otherwise specified as a component of:
 - RCHOP
 - Dose-adjusted EPOCH
 - Hyper-CVAD alternating with high-dose methotrexate and cytarabine regimen with rituximab
 - R-CODOX-M regimen alternating with R-IVAC regimen
- Induction therapy for HGBLs with MYC and BCL2 with or without BCL6 rearrangements and HGBL, not otherwise specified as a component of R-mini-CHOP regimen
- **Mantle cell lymphoma**
 - Aggressive induction therapy when both of the following criteria are met:

- One of the following conditions:
 - Additional therapy for stage I-II disease following partial response, progression, or relapse after initial treatment with ISRT alone
 - Re-induction therapy for stage I-II disease (in selected cases outlined in NCCN guidelines) for relapse after initial treatment with chemoimmunotherapy
 - For classical or symptomatic indolent TP53 wildtype stage II bulky noncontiguous or stage III, IV disease
- As a component of one of the following regimens:
 - LyMA regimen: RDHA regimen conditionally followed by RCHOP for non-PET complete response (NCCN-preferred)
 - HyperCVAD alternating with high-dose methotrexate and cytarabine regimen with rituximab (Note: rituximab + covalent BTKi (acalabrutinib, ibrutinib, or zanubrutinib) can be used as a pretreatment to limit the number of cycles of R-HyperCVAD/rituximab maintenance)
 - NORDIC (dose-intensified induction immunochemotherapy with rituximab, cyclophosphamide, vincristine, doxorubicin, and prednisone [maxi-CHOP] alternating with rituximab and high-dose cytarabine) regimen (NCCN-preferred)
 - Bendamustine with rituximab followed by rituximab in combination with high-dose cytarabine (NCCN-preferred)
 - TRIANGLE regimen: alternating RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone) + ibrutinib/RDHAP (rituximab, dexamethasone, and cytarabine) + platinum (carboplatin, cisplatin, or oxaliplatin) regimen (NCCN-preferred)
 - RBAC500 (rituximab, bendamustine, and cytarabine) regimen
- Less-aggressive induction therapy, when they meet both of the following criteria:
 - One of the following conditions:
 - Initial therapy for stage I-II disease
 - Additional therapy for stage I-II disease for partial response, progression, or relapse after initial treatment with ISRT alone
 - Re-induction therapy for stage I-II disease (in selected cases outlined in NCCN guidelines) for relapse after initial treatment with chemoimmunotherapy in those who are not suitable for aggressive therapy

- For classical or indolent TP53 wildtype stage II bulky noncontiguous or stage III, IV disease in those who are not suitable for aggressive therapy
 - As a component of one of the following regimens:
 - In combination with bendamustine or lenalidomide (NCCN-preferred)
 - VR-CAP regimen (NCCN-preferred)
 - RCHOP (NCCN-preferred)
 - In combination with acalabrutinib
- NCCN-preferred less-aggressive induction therapy classical indolent TP53 mutated stage II bulky noncontiguous or stage III, IV disease (in absence of clinical trial) with the following:
 - In combination with bendamustine or lenalidomide
 - VR-CAP regimen
 - RCHOP regimen
- In combination with acalabrutinib as less-aggressive therapy if not suitable for aggressive therapy
- As a component of TRIANGLE regimen: alternating RCHOP + ibrutinib/RDHAP (rituximab, dexamethasone, and cytarabine) + platinum (carboplatin, cisplatin, or oxaliplatin) regimen (NCCN-preferred), if suitable for aggressive therapy
- Maintenance therapy, in combination with ibrutinib as:
 - For complete response following aggressive induction therapy
 - Following high dose therapy/autologous stem cell rescue
- Maintenance therapy, as a single agent, for classical or indolent TP53 wildtype following complete response or very good partial response to less-aggressive induction therapy with BR (bendamustine and rituximab) regimen or RCHOP
- Second-line and subsequent therapy in combination with lenalidomide (NCCN-preferred) or in combination with ibrutinib for:
 - Stage I-II disease with partial response, relapse, or progression after prior treatment with chemoimmunotherapy
 - Classical or indolent TP53 wildtype stage II bulky noncontiguous or stage III, IV disease in individuals who have no response or progressive disease or partial response with substantial disease after induction therapy
 - Relapsed or refractory disease (if not previously given)
- Second-line therapy or subsequent therapy (in certain circumstances outlined in NCCN guidelines) for stage I-II disease with partial response, relapse, or progression after prior treatment with chemoimmunotherapy; or for classical or indolent stage II bulky noncontiguous or stage III, IV disease in those with no response or progressive disease or partial response with substantial disease after

induction therapy; or for relapsed or refractory disease in one of the following regimens:

- In combination with bendamustine (if not previously given)
- RBAC500 (rituximab, bendamustine, and cytarabine) regimen (if not previously treated with bendamustine)
- In combination with bortezomib
- RDHA (dexamethasone and cytarabine) + platinum (carboplatin, cisplatin, or oxaliplatin) + rituximab regimen (if not previously given)
- GemOx with rituximab
- In combination with venetoclax

○ **Nodal Marginal Zone Lymphoma**

- First-line, second-line, or subsequent therapy for relapsed, refractory, or progressive disease, as a single agent (NCCN-preferred) or in combination with chlorambucil or cyclophosphamide for the following:
 - Stage I
 - Contiguous stage II
 - Stage III or IV disease in elderly or infirm individuals with indications for treatment[‡] where tolerability of combination chemotherapy is a concern
- NCCN-preferred first-line therapy for stage I, contiguous stage II, noncontiguous stage II, or stage III, IV disease in individuals with indications for treatment[‡] in one of the following regimens:
 - RCHOP
 - RCVP
 - Bendamustine with rituximab
- First-line therapy as a single agent for stage I, contiguous stage II, noncontiguous stage II, or stage III, IV disease in individuals with indications for treatment[‡]
- NCCN-preferred second-line or subsequent therapy for relapsed, refractory, or progressive disease in individuals with indications for treatment[‡] in one of the following regimens:
 - Bendamustine with rituximab (if not previously treated with bendamustine)
 - RCHOP
 - RCVP
 - Lenalidomide with rituximab including for the elderly or infirm when tolerability of combination therapy is a concern
- Maintenance as optional first-line extended therapy
- Second-line or subsequent therapy as a single agent for relapsed, refractory or progressive disease in individuals with the indications for treatment[‡] (if longer duration of remission)

‡Indications for treatment of nodal marginal zone lymphoma include: candidate for clinical trial, symptoms, threatened end-organ function, clinically significant or progressive cytopenia secondary to the lymphoma, clinically significant bulky disease, steady or rapid progression.

- **Nongastric MALT lymphoma (noncutaneous)**

- First-line therapy for stage IE or contiguous IIE disease in selected cases
- First-line, second-line, or subsequent therapy for relapsed, refractory, or progressive disease as a single agent (NCCN-preferred) or in combination with chlorambucil or cyclophosphamide for stage IV disease or in recurrent stage IE or contiguous stage IIE disease in elderly or infirm individuals with the indications for treatment**** where tolerability of combination chemotherapy is a concern
- First-line therapy (NCCN-preferred) for stage IV disease or recurrent stage IE or contiguous stage IIE disease in individuals with the indications for treatment**** in one of the following regimens:
 - RCHOP
 - RCVP
 - Bendamustine with rituximab
- First-line therapy as a single agent for stage IV disease or recurrent stage IE or contiguous stage IIE disease in individuals with the indications for treatment****
- Maintenance as optional first-line extended therapy
- NCCN-preferred second-line or subsequent therapy for relapsed, refractory, or for progressive disease in individuals with the indications for treatment**** in one of the following regimens:
 - Bendamustine with rituximab (if not previously given)
 - RCHOP
 - RCVP
 - In combination with lenalidomide, including for the elderly or infirm when tolerability of combination chemotherapy is a concern
- Second-line or subsequent therapy as a single agent for relapsed, refractory, or progressive disease in individuals with the indications for treatment**** (if longer duration of remission)

****Indications for treatment of nongastric MALT lymphoma include: candidate for clinical trial, symptoms, gastrointestinal bleeding, threatened end-organ function, clinically significant bulky disease, steady or rapid progression.

- **Pediatric aggressive mature B-cell lymphomas (age ≥6 months) - Burkitt Lymphoma and Diffuse Large B-cell Lymphoma**

- Induction therapy for individuals with 20% or greater size reduction after COP reduction phase as a component of Children's Oncology Group (COG) Adolescent Non-Hodgkin's Lymphoma (ANHL)1131 regimen B/induction 1 and 2 with COPADM with rituximab regimen (NCCN preferred) for:

- Group B individuals with low-risk disease (unresected stage I or nonabdominal stage II individuals or any stage III individual with lactate dehydrogenase [LDH] 2 or less times the upper limit of normal [ULN])
 - Group B individuals with high-risk disease (any stage III individual with LDH >2 times ULN, and all non-CNS stage IV individuals with <25% bone marrow involvement)
- Consolidation therapy 1 for individuals with 20% or greater size reduction after COP reduction phase as a component of COG ANHL1131 regimen B with CYM (cytarabine, methotrexate, and intrathecal therapy with methotrexate, cytarabine, and hydrocortisone) with rituximab regimen (NCCN preferred) for:
 - Group B individuals with low-risk disease (unresected stage I or nonabdominal stage II individuals or any stage III individual with LDH ≤2 times the ULN)
 - Group B individuals with high-risk disease (any stage III individual with LDH >2 times ULN, and all non-CNS stage IV individuals with <25% bone marrow involvement)
- Induction therapy as a component of COG ANHL1131 regimen C1/induction 1 and 2 with R-COPADM with rituximab regimen (NCCN preferred) for:
 - Group B individuals with <20% size reduction after COP reduction phase
 - Group C individuals with CNS-negative disease after initial treatment with COP reduction phase
 - Group C individuals with CNS-positive and CSF-negative or -positive disease after initial treatment with COP reduction phase
- Alternative induction therapy as a component of COG ANHL1131 regimen C3/induction 1 and 2 with R-COPADM with rituximab regimen (NCCN preferred) for:
 - Group C individuals with CNS- and CSF-positive disease
 - Group C individuals on regimen C1 therapy with less than 20% size reduction after COP reduction phase
- Consolidation therapy 1 and 2 as a component of COG ANHL1131 regimen C1 with R-CYVE with rituximab regimen (NCCN preferred) for:
 - Group B individuals with less than complete response after first cycle of consolidation with CYM regimen
 - Group C individuals with CNS-negative disease
 - Group C individuals with CNS-positive disease, plus high-dose methotrexate and additional intrathecal therapy with methotrexate, cytarabine, and hydrocortisone after R-CYVE 1 only
- Consolidation therapy 1 and 2 as a component of COG ANHL1131 regimen C3 with R-CYVE with rituximab regimen (NCCN preferred) for group C individuals with CNS- and CSF-positive disease, plus high-dose

- methotrexate and additional intrathecal therapy with methotrexate, cytarabine, and hydrocortisone after R-CYVE 1 only
- As a component of R-CYVE with rituximab regimen as treatment for relapsed/refractory disease if not previously received as a part of initial therapy (NCCN preferred)
- As a component of R-ICE (ifosfamide, carboplatin, and etoposide) with rituximab regimen as treatment for relapsed/refractory disease (NCCN preferred)
- **Pediatric aggressive mature B-cell lymphomas (age ≥6 months) - Primary Mediastinal Large B-Cell Lymphoma**
 - Induction therapy/initial treatment as a component of:
 - DA-EPOCH (etoposide, prednisolone, vincristine, cyclophosphamide, and doxorubicin) with rituximab regimen (NCCN preferred)
 - R-CHOP (NCCN preferred)
 - Relapsed or refractory disease as a component of:
 - DHAP with rituximab regimen (NCCN preferred)
 - ICE with rituximab regimen (NCCN preferred)
 - Induction therapy/initial treatment as a component of LMB-modified B/C chemotherapy with rituximab for R-COPADM (cyclophosphamide, vincristine, prednisone, doxorubicin, methotrexate, and intrathecal therapy with methotrexate and hydrocortisone) with rituximab regimen
 - Consolidation therapy as a component of LMB-modified B/C chemotherapy with rituximab for R-CYVE with rituximab regimen
- **Post-transplantation lymphoproliferative disorder (PTLD)**
 - Used as clinically indicated as a bridging option until CAR T-cell product is available for individuals with primary refractory disease or relapsed disease less than 12 months after completion of first-line therapy as a component of one of the following:
 - DHA regimen
 - Polatuzumab vedotin-piiq with or without bendamustine (consider/add bendamustine only after leukapheresis)
 - GDP regimen
 - Gemcitabine, dexamethasone, and carboplatin regimen
 - GemOx regimen
 - ICE regimen
 - Single-agent therapy as:
 - First-line therapy for monomorphic (B-cell type) or polymorphic (B-cell type) PTLD
 - Second-line therapy for partial response, persistent or progressive nondestructive lesions or for partial response, persistent or progressive monomorphic (B-cell type) PTLD if immunosuppressive was reduced in first-line therapy (or for

those with partial response to initial treatment with rituximab monotherapy and IPI 0-2)

- Maintenance therapy for polymorphic (B-cell type) PTLD achieving complete response on first-line therapy
- Concurrent chemoimmunotherapy for CD20+ disease as a component of RCHOP, RCVP, RCEPP, or RCEOP regimen
- with rituximab for frail individuals who cannot tolerate anthracyclines as:
 - First-line therapy for monomorphic (B-cell type) or systemic polymorphic (B-cell type) PTLD
 - Second-line therapy for persistent or progressive monomorphic (B-cell type) or polymorphic (B-cell type) PTLD
- Sequential chemoimmunotherapy as a single agent followed by CHOP regimen as:
 - First-line therapy for monomorphic (B-cell type) or systemic polymorphic (B-cell type) PTLD
 - Second-line therapy for partial response, persistent or progressive monomorphic (B-cell type) or polymorphic (B-cell type) PTLD
- In combination with high-dose methotrexate for primary CNS PTLD (B-cell type)
- Second-line and subsequent therapy for individuals with monomorphic PTLD (B-cell type) for one of the following:
 - Relapsed disease less than 12 months after completion of initial treatment with chemoimmunotherapy
 - Primary refractory disease (partial response, no response, or progression) or relapsed disease less than 12 months after completion of initial treatment with chemoimmunotherapy in noncandidates for CAR T-cell therapy
 - Alternative systemic therapy (if not previously used) for relapsed/refractory disease in noncandidates for CAR T-cell therapy
- Second-line and subsequent therapy for individuals with monomorphic PTLD (B-cell type) with intention to proceed to transplant, as a component of:
 - DHA regimen
 - ESHAP
 - GDP regimen
 - Gemcitabine, dexamethasone, and carboplatin regimen
 - GemOX regimen
 - ICE
 - MINE

- Second-line and subsequent therapy for individuals with monomorphic PTLD (B-cell type) in noncandidates for transplant when they meet both of the following criteria:
 - One of the following conditions:
 - Relapsed disease less than 12 months after completion of initial treatment with chemoimmunotherapy
 - Primary refractory disease (partial response, no response, or progression) or relapsed disease less than 12 months after completion of initial treatment with chemoimmunotherapy in noncandidates for CAR T-cell therapy
 - Alternative systemic therapy (if not previously used) for relapsed/refractory disease in noncandidates for CAR T-cell therapy
 - As a component of one of the following regimens:
 - Polatuzumab vedotin-piiq with or without bendamustine
 - As a single agent
 - In combination with lenalidomide (nongerminal center diffuse large B-cell lymphoma), or bendamustine
 - Dose-adjusted EPOCH regimen (if not previously given)
 - CEOP
 - GDP
 - GemOx
 - Gemcitabine, dexamethasone, carboplatin
- **Primary cutaneous B-cell lymphoma**
 - Therapy for primary cutaneous marginal zone or follicle center lymphoma with:
 - Generalized disease (skin only), T3
 - Solitary/regional, T1-2 disease that is refractory to initial therapy
- **Splenic marginal zone lymphoma**
 - Single-agent therapy (NCCN-preferred) for symptomatic individuals with splenomegaly who have one of the following features:
 - Hepatitis C negative
 - Hepatitis C positive with contraindications for hepatitis treatment
 - Hepatitis C positive with no response to appropriate hepatitis treatment
 - First-line (if treatment naive), second-line or subsequent therapy as a single agent (NCCN-preferred) or in combination with chlorambucil or cyclophosphamide in elderly or infirm individuals with the indications for treatment[†] upon disease recurrence following initial treatment for splenomegaly where tolerability of combination chemotherapy is a concern

- First-line therapy (NCCN-preferred) in treatment-naïve individuals with the indications for treatment[†] for disease recurrence following initial treatment for splenomegaly in one of the following regimens:
 - As a single agent
 - RCHOP
 - RCVP
 - Bendamustine with rituximab
- Maintenance as optional first-line extended therapy in individuals
- NCCN-preferred second-line (if previously treated with rituximab) and subsequent therapy for disease recurrence in combination with lenalidomide for disease recurrence in those with indications for treatment[†], including elderly or infirm when tolerability of combination chemotherapy is a concern
- Second-line and subsequent therapy as a single agent for disease recurrence in those with indications for treatment[†] (if previously treated with rituximab with a longer duration of remission)
- NCCN-preferred second-line (if prior treatment with rituximab) or subsequent therapy for disease recurrence in individuals with the indications for treatment[†] in one of the following regimens:
 - Bendamustine with rituximab (if not previously given)
 - RCHOP
 - RCVP

[†]Indications for treatment of splenic marginal cell lymphoma include: candidate for clinical trial, symptoms, cytopenias including autoimmune cytopenia, threatened end-organ function, clinically significant bulky disease, steady or rapid progression.

- **Multiple sclerosis, relapsing-remitting, after documented failure, contraindication or intolerance to at least two other disease-modifying treatments (DMTs)**
- **Myasthenia gravis**
 - Refractory to previous treatments (e.g., corticosteroids, immunosuppressants, plasma exchange, IVIG, thymectomy) as demonstrated through baseline and periodic evaluation of disease status through 1) the Myasthenia Gravis Foundation of America (MGFA) clinical classification, or 2) the Myasthenia Gravis Activities of Daily Living (MG-ADL) score
- **Nephrotic syndrome, including minimal change disease, in pediatric individuals when disease is refractory to corticosteroids or other immunosuppressive therapies (e.g., cyclophosphamide, cyclosporine, mycophenolate mofetil)**
- **Neuromyelitis optica (NMO)**
- **Pemphigoid diseases refractory to corticosteroids or other immunosuppressive therapies**
 - Bullous pemphigoid
 - Mucous membrane pemphigoid, including ocular cicatricial pemphigoid
 - Epidermolysis bullosa acquisita
- **Pemphigus diseases (i.e., pemphigus vulgaris, pemphigus foliaceus, and paraneoplastic pemphigus) as first-line or subsequent-line of treatment**
- **Pure red cell aplasia, refractory to other standard therapies (e.g., corticosteroids, cyclophosphamide, cyclosporine)**
- **Rheumatoid arthritis, active**

- In combination with methotrexate, unless documented failure, contraindication or intolerance exists, in adults with moderate-to-severe active rheumatoid arthritis who have had an inadequate response to at least a 3-month trial of one or more tumor necrosis factor (TNF)–antagonist therapies
- **Scleroderma refractory to at least 3 months of corticosteroids or other immunosuppressive therapies (e.g., methotrexate, cyclophosphamide, azathioprine, mycophenolate mofetil)**
- **Sjögren syndrome, primary, refractory to corticosteroids and other immunosuppressive therapies (e.g., methotrexate, cyclophosphamide, azathioprine)**
- **Systemic lupus erythematosus (SLE), refractory to other immunosuppressive therapies (e.g., azathioprine, cyclophosphamide, mycophenolate mofetil)**
- **Thrombocytopenic purpura, immune or idiopathic (ITP) when the individual has a documented platelet count $<30 \times 10^9/L$**
- **Thrombocytopenic purpura, thrombotic (TTP)**
 - In combination with corticosteroids and therapeutic plasma exchange (TPE), unless documented failure, contraindication, or intolerance exists.
- **Transplantation, prophylaxis**
 - For prophylaxis, to reduce cardiac or renal transplantation rejection (pre- and post-) by reducing HLA antibodies in previously sensitized individuals
 - In combination with IVIG alone, or in combination with IVIG and TPE
- **Transplantation, antibody-mediated rejection (AMR)**
 - For refractory cardiac, lung, pancreas, or renal transplantation AMR
 - In combination or after failure of either IVIG alone, or IVIG in combination with TPE
- **Waldenström macroglobulinemia/lymphoplasmacytic lymphoma**
 - Used as a component of CaRD as primary therapy or for relapse if previously used as primary therapy that was well tolerated and elicited a prolonged response
 - Primary therapy, for relapse if previously used as primary therapy that was well tolerated and elicited a prolonged response, or as alternative therapy for previously treated disease with persistent symptoms following primary therapy, or that does not respond to primary therapy, or for progressive or relapsed disease
 - As a single agent
 - In combination with bendamustine (NCCN-preferred regimen)
 - In combination with bortezomib with dexamethasone (NCCN-preferred regimen)
 - In combination with cyclophosphamide and prednisone
 - In combination with cyclophosphamide and dexamethasone (NCCN-preferred when not used as primary therapy)
 - In combination with ibrutinib (NCCN-preferred)
 - In combination with ixazomib and dexamethasone
 - Maintenance therapy in select individuals after chemoimmunotherapy regimens
 - Management of symptomatic Bing-Neel syndrome if systemic control is needed in combination with one of the following:
 - Ibrutinib (NCCN-preferred)
 - Zanubrutinib (NCCN-preferred)
 - Bendamustine

- Methotrexate (intravenous)
- Fludarabine
- Cytarabine
- Alternative therapy for previously treated disease with persistent symptoms following primary therapy or that does not respond to primary therapy or for progressive or relapsed disease
 - As a component of RCHOP
 - In combination with cladribine or fludarabine, or as a component of FCR (fludarabine, cyclophosphamide, and rituximab) regimen in individuals who are not potential autologous stem cell transplant candidates

RITUXIMAB AND HYALURONIDASE HUMAN (RITUXAN HYCELA)

Rituximab and hyaluronidase human (Rituxan Hycela) for subcutaneous injection is considered medically necessary and, therefore, covered as a substitute for rituximab and related biosimilars after at least one full dose of rituximab infusion or related biosimilars is administered, and when the following criteria are met:

- **Castleman Disease (CD)**
 - As a single agent or in combination with other systemic therapies
- **Lymphoma, Hodgkin**
 - As a single agent
- **Lymphoma, non-Hodgkin (NHL)**
 - **Chronic lymphocytic leukemia (CLL)**
 - With fludarabine, cyclophosphamide (FCR), for the treatment of previously untreated and previously treated CLL
 - As a single agent or in combination with other systemic therapies
 - **Diffuse large B-cell lymphoma (DLBCL)**
 - Previously untreated DLBCL in combination with CHOP or other anthracycline-based chemotherapy regimens
 - As a single agent or in combination with other systemic therapies
 - **Follicular lymphoma**
 - Relapsed or refractory, follicular lymphoma as a single agent
 - Previously untreated follicular lymphoma in combination with first-line chemotherapy and, in individuals achieving a complete or partial response to rituximab in combination with chemotherapy, as single-agent maintenance therapy
 - Nonprogressing (including stable disease) follicular lymphoma as a single agent after first-line CVP chemotherapy
 - Classic follicular lymphoma as a single agent or in combination with other systemic therapies
 - **Gastric MALT lymphoma**
 - As a single agent or in combination with other systemic therapies
 - **Hairy cell leukemia**
 - As a single agent or in combination with other systemic therapies
 - **High-grade B-cell lymphomas**
 - As a single agent or in combination with other systemic therapies
 - **Histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma**
 - As a single agent or in combination with other systemic therapies
 - **Mantle cell lymphoma**
 - As a single agent or in combination with other systemic therapies
 - **Nodal marginal zone lymphoma**
 - As a single agent or in combination with other systemic therapies
 - **Nongastric MALT lymphoma (noncutaneous)**

- As a single agent or in combination with other systemic therapies
- **Post-transplantation lymphoproliferative disorder (PTLD)**
 - As a single agent or in combination with other systemic therapies
- **Primary cutaneous B-cell lymphomas**
 - Primary cutaneous marginal zone or follicle center lymphoma with one of the following: solitary/regional, T1-2 disease that is refractory to initial therapy or generalized disease (skin only), T3
- **Splenic marginal zone lymphoma**
 - As a single agent or in combination with other systemic therapies
- **Waldenström macroglobulinemia/lymphoplasmacytic lymphoma**
 - As a single agent

Duration of authorization: 12 months

Version Effective Date: 10/07/2024

Title: Rituximab (Rituxan®) Infusion and Related Biosimilars, and Rituximab/Hyaluronidase Human for Subcutaneous Injection (Rituxan Hycela®)

MEDICALLY NECESSARY

ICD-10 CODES AND NARRATIVES

RITUXIMAB AND RELATED BIOSIMILARS ARE MEDICALLY NECESSARY WHEN REPORTED WITH THE FOLLOWING DIAGNOSIS CODES:

C79.32 Secondary malignant neoplasm of cerebral meninges

C79.49 Secondary malignant neoplasm of other parts of nervous system

C81.00 Nodular lymphocyte predominant Hodgkin lymphoma, unspecified site

C81.01 Nodular lymphocyte predominant Hodgkin lymphoma, lymph nodes of head, face, and neck

C81.02 Nodular lymphocyte predominant Hodgkin lymphoma, intrathoracic lymph nodes

C81.03 Nodular lymphocyte predominant Hodgkin lymphoma, intra-abdominal lymph nodes

C81.04 Nodular lymphocyte predominant Hodgkin lymphoma, lymph nodes of axilla and upper limb

C81.05 Nodular lymphocyte predominant Hodgkin lymphoma, lymph nodes of inguinal region and lower limb

C81.06 Nodular lymphocyte predominant Hodgkin lymphoma, intrapelvic lymph nodes

C81.07 Nodular lymphocyte predominant Hodgkin lymphoma, spleen

C81.08 Nodular lymphocyte predominant Hodgkin lymphoma, lymph nodes of multiple sites

C81.09 Nodular lymphocyte predominant Hodgkin lymphoma, extranodal and solid organ sites

C81.70 Other Hodgkin lymphoma, unspecified site

C81.71 Other Hodgkin lymphoma, lymph nodes of head, face, and neck

C81.72 Other Hodgkin lymphoma, intrathoracic lymph nodes

C81.73 Other Hodgkin lymphoma, intra-abdominal lymph nodes

C81.74 Other Hodgkin lymphoma, lymph nodes of axilla and upper limb

C81.75 Other Hodgkin lymphoma, lymph nodes of inguinal region and lower limb

C81.76 Other Hodgkin lymphoma, intrapelvic lymph nodes

C81.77 Other Hodgkin lymphoma, spleen

C81.78 Other Hodgkin lymphoma, lymph nodes of multiple sites

C81.79 Other Hodgkin lymphoma, extranodal and solid organ sites

C82.00 Follicular lymphoma grade I, unspecified site

C82.01 Follicular lymphoma grade I, lymph nodes of head, face, and neck

C82.02 Follicular lymphoma grade I, intrathoracic lymph nodes

C82.03 Follicular lymphoma grade I, intra-abdominal lymph nodes

C82.04 Follicular lymphoma grade I, lymph nodes of axilla and upper limb

C82.05 Follicular lymphoma grade I, lymph nodes of inguinal region and lower limb

C82.06 Follicular lymphoma grade I, intrapelvic lymph nodes

C82.07 Follicular lymphoma grade I, spleen

C82.08 Follicular lymphoma grade I, lymph nodes of multiple sites

C82.09 Follicular lymphoma grade I, extranodal and solid organ sites

C82.10 Follicular lymphoma grade II, unspecified site

C82.11 Follicular lymphoma grade II, lymph nodes of head, face, and neck

C82.12 Follicular lymphoma grade II, intrathoracic lymph nodes

C82.13 Follicular lymphoma grade II, intra-abdominal lymph nodes

C82.14 Follicular lymphoma grade II, lymph nodes of axilla and upper limb

C82.15 Follicular lymphoma grade II, lymph nodes of inguinal region and lower limb

C82.16 Follicular lymphoma grade II, intrapelvic lymph nodes

C82.17 Follicular lymphoma grade II, spleen

C82.18 Follicular lymphoma grade II, lymph nodes of multiple sites

C82.19 Follicular lymphoma grade II, extranodal and solid organ sites

C82.30 Follicular lymphoma grade IIIa, unspecified site

C82.31 Follicular lymphoma grade IIIa, lymph nodes of head, face, and neck

C82.32 Follicular lymphoma grade IIIa, intrathoracic lymph nodes

C82.33 Follicular lymphoma grade IIIa, intra-abdominal lymph nodes

C82.34 Follicular lymphoma grade IIIa, lymph nodes of axilla and upper limb

C82.35 Follicular lymphoma grade IIIa, lymph nodes of inguinal region and lower limb

C82.36 Follicular lymphoma grade IIIa, intrapelvic lymph nodes

C82.37 Follicular lymphoma grade IIIa, spleen

C82.38 Follicular lymphoma grade IIIa, lymph nodes of multiple sites

C82.39 Follicular lymphoma grade IIIa, extranodal and solid organ sites

C82.50 Diffuse follicle center lymphoma, unspecified site

C82.51 Diffuse follicle center lymphoma, lymph nodes of head, face, and neck

C82.52 Diffuse follicle center lymphoma, intrathoracic lymph nodes

C82.53 Diffuse follicle center lymphoma, intra-abdominal lymph nodes

C82.54 Diffuse follicle center lymphoma, lymph nodes of axilla and upper limb

C82.55 Diffuse follicle center lymphoma, lymph nodes of inguinal region and lower limb

C82.56 Diffuse follicle center lymphoma, intrapelvic lymph nodes

C82.57 Diffuse follicle center lymphoma, spleen

C82.58 Diffuse follicle center lymphoma, lymph nodes of multiple sites

C82.59 Diffuse follicle center lymphoma, extranodal and solid organ sites

C82.60 Cutaneous follicle center lymphoma, unspecified site

C82.61 Cutaneous follicle center lymphoma, lymph nodes of head, face, and neck

C82.62 Cutaneous follicle center lymphoma, intrathoracic lymph nodes

C82.63 Cutaneous follicle center lymphoma, intra-abdominal lymph nodes

C82.64 Cutaneous follicle center lymphoma, lymph nodes of axilla and upper limb

C82.65 Cutaneous follicle center lymphoma, lymph nodes of inguinal region and lower limb

C82.66 Cutaneous follicle center lymphoma, intrapelvic lymph nodes

C82.67 Cutaneous follicle center lymphoma, spleen

C82.68 Cutaneous follicle center lymphoma, lymph nodes of multiple sites

C82.69 Cutaneous follicle center lymphoma, extranodal and solid organ sites

C82.80 Other types of follicular lymphoma, unspecified site

C82.81 Other types of follicular lymphoma, lymph nodes of head, face, and neck

C82.82 Other types of follicular lymphoma, intrathoracic lymph nodes

C82.83 Other types of follicular lymphoma, intra-abdominal lymph nodes

C82.84 Other types of follicular lymphoma, lymph nodes of axilla and upper limb

C82.85 Other types of follicular lymphoma, lymph nodes of inguinal region and lower limb

C82.86 Other types of follicular lymphoma, intrapelvic lymph nodes

C82.87 Other types of follicular lymphoma, spleen

C82.88 Other types of follicular lymphoma, lymph nodes of multiple sites

C82.89 Other types of follicular lymphoma, extranodal and solid organ sites

C82.90 Follicular lymphoma, unspecified, unspecified site

C82.91 Follicular lymphoma, unspecified, lymph nodes of head, face, and neck

C82.92 Follicular lymphoma, unspecified, intrathoracic lymph nodes

C82.93 Follicular lymphoma, unspecified, intra-abdominal lymph nodes

C82.94 Follicular lymphoma, unspecified, lymph nodes of axilla and upper limb

C82.95 Follicular lymphoma, unspecified, lymph nodes of inguinal region and lower limb

C82.96 Follicular lymphoma, unspecified, intrapelvic lymph nodes

C82.97 Follicular lymphoma, unspecified, spleen

C82.98 Follicular lymphoma, unspecified, lymph nodes of multiple sites

C82.99 Follicular lymphoma, unspecified, extranodal and solid organ sites

C83.00 Small cell B-cell lymphoma, unspecified site

C83.01 Small cell B-cell lymphoma, lymph nodes of head, face, and neck

C83.02 Small cell B-cell lymphoma, intrathoracic lymph nodes

C83.03 Small cell B-cell lymphoma, intra-abdominal lymph nodes

C83.04 Small cell B-cell lymphoma, lymph nodes of axilla and upper limb

C83.05 Small cell B-cell lymphoma, lymph nodes of inguinal region and lower limb

C83.06 Small cell B-cell lymphoma, intrapelvic lymph nodes

C83.07 Small cell B-cell lymphoma, spleen

C83.08 Small cell B-cell lymphoma, lymph nodes of multiple sites

C83.09 Small cell B-cell lymphoma, extranodal and solid organ sites

C83.10 Mantle cell lymphoma, unspecified site

C83.11 Mantle cell lymphoma, lymph nodes of head, face, and neck

C83.12 Mantle cell lymphoma, intrathoracic lymph nodes

C83.13 Mantle cell lymphoma, intra-abdominal lymph nodes

C83.14 Mantle cell lymphoma, lymph nodes of axilla and upper limb

C83.15 Mantle cell lymphoma, lymph nodes of inguinal region and lower limb

C83.16 Mantle cell lymphoma, intrapelvic lymph nodes

C83.17 Mantle cell lymphoma, spleen

C83.18 Mantle cell lymphoma, lymph nodes of multiple sites

C83.19 Mantle cell lymphoma, extranodal and solid organ sites

C83.30 Diffuse large B-cell lymphoma, unspecified site

C83.31 Diffuse large B-cell lymphoma, lymph nodes of head, face, and neck

C83.32 Diffuse large B-cell lymphoma, intrathoracic lymph nodes

C83.33 Diffuse large B-cell lymphoma, intra-abdominal lymph nodes

C83.34 Diffuse large B-cell lymphoma, lymph nodes of axilla and upper limb

C83.35 Diffuse large B-cell lymphoma, lymph nodes of inguinal region and lower limb

C83.36 Diffuse large B-cell lymphoma, intrapelvic lymph nodes

C83.37 Diffuse large B-cell lymphoma, spleen

C83.38 Diffuse large B-cell lymphoma, lymph nodes of multiple sites

C83.390 Primary central nervous system lymphoma

C83.398 Diffuse large B-cell lymphoma of other extranodal and solid organ sites

C83.70 Burkitt lymphoma, unspecified site

C83.71 Burkitt lymphoma, lymph nodes of head, face, and neck

C83.72 Burkitt lymphoma, intrathoracic lymph nodes

C83.73 Burkitt lymphoma, intra-abdominal lymph nodes

C83.74 Burkitt lymphoma, lymph nodes of axilla and upper limb

C83.75 Burkitt lymphoma, lymph nodes of inguinal region and lower limb

C83.76 Burkitt lymphoma, intrapelvic lymph nodes

C83.77 Burkitt lymphoma, spleen

C83.78 Burkitt lymphoma, lymph nodes of multiple sites

C83.79 Burkitt lymphoma, extranodal and solid organ sites

C85.10 Unspecified B-cell lymphoma, unspecified site

C85.11 Unspecified B-cell lymphoma, lymph nodes of head, face, and neck

C85.12 Unspecified B-cell lymphoma, intrathoracic lymph nodes

C85.13 Unspecified B-cell lymphoma, intra-abdominal lymph nodes

C85.14 Unspecified B-cell lymphoma, lymph nodes of axilla and upper limb

C85.15 Unspecified B-cell lymphoma, lymph nodes of inguinal region and lower limb

C85.16 Unspecified B-cell lymphoma, intrapelvic lymph nodes

C85.17 Unspecified B-cell lymphoma, spleen

C85.18 Unspecified B-cell lymphoma, lymph nodes of multiple sites

C85.19 Unspecified B-cell lymphoma, extranodal and solid organ sites

C85.20 Mediastinal (thymic) large B-cell lymphoma, unspecified site

C85.21 Mediastinal (thymic) large B-cell lymphoma, lymph nodes of head, face, and neck

C85.22 Mediastinal (thymic) large B-cell lymphoma, intrathoracic lymph nodes

C85.23 Mediastinal (thymic) large B-cell lymphoma, intra-abdominal lymph nodes

C85.24 Mediastinal (thymic) large B-cell lymphoma, lymph nodes of axilla and upper limb

C85.25 Mediastinal (thymic) large B-cell lymphoma, lymph nodes of inguinal region and lower limb

C85.26 Mediastinal (thymic) large B-cell lymphoma, intrapelvic lymph nodes

C85.27 Mediastinal (thymic) large B-cell lymphoma, spleen

C85.28 Mediastinal (thymic) large B-cell lymphoma, lymph nodes of multiple sites

C85.29 Mediastinal (thymic) large B-cell lymphoma, extranodal and solid organ sites

C85.80 Other specified types of non-Hodgkin lymphoma, unspecified site

C85.81 Other specified types of non-Hodgkin lymphoma, lymph nodes of head, face, and neck

C85.82 Other specified types of non-Hodgkin lymphoma, intrathoracic lymph nodes

C85.83 Other specified types of non-Hodgkin lymphoma, intra-abdominal lymph nodes

C85.84 Other specified types of non-Hodgkin lymphoma, lymph nodes of axilla and upper limb

C85.85 Other specified types of non-Hodgkin lymphoma, lymph nodes of inguinal region and lower limb

C85.86 Other specified types of non-Hodgkin lymphoma, intrapelvic lymph nodes

C85.87 Other specified types of non-Hodgkin lymphoma, spleen

C85.88 Other specified types of non-Hodgkin lymphoma, lymph nodes of multiple sites

C85.89 Other specified types of non-Hodgkin lymphoma, extranodal and solid organ sites

C88.00 Waldenstrom macroglobulinemia not having achieved remission

C88.40 Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue [MALT-lymphoma] not having achieved remission

C91.00 Acute lymphoblastic leukemia not having achieved remission

C91.02 Acute lymphoblastic leukemia, in relapse

C91.10 Chronic lymphocytic leukemia of B-cell type not having achieved remission

C91.12 Chronic lymphocytic leukemia of B-cell type in relapse

C91.40 Hairy cell leukemia not having achieved remission

C91.42 Hairy cell leukemia, in relapse

C91.A0 Mature B-cell leukemia Burkitt-type not having achieved remission

C91.A2 Mature B-cell leukemia Burkitt-type, in relapse

D47.Z1 Post-transplant lymphoproliferative disorder (PTLD)

D47.Z2 Castleman disease

D59.0 Drug-induced autoimmune hemolytic anemia

D59.10 Autoimmune hemolytic anemia, unspecified

D59.11 Warm autoimmune hemolytic anemia

D59.12 Cold autoimmune hemolytic anemia

D59.13 Mixed type autoimmune hemolytic anemia

D59.19 Other autoimmune hemolytic anemia

D60.0 Chronic acquired pure red cell aplasia

D60.1 Transient acquired pure red cell aplasia

D60.8 Other acquired pure red cell aplasias

D60.9 Acquired pure red cell aplasia, unspecified

D61.01 Constitutional (pure) red blood cell aplasia

D69.3 Immune thrombocytopenic purpura

D76.3 Other histiocytosis syndromes

D89.84 IgG4-related disease

D89.811 Chronic graft-versus-host disease

D89.812 Acute on chronic graft-versus-host disease

G35 Multiple sclerosis

G36.0 Neuromyelitis optica [Devic]

G70.00 Myasthenia gravis without (acute) exacerbation

G92.00 Immune effector cell-associated neurotoxicity syndrome, grade unspecified

G92.01 Immune effector cell-associated neurotoxicity syndrome, grade 1

G92.02 Immune effector cell-associated neurotoxicity syndrome, grade 2

G92.03 Immune effector cell-associated neurotoxicity syndrome, grade 3

G92.04 Immune effector cell-associated neurotoxicity syndrome, grade 4

G92.05 Immune effector cell-associated neurotoxicity syndrome, grade 5

I77.82 Antineutrophilic cytoplasmic antibody [ANCA] vasculitis

L10.0 Pemphigus vulgaris

L10.2 Pemphigus foliaceus

L10.81 Paraneoplastic pemphigus

L12.0 Bullous pemphigoid

L12.1 Cicatricial pemphigoid

L12.30 Acquired epidermolysis bullosa, unspecified

L94.0 Localized scleroderma [morphea]

L94.1 Linear scleroderma

M05.011 Felty's syndrome, right shoulder

M05.012 Felty's syndrome, left shoulder

M05.021 Felty's syndrome, right elbow

M05.022 Felty's syndrome, left elbow

M05.031 Felty's syndrome, right wrist

M05.032 Felty's syndrome, left wrist

M05.041 Felty's syndrome, right hand

M05.042 Felty's syndrome, left hand

M05.051 Felty's syndrome, right hip

M05.052 Felty's syndrome, left hip

M05.061 Felty's syndrome, right knee

M05.062 Felty's syndrome, left knee

M05.071 Felty's syndrome, right ankle and foot

M05.072 Felty's syndrome, left ankle and foot

M05.09 Felty's syndrome, multiple sites

M05.111 Rheumatoid lung disease with rheumatoid arthritis of right shoulder

M05.112 Rheumatoid lung disease with rheumatoid arthritis of left shoulder

M05.121 Rheumatoid lung disease with rheumatoid arthritis of right elbow

M05.122 Rheumatoid lung disease with rheumatoid arthritis of left elbow

M05.131 Rheumatoid lung disease with rheumatoid arthritis of right wrist

M05.132 Rheumatoid lung disease with rheumatoid arthritis of left wrist

M05.141 Rheumatoid lung disease with rheumatoid arthritis of right hand

M05.142 Rheumatoid lung disease with rheumatoid arthritis of left hand

M05.151 Rheumatoid lung disease with rheumatoid arthritis of right hip

M05.152 Rheumatoid lung disease with rheumatoid arthritis of left hip

M05.161 Rheumatoid lung disease with rheumatoid arthritis of right knee

M05.162 Rheumatoid lung disease with rheumatoid arthritis of left knee

M05.171 Rheumatoid lung disease with rheumatoid arthritis of right ankle and foot

M05.172 Rheumatoid lung disease with rheumatoid arthritis of left ankle and foot

M05.19 Rheumatoid lung disease with rheumatoid arthritis of multiple sites

M05.211 Rheumatoid vasculitis with rheumatoid arthritis of right shoulder

M05.212 Rheumatoid vasculitis with rheumatoid arthritis of left shoulder

M05.221 Rheumatoid vasculitis with rheumatoid arthritis of right elbow

M05.222 Rheumatoid vasculitis with rheumatoid arthritis of left elbow

M05.231 Rheumatoid vasculitis with rheumatoid arthritis of right wrist

M05.232 Rheumatoid vasculitis with rheumatoid arthritis of left wrist

M05.241 Rheumatoid vasculitis with rheumatoid arthritis of right hand

M05.242 Rheumatoid vasculitis with rheumatoid arthritis of left hand

M05.251 Rheumatoid vasculitis with rheumatoid arthritis of right hip

M05.252 Rheumatoid vasculitis with rheumatoid arthritis of left hip

M05.261 Rheumatoid vasculitis with rheumatoid arthritis of right knee

M05.262 Rheumatoid vasculitis with rheumatoid arthritis of left knee

M05.271 Rheumatoid vasculitis with rheumatoid arthritis of right ankle and foot

M05.272 Rheumatoid vasculitis with rheumatoid arthritis of left ankle and foot

M05.29 Rheumatoid vasculitis with rheumatoid arthritis of multiple sites

M05.311 Rheumatoid heart disease with rheumatoid arthritis of right shoulder

M05.312 Rheumatoid heart disease with rheumatoid arthritis of left shoulder

M05.321 Rheumatoid heart disease with rheumatoid arthritis of right elbow

M05.322 Rheumatoid heart disease with rheumatoid arthritis of left elbow

M05.331 Rheumatoid heart disease with rheumatoid arthritis of right wrist

M05.332 Rheumatoid heart disease with rheumatoid arthritis of left wrist

M05.341 Rheumatoid heart disease with rheumatoid arthritis of right hand

M05.342 Rheumatoid heart disease with rheumatoid arthritis of left hand

M05.351 Rheumatoid heart disease with rheumatoid arthritis of right hip

M05.352 Rheumatoid heart disease with rheumatoid arthritis of left hip

M05.361 Rheumatoid heart disease with rheumatoid arthritis of right knee

M05.362 Rheumatoid heart disease with rheumatoid arthritis of left knee

M05.371 Rheumatoid heart disease with rheumatoid arthritis of right ankle and foot

M05.372 Rheumatoid heart disease with rheumatoid arthritis of left ankle and foot

M05.39 Rheumatoid heart disease with rheumatoid arthritis of multiple sites

M05.411 Rheumatoid myopathy with rheumatoid arthritis of right shoulder

M05.412 Rheumatoid myopathy with rheumatoid arthritis of left shoulder

M05.421 Rheumatoid myopathy with rheumatoid arthritis of right elbow

M05.422 Rheumatoid myopathy with rheumatoid arthritis of left elbow

M05.431 Rheumatoid myopathy with rheumatoid arthritis of right wrist

M05.432 Rheumatoid myopathy with rheumatoid arthritis of left wrist

M05.441 Rheumatoid myopathy with rheumatoid arthritis of right hand

M05.442 Rheumatoid myopathy with rheumatoid arthritis of left hand

M05.451 Rheumatoid myopathy with rheumatoid arthritis of right hip

M05.452 Rheumatoid myopathy with rheumatoid arthritis of left hip

M05.461 Rheumatoid myopathy with rheumatoid arthritis of right knee

M05.462 Rheumatoid myopathy with rheumatoid arthritis of left knee

M05.471 Rheumatoid myopathy with rheumatoid arthritis of right ankle and foot

M05.472 Rheumatoid myopathy with rheumatoid arthritis of left ankle and foot

M05.49 Rheumatoid myopathy with rheumatoid arthritis of multiple sites

M05.511 Rheumatoid polyneuropathy with rheumatoid arthritis of right shoulder

M05.512 Rheumatoid polyneuropathy with rheumatoid arthritis of left shoulder

M05.521 Rheumatoid polyneuropathy with rheumatoid arthritis of right elbow

M05.522 Rheumatoid polyneuropathy with rheumatoid arthritis of left elbow

M05.531 Rheumatoid polyneuropathy with rheumatoid arthritis of right wrist

M05.532 Rheumatoid polyneuropathy with rheumatoid arthritis of left wrist

M05.541 Rheumatoid polyneuropathy with rheumatoid arthritis of right hand

M05.542 Rheumatoid polyneuropathy with rheumatoid arthritis of left hand

M05.551 Rheumatoid polyneuropathy with rheumatoid arthritis of right hip

M05.552 Rheumatoid polyneuropathy with rheumatoid arthritis of left hip

M05.561 Rheumatoid polyneuropathy with rheumatoid arthritis of right knee

M05.562 Rheumatoid polyneuropathy with rheumatoid arthritis of left knee

M05.571 Rheumatoid polyneuropathy with rheumatoid arthritis of right ankle and foot

M05.572 Rheumatoid polyneuropathy with rheumatoid arthritis of left ankle and foot

M05.59 Rheumatoid polyneuropathy with rheumatoid arthritis of multiple sites

M05.611 Rheumatoid arthritis of right shoulder with involvement of other organs and systems

M05.612 Rheumatoid arthritis of left shoulder with involvement of other organs and systems

M05.621 Rheumatoid arthritis of right elbow with involvement of other organs and systems

M05.622 Rheumatoid arthritis of left elbow with involvement of other organs and systems

M05.631 Rheumatoid arthritis of right wrist with involvement of other organs and systems

M05.632 Rheumatoid arthritis of left wrist with involvement of other organs and systems

M05.641 Rheumatoid arthritis of right hand with involvement of other organs and systems

M05.642 Rheumatoid arthritis of left hand with involvement of other organs and systems

M05.651 Rheumatoid arthritis of right hip with involvement of other organs and systems

M05.652 Rheumatoid arthritis of left hip with involvement of other organs and systems

M05.661 Rheumatoid arthritis of right knee with involvement of other organs and systems

M05.662 Rheumatoid arthritis of left knee with involvement of other organs and systems

M05.671 Rheumatoid arthritis of right ankle and foot with involvement of other organs and systems

M05.672 Rheumatoid arthritis of left ankle and foot with involvement of other organs and systems

M05.69 Rheumatoid arthritis of multiple sites with involvement of other organs and systems

M05.7A Rheumatoid arthritis with rheumatoid factor of other specified site without organ or systems involvement

M05.8A Other rheumatoid arthritis with rheumatoid factor of other specified site

M05.711 Rheumatoid arthritis with rheumatoid factor of right shoulder without organ or systems involvement

M05.712 Rheumatoid arthritis with rheumatoid factor of left shoulder without organ or systems involvement

M05.721 Rheumatoid arthritis with rheumatoid factor of right elbow without organ or systems involvement

M05.722 Rheumatoid arthritis with rheumatoid factor of left elbow without organ or systems involvement

M05.731 Rheumatoid arthritis with rheumatoid factor of right wrist without organ or systems involvement

M05.732 Rheumatoid arthritis with rheumatoid factor of left wrist without organ or systems involvement

M05.741 Rheumatoid arthritis with rheumatoid factor of right hand without organ or systems involvement

M05.742 Rheumatoid arthritis with rheumatoid factor of left hand without organ or systems involvement

M05.751 Rheumatoid arthritis with rheumatoid factor of right hip without organ or systems involvement

M05.752 Rheumatoid arthritis with rheumatoid factor of left hip without organ or systems involvement

M05.761 Rheumatoid arthritis with rheumatoid factor of right knee without organ or systems involvement

M05.762 Rheumatoid arthritis with rheumatoid factor of left knee without organ or systems involvement

M05.771 Rheumatoid arthritis with rheumatoid factor of right ankle and foot without organ or systems involvement

M05.772 Rheumatoid arthritis with rheumatoid factor of left ankle and foot without organ or systems involvement

M05.79 Rheumatoid arthritis with rheumatoid factor of multiple sites without organ or systems involvement

M05.811 Other rheumatoid arthritis with rheumatoid factor of right shoulder

M05.812 Other rheumatoid arthritis with rheumatoid factor of left shoulder

M05.821 Other rheumatoid arthritis with rheumatoid factor of right elbow

M05.822 Other rheumatoid arthritis with rheumatoid factor of left elbow

M05.831 Other rheumatoid arthritis with rheumatoid factor of right wrist

M05.832 Other rheumatoid arthritis with rheumatoid factor of left wrist

M05.841 Other rheumatoid arthritis with rheumatoid factor of right hand

M05.842 Other rheumatoid arthritis with rheumatoid factor of left hand

M05.851 Other rheumatoid arthritis with rheumatoid factor of right hip

M05.852 Other rheumatoid arthritis with rheumatoid factor of left hip

M05.861 Other rheumatoid arthritis with rheumatoid factor of right knee

M05.862 Other rheumatoid arthritis with rheumatoid factor of left knee

M05.871 Other rheumatoid arthritis with rheumatoid factor of right ankle and foot

M05.872 Other rheumatoid arthritis with rheumatoid factor of left ankle and foot

M05.89 Other rheumatoid arthritis with rheumatoid factor of multiple sites

M05.9 Rheumatoid arthritis with rheumatoid factor, unspecified

M06.0A Rheumatoid arthritis without rheumatoid factor, other specified site

M06.8A Other specified rheumatoid arthritis, other specified site

M06.011 Rheumatoid arthritis without rheumatoid factor, right shoulder

M06.012 Rheumatoid arthritis without rheumatoid factor, left shoulder

M06.021 Rheumatoid arthritis without rheumatoid factor, right elbow

M06.022 Rheumatoid arthritis without rheumatoid factor, left elbow

M06.031 Rheumatoid arthritis without rheumatoid factor, right wrist

M06.032 Rheumatoid arthritis without rheumatoid factor, left wrist

M06.041 Rheumatoid arthritis without rheumatoid factor, right hand

M06.042 Rheumatoid arthritis without rheumatoid factor, left hand

M06.051 Rheumatoid arthritis without rheumatoid factor, right hip

M06.052 Rheumatoid arthritis without rheumatoid factor, left hip

M06.061 Rheumatoid arthritis without rheumatoid factor, right knee

M06.062 Rheumatoid arthritis without rheumatoid factor, left knee

M06.071 Rheumatoid arthritis without rheumatoid factor, right ankle and foot

M06.072 Rheumatoid arthritis without rheumatoid factor, left ankle and foot

M06.08 Rheumatoid arthritis without rheumatoid factor, vertebrae

M06.09 Rheumatoid arthritis without rheumatoid factor, multiple sites

M06.1 Adult-onset Still's disease

M06.811 Other specified rheumatoid arthritis, right shoulder

M06.812 Other specified rheumatoid arthritis, left shoulder

M06.821 Other specified rheumatoid arthritis, right elbow

M06.822 Other specified rheumatoid arthritis, left elbow

M06.831 Other specified rheumatoid arthritis, right wrist

M06.832 Other specified rheumatoid arthritis, left wrist

M06.841 Other specified rheumatoid arthritis, right hand

M06.842 Other specified rheumatoid arthritis, left hand

M06.851 Other specified rheumatoid arthritis, right hip

M06.852 Other specified rheumatoid arthritis, left hip

M06.861 Other specified rheumatoid arthritis, right knee

M06.862 Other specified rheumatoid arthritis, left knee

M06.871 Other specified rheumatoid arthritis, right ankle and foot

M06.872 Other specified rheumatoid arthritis, left ankle and foot

M06.88 Other specified rheumatoid arthritis, vertebrae

M06.89 Other specified rheumatoid arthritis, multiple sites

M06.9 Rheumatoid arthritis, unspecified

M30.1 Polyarteritis with lung involvement [Churg-Strauss]

M31.10 Thrombotic microangiopathy, unspecified

M31.11 Hematopoietic stem cell transplantation-associated thrombotic microangiopathy [HSCT-TMA]

M31.19 Other thrombotic microangiopathy

M31.30 Wegener's granulomatosis without renal involvement

M31.31 Wegener's granulomatosis with renal involvement

M31.7 Microscopic polyangiitis

M32.14 Glomerular disease in systemic lupus erythematosus

M34.0 Progressive systemic sclerosis

M34.1 CR(E)ST syndrome

M34.2 Systemic sclerosis induced by drug and chemical

M34.81 Systemic sclerosis with lung involvement

M34.82 Systemic sclerosis with myopathy

M34.83 Systemic sclerosis with polyneuropathy

M34.89 Other systemic sclerosis

M34.9 Systemic sclerosis, unspecified

M35.00 Sjogren syndrome, unspecified

M35.01 Sjogren syndrome with keratoconjunctivitis

M35.02 Sjogren syndrome with lung involvement

M35.03 Sjogren syndrome with myopathy

M35.04 Sjogren syndrome with tubulo-interstitial nephropathy

M35.05 Sjogren syndrome with inflammatory arthritis

M35.06 Sjogren syndrome with peripheral nervous system involvement

M35.07 Sjogren syndrome with central nervous system involvement

M35.08 Sjogren syndrome with gastrointestinal involvement

M35.09 Sjogren syndrome with other organ involvement

M35.0A Sjogren syndrome with glomerular disease

M35.0B Sjogren syndrome with vasculitis

M35.0C Sjogren syndrome with dental involvement

M35.5 Multifocal fibrosclerosis

M35.9 Systemic involvement of connective tissue, unspecified

N01.0 Rapidly progressive nephritic syndrome with minor glomerular abnormality

N01.2 Rapidly progressive nephritic syndrome with diffuse membranous glomerulonephritis

N01.3 Rapidly progressive nephritic syndrome with diffuse mesangial proliferative glomerulonephritis

N01.4 Rapidly progressive nephritic syndrome with diffuse endocapillary proliferative glomerulonephritis

N01.5 Rapidly progressive nephritic syndrome with diffuse mesangiocapillary glomerulonephritis

N01.6 Rapidly progressive nephritic syndrome with dense deposit disease

N01.7 Rapidly progressive nephritic syndrome with diffuse crescentic glomerulonephritis

N01.8 Rapidly progressive nephritic syndrome with other morphologic changes

N01.9 Rapidly progressive nephritic syndrome with unspecified morphologic changes

N04.20 Nephrotic syndrome with diffuse membranous glomerulonephritis, unspecified

N04.21 Primary membranous nephropathy with nephrotic syndrome

N04.22 Secondary membranous nephropathy with nephrotic syndrome

N04.29 Other nephrotic syndrome with diffuse membranous glomerulonephritis

N04.3 Nephrotic syndrome with diffuse mesangial proliferative glomerulonephritis

N04.4 Nephrotic syndrome with diffuse endocapillary proliferative glomerulonephritis

N04.5 Nephrotic syndrome with diffuse mesangiocapillary glomerulonephritis

N04.6 Nephrotic syndrome with dense deposit disease

N04.7 Nephrotic syndrome with diffuse crescentic glomerulonephritis

N04.8 Nephrotic syndrome with other morphologic changes

N04.9 Nephrotic syndrome with unspecified morphologic changes

N05.0 Unspecified nephritic syndrome with minor glomerular abnormality

N05.2 Unspecified nephritic syndrome with diffuse membranous glomerulonephritis

N05.3 Unspecified nephritic syndrome with diffuse mesangial proliferative glomerulonephritis

N05.4 Unspecified nephritic syndrome with diffuse endocapillary proliferative glomerulonephritis

N05.5 Unspecified nephritic syndrome with diffuse mesangiocapillary glomerulonephritis

N05.6 Unspecified nephritic syndrome with dense deposit disease

N05.7 Unspecified nephritic syndrome with diffuse crescentic glomerulonephritis

N05.8 Unspecified nephritic syndrome with other morphologic changes

N05.9 Unspecified nephritic syndrome with unspecified morphologic changes

T86.11 Kidney transplant rejection

T86.21 Heart transplant rejection

T86.31 Heart-lung transplant rejection

T86.810 Lung transplant rejection

T86.99 Other complications of unspecified transplanted organ and tissue

Z29.89 Encounter for other specified prophylactic measures

RITUXIMAB AND HYALURONIDASE HUMAN (RITUXAN HYCELA) FOR SUBCUTANEOUS INJECTION ARE MEDICALLY NECESSARY WHEN REPORTED WITH THE FOLLOWING DIAGNOSIS CODES:

C81.70 Other Hodgkin lymphoma, unspecified site

C81.71 Other Hodgkin lymphoma, lymph nodes of head, face, and neck

C81.72 Other Hodgkin lymphoma, intrathoracic lymph nodes

C81.73 Other Hodgkin lymphoma, intra-abdominal lymph nodes

C81.74 Other Hodgkin lymphoma, lymph nodes of axilla and upper limb

C81.75 Other Hodgkin lymphoma, lymph nodes of inguinal region and lower limb

C81.76 Other Hodgkin lymphoma, intrapelvic lymph nodes

C81.77 Other Hodgkin lymphoma, spleen

C81.78 Other Hodgkin lymphoma, lymph nodes of multiple sites

C81.79 Other Hodgkin lymphoma, extranodal and solid organ sites

C82.00 Follicular lymphoma grade I, unspecified site

C82.01 Follicular lymphoma grade I, lymph nodes of head, face, and neck

C82.02 Follicular lymphoma grade I, intrathoracic lymph nodes

C82.03 Follicular lymphoma grade I, intra-abdominal lymph nodes

C82.04 Follicular lymphoma grade I, lymph nodes of axilla and upper limb

C82.05 Follicular lymphoma grade I, lymph nodes of inguinal region and lower limb

C82.06 Follicular lymphoma grade I, intrapelvic lymph nodes

C82.07 Follicular lymphoma grade I, spleen

C82.08 Follicular lymphoma grade I, lymph nodes of multiple sites

C82.09 Follicular lymphoma grade I, extranodal and solid organ sites

C82.10 Follicular lymphoma grade II, unspecified site

C82.11 Follicular lymphoma grade II, lymph nodes of head, face, and neck

C82.12 Follicular lymphoma grade II, intrathoracic lymph nodes

C82.13 Follicular lymphoma grade II, intra-abdominal lymph nodes

C82.14 Follicular lymphoma grade II, lymph nodes of axilla and upper limb

C82.15 Follicular lymphoma grade II, lymph nodes of inguinal region and lower limb

C82.16 Follicular lymphoma grade II, intrapelvic lymph nodes

C82.17 Follicular lymphoma grade II, spleen

C82.18 Follicular lymphoma grade II, lymph nodes of multiple sites

C82.19 Follicular lymphoma grade II, extranodal and solid organ sites

C82.30 Follicular lymphoma grade IIIa, unspecified site

C82.31 Follicular lymphoma grade IIIa, lymph nodes of head, face, and neck

C82.32 Follicular lymphoma grade IIIa, intrathoracic lymph nodes

C82.33 Follicular lymphoma grade IIIa, intra-abdominal lymph nodes

C82.34 Follicular lymphoma grade IIIa, lymph nodes of axilla and upper limb

C82.35 Follicular lymphoma grade IIIa, lymph nodes of inguinal region and lower limb

C82.36 Follicular lymphoma grade IIIa, intrapelvic lymph nodes

C82.37 Follicular lymphoma grade IIIa, spleen

C82.38 Follicular lymphoma grade IIIa, lymph nodes of multiple sites

C82.39 Follicular lymphoma grade IIIa, extranodal and solid organ sites

C82.50 Diffuse follicle center lymphoma, unspecified site

C82.51 Diffuse follicle center lymphoma, lymph nodes of head, face, and neck

C82.52 Diffuse follicle center lymphoma, intrathoracic lymph nodes

C82.53 Diffuse follicle center lymphoma, intra-abdominal lymph nodes

C82.54 Diffuse follicle center lymphoma, lymph nodes of axilla and upper limb

C82.55 Diffuse follicle center lymphoma, lymph nodes of inguinal region and lower limb

C82.56 Diffuse follicle center lymphoma, intrapelvic lymph nodes

C82.57 Diffuse follicle center lymphoma, spleen

C82.58 Diffuse follicle center lymphoma, lymph nodes of multiple sites

C82.59 Diffuse follicle center lymphoma, extranodal and solid organ sites

C82.60 Cutaneous follicle center lymphoma, unspecified site

C82.61 Cutaneous follicle center lymphoma, lymph nodes of head, face, and neck

C82.62 Cutaneous follicle center lymphoma, intrathoracic lymph nodes

C82.63 Cutaneous follicle center lymphoma, intra-abdominal lymph nodes

C82.64 Cutaneous follicle center lymphoma, lymph nodes of axilla and upper limb

C82.65 Cutaneous follicle center lymphoma, lymph nodes of inguinal region and lower limb

C82.66 Cutaneous follicle center lymphoma, intrapelvic lymph nodes

C82.67 Cutaneous follicle center lymphoma, spleen

C82.68 Cutaneous follicle center lymphoma, lymph nodes of multiple sites

C82.69 Cutaneous follicle center lymphoma, extranodal and solid organ sites

C82.80 Other types of follicular lymphoma, unspecified site

C82.81 Other types of follicular lymphoma, lymph nodes of head, face, and neck

C82.82 Other types of follicular lymphoma, intrathoracic lymph nodes

C82.83 Other types of follicular lymphoma, intra-abdominal lymph nodes

C82.84 Other types of follicular lymphoma, lymph nodes of axilla and upper limb

C82.85 Other types of follicular lymphoma, lymph nodes of inguinal region and lower limb

C82.86 Other types of follicular lymphoma, intrapelvic lymph nodes

C82.87 Other types of follicular lymphoma, spleen

C82.88 Other types of follicular lymphoma, lymph nodes of multiple sites

C82.89 Other types of follicular lymphoma, extranodal and solid organ sites

C82.90 Follicular lymphoma, unspecified, unspecified site

C82.91 Follicular lymphoma, unspecified, lymph nodes of head, face, and neck

C82.92 Follicular lymphoma, unspecified, intrathoracic lymph nodes

C82.93 Follicular lymphoma, unspecified, intra-abdominal lymph nodes

C82.94 Follicular lymphoma, unspecified, lymph nodes of axilla and upper limb

C82.95 Follicular lymphoma, unspecified, lymph nodes of inguinal region and lower limb

C82.96 Follicular lymphoma, unspecified, intrapelvic lymph nodes

C82.97 Follicular lymphoma, unspecified, spleen

C82.98 Follicular lymphoma, unspecified, lymph nodes of multiple sites

C82.99 Follicular lymphoma, unspecified, extranodal and solid organ sites

C83.00 Small cell B-cell lymphoma, unspecified site

C83.01 Small cell B-cell lymphoma, lymph nodes of head, face, and neck

C83.02 Small cell B-cell lymphoma, intrathoracic lymph nodes

C83.03 Small cell B-cell lymphoma, intra-abdominal lymph nodes

C83.04 Small cell B-cell lymphoma, lymph nodes of axilla and upper limb

C83.05 Small cell B-cell lymphoma, lymph nodes of inguinal region and lower limb

C83.06 Small cell B-cell lymphoma, intrapelvic lymph nodes

C83.07 Small cell B-cell lymphoma, spleen

C83.08 Small cell B-cell lymphoma, lymph nodes of multiple sites

C83.09 Small cell B-cell lymphoma, extranodal and solid organ sites

C83.10 Mantle cell lymphoma, unspecified site

C83.11 Mantle cell lymphoma, lymph nodes of head, face, and neck

C83.12 Mantle cell lymphoma, intrathoracic lymph nodes

C83.13 Mantle cell lymphoma, intra-abdominal lymph nodes

C83.14 Mantle cell lymphoma, lymph nodes of axilla and upper limb

C83.15 Mantle cell lymphoma, lymph nodes of inguinal region and lower limb

C83.16 Mantle cell lymphoma, intrapelvic lymph nodes

C83.17 Mantle cell lymphoma, spleen

C83.18 Mantle cell lymphoma, lymph nodes of multiple sites

C83.19 Mantle cell lymphoma, extranodal and solid organ sites

C83.30 Diffuse large B-cell lymphoma, unspecified site

C83.31 Diffuse large B-cell lymphoma, lymph nodes of head, face, and neck

C83.32 Diffuse large B-cell lymphoma, intrathoracic lymph nodes

C83.33 Diffuse large B-cell lymphoma, intra-abdominal lymph nodes

C83.34 Diffuse large B-cell lymphoma, lymph nodes of axilla and upper limb

C83.35 Diffuse large B-cell lymphoma, lymph nodes of inguinal region and lower limb

C83.36 Diffuse large B-cell lymphoma, intrapelvic lymph nodes

C83.37 Diffuse large B-cell lymphoma, spleen

C83.38 Diffuse large B-cell lymphoma, lymph nodes of multiple sites

C83.390 Primary central nervous system lymphoma

C83.398 Diffuse large B-cell lymphoma of other extranodal and solid organ sites

C85.10 Unspecified B-cell lymphoma, unspecified site

C85.11 Unspecified B-cell lymphoma, lymph nodes of head, face, and neck

C85.12 Unspecified B-cell lymphoma, intrathoracic lymph nodes

C85.13 Unspecified B-cell lymphoma, intra-abdominal lymph nodes

C85.14 Unspecified B-cell lymphoma, lymph nodes of axilla and upper limb

C85.15 Unspecified B-cell lymphoma, lymph nodes of inguinal region and lower limb

C85.16 Unspecified B-cell lymphoma, intrapelvic lymph nodes

C85.17 Unspecified B-cell lymphoma, spleen

C85.18 Unspecified B-cell lymphoma, lymph nodes of multiple sites

C85.19 Unspecified B-cell lymphoma, extranodal and solid organ sites

C85.20 Mediastinal (thymic) large B-cell lymphoma, unspecified site

C85.21 Mediastinal (thymic) large B-cell lymphoma, lymph nodes of head, face, and neck

C85.22 Mediastinal (thymic) large B-cell lymphoma, intrathoracic lymph nodes

C85.23 Mediastinal (thymic) large B-cell lymphoma, intra-abdominal lymph nodes

C85.24 Mediastinal (thymic) large B-cell lymphoma, lymph nodes of axilla and upper limb

C85.25 Mediastinal (thymic) large B-cell lymphoma, lymph nodes of inguinal region and lower limb

C85.26 Mediastinal (thymic) large B-cell lymphoma, intrapelvic lymph nodes

C85.27 Mediastinal (thymic) large B-cell lymphoma, spleen

C85.28 Mediastinal (thymic) large B-cell lymphoma, lymph nodes of multiple sites

C85.29 Mediastinal (thymic) large B-cell lymphoma, extranodal and solid organ sites

C88.00 Waldenstrom macroglobulinemia not having achieved remission

C88.40 Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue [MALT-lymphoma] not having achieved remission

C91.10 Chronic lymphocytic leukemia of B-cell type not having achieved remission

C91.12 Chronic lymphocytic leukemia of B-cell type in relapse

C91.40 Hairy cell leukemia not having achieved remission

C91.42 Hairy cell leukemia, in relapse

D47.Z1 Post-transplant lymphoproliferative disorder (PTLD)

D47.Z2 Castleman disease

Duration of authorization: 12 months

Version Effective Date: 10/07/2024

Title: Routine/Non-routine Vaccines**MEDICALLY NECESSARY**

Non-routine vaccines for the indications described below are considered medically necessary and, therefore, covered in accordance with Advisory Committee for Immunization Practices (ACIP) recommendations. In addition, vaccines approved by the FDA that have not been recognized by the ACIP are considered non-routine. The following vaccine indications are considered non-routine and non-preventive and are subject to applicable member cost sharing.

BCG Vaccine

Bacille Calmette-Guerin (BCG) vaccine is considered medically necessary and, therefore, covered for individuals when either of the following criteria are met:

- For children who have a negative tuberculin skin test and who are continually exposed to, and cannot be separated from, adults who are untreated or ineffectively treated for tuberculosis (TB) disease (if the child cannot be given long-term treatment for infection).
- For children who have a negative tuberculin skin test and who are continually exposed to, and cannot be separated from, adults who have TB caused by strains resistant to isoniazid and rifampin.

Pneumococcal Vaccine

13- valent Pneumococcal conjugate vaccine (PCV) is considered medically necessary and, therefore, covered for individuals.

21- valent Pneumococcal conjugate vaccine (PCV) is considered medically necessary and, therefore, covered for individuals 18 years of age.

Post-Exposure Rabies Vaccine

Post-exposure rabies vaccine, for intramuscular use, is considered medically necessary and, therefore, covered for the following individuals:

- A four-dose regimen in combination with rabies immune globulin (RIG) for healthy individuals as treatment of an injury or direct exposure to rabies disease or condition.
- A five-dose regimen with one dose of RIG for individuals with altered immunocompetence.

Preexposure Prophylaxis for Prevention of Anthrax Booster

An anthrax booster for the preexposure prophylaxis for prevention of anthrax every three years is considered medically necessary and, therefore, covered for individuals not at high risk for exposure for B. anthracis who previously completed the three dose primary series and the initial two dose booster series who want to maintain protection.

Respiratory Syncytial Virus Vaccine

Respiratory syncytial virus vaccine, adjuvanted (Arexvy) is considered medically necessary and, therefore, covered as a one-time dose regimen for individuals 50 through 59 years of age.

Tdap/Td Vaccines

Tdap or Td vaccine (tetanus toxoid-containing vaccine) is considered medically necessary and, therefore, covered for tetanus wound management for the following individuals:

- For individuals with a history of three or more doses of absorbed tetanus toxoid vaccination:
 - Td vaccine (Tdap may be substituted for Td in individuals older than 10 years who have previously not received Tdap, or in individuals 7 to 10 years of age who are under-vaccinated against pertussis).

- A booster dose of tetanus toxoid-containing vaccine if it has been more than 10 years since the last tetanus toxoid dose and the wound is clean and minor.
- A booster dose of tetanus toxoid-containing vaccine if it has been 5 years or more since the last tetanus toxoid dose and the wound is other than clean and minor.
- For individuals with an unknown history or a history of less than three doses of absorbed tetanus toxoid vaccination:
 - Td vaccine (Tdap for individuals older than 10 years who have previously not received Tdap, or in individuals 7 to 10 years of age who are under-vaccinated against pertussis).

Typhoid Vaccine

Typhoid vaccine is considered medically necessary and, therefore, covered for individuals with intimate exposure (e.g., household contact) to a documented *Salmonella* serotype Typhi chronic carrier (defined as excretion of *Salmonella* serotype Typhi in urine or stool for more than one year).

Zoster (Shingles) Vaccine

Recombinant zoster vaccine is considered medically necessary and, therefore, covered for individuals aged 18 years and older who are or will be at increased risk of herpes zoster due to immunodeficiency or immunosuppression caused by known disease or therapy.

EXPERIMENTAL/INVESTIGATIONAL

Rabies Vaccine

The rabies vaccine for intradermal use is considered experimental/investigational and, therefore, not covered because the safety and/or effectiveness of this service cannot be established by review of the available published peer-reviewed literature.

TRAVEL-RELATED VACCINES

Travel-related vaccines are benefit contract exclusions for most plans, and therefore, not eligible for reimbursement consideration. Individual benefits must be verified.

Travel-related vaccines includes, but is not limited to, the following diseases:

- Japanese encephalitis (JE)
- Yellow fever (has country-specific requirements)
- Cholera
- Ebola
- Tick-borne encephalitis
- Chikungunya

There are additional vaccines, both routine and non-routine that are commonly, but not exclusively, used for travel purposes. When routine vaccines are used solely for travel-related purposes in accordance with the ACIP recommendations, the routine vaccines are considered medically necessary and, therefore, covered by the Company.

EMPLOYMENT/OCCUPATION-RELATED VACCINES

Vaccines used prophylactically for employment purposes, occupational requirements, or work-related injuries are benefit contract exclusions for most plans, and therefore, not eligible for reimbursement consideration. Individual benefits must be verified.

Vaccines include, but are not limited to, pre-exposure rabies vaccine.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to, records from the professional providers' office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation must be made available to the Company upon request. Failure to produce the requested information may result in a denial for the service.

Duration of authorization: 12 months

Version Effective Date: 01/01/2025

Title: Rozanolixizumab-noli (Rystiggo)

MEDICALLY NECESSARY

ROZANOLIXIZUMAB-NOLI (RYSTIGGO)

Rozanolixizumab-noli (Rystiggo) is considered medically necessary and, therefore, covered for the treatment of adult individuals 18 years of age or older with generalized myasthenia gravis (gMG), when all of the following criteria are met, including dosing and frequency:

Initial Criteria

- The individual has documented diagnosis of gMG based individual's history and supported by previous evaluations
- The individual has a confirmed positive record of autoantibodies against acetylcholine receptor (AChR) or muscle-specific kinase (MuSK) .
- The individual has Myasthenia Gravis Foundation of America (MGFA) Class II, III, IVa
- The individual has Myasthenia Gravis-Activities of Daily Living (MG-ADL) score of at least 3 (with ≥ 3 points from non-ocular symptom) AND a quantitative myasthenia gravis (QMG) score of at least 11
- The individual has a history of inadequate response or intolerance one of the following :
 - standard-of-care therapy (i.e, acetylcholinesterase inhibitors [AChEIs] e.g., pyridostigmine or corticosteroids e.g., prednisone)
 - use of immunoglobulin g (IVIg)/ plasma exchange (PLEX) as rescue therapy
- The individual is not receiving rozanolixizumab-noli (Rystiggo) in combination with eculizumab (Soliris), ravulizumab (Ultomiris) or efgartigimod alfa-fcab (Vyvgart)
- Dosing and frequency for rozanolixizumab-noli (Rystiggo) is based on a body weight (BW) of the individual, once weekly for six weeks with every next cycle initiated not sooner than 63 days from the start of the previous treatment cycle:
 - if (BW) less than 50 kg: 420 mg
 - if (BW) 50 kg to less than 100 kg 560 mg
 - if (BW) 100 kg and above 840 mg

Continuation Criteria

Submission of medical records to demonstrate a positive clinical response from baseline (e.g., two-point reduction in MG-ADL total score). The safety of initiating subsequent cycles sooner than 63 days from the start of the previous treatment cycle has not been established.

EXPERIMENTAL/INVESTIGATIONAL

All other uses for moxetumomab Rozanolixizumab-noli (Rystiggo) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

DOSING AND FREQUENCY REQUIREMENTS

The Company reserves the right to modify the Dosing and Frequency Requirements listed in this policy to ensure consistency with the most recently published recommendations for the use of rozanolixizumab-noli (Rystiggo). Changes to these guidelines are based on a consensus of information obtained from resources such as, but not limited to: the US Food and Drug Administration (FDA); Company-recognized authoritative pharmacology compendia; or published peer-reviewed clinical research. The professional provider must supply supporting documentation (i.e., published peer-reviewed literature) in order to request coverage for an amount of rozanolixizumab-noli (Rystiggo) outside of the Dosing and Frequency Requirements listed in this policy. For a list of Company-recognized pharmacology compendia, view our policy on off-label coverage for prescription drugs and biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of this drug. If the member's dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider must submit those changes to the Company for a new approval based on those changes as part of the utilization management activities. The Company reserves the right to conduct postpayment review and audit procedures for any claims submitted for rozanolixizumab-noli (Rystiggo).

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

When coverage of rozanolixizumab-noli (Rystiggo) is requested outside of the Dosing and Frequency Requirements listed in this policy, the prescribing professional provider must supply documentation (i.e., published peer-reviewed literature) to the Company that supports this request.

Duration of authorization: 12 months

Version Effective Date: 05/28/2025

Title: Sacituzumab govitecan-hziy (Trodelvy™)

MEDICALLY NECESSARY

SACITUZUMAB GOVITECAN-HZIY (TRODELVY)

Sacituzumab govitecan-hziy (Trodelvy) injection is considered medically necessary and, therefore, covered as monotherapy in individuals who meet the applicable criteria including dosing and frequency requirements outlined below for the following indications:

Bladder Cancer

- As second-line systemic therapy (if a first-line therapy containing both platinum chemotherapy and an immune checkpoint inhibitor was used, including maintenance checkpoint inhibitor), or subsequent-line systemic therapy (for individuals who have already received platinum and a checkpoint inhibitor, if eligible) as a single agent for any of the following:
 - stage II (cT2, N0) disease or stage IIIA (cT3, N0; cT4a, N0; cT1-T4a, N1) disease if tumor is present following reassessment of tumor status 2 to 3 months after primary treatment with concurrent bladder-preserving chemoradiotherapy and maximal transurethral resection of bladder tumor (TURBT)
 - stage IIIB (cT1-T4a, N2,3) disease following partial response or progression after primary treatment with downstaging systemic therapy or concurrent chemoradiotherapy
 - stage IVA (cT4b, any N, M0) disease if the tumor is present following reassessment of tumor status after primary treatment with first-line systemic therapy or concurrent chemoradiotherapy
 - stage IVA (any T, any N, M1a) disease if stable disease or progression following reassessment of tumor status after primary treatment with first-line systemic therapy

- metastatic stage IVB (any T, any N, M1b) disease
- muscle-invasive local recurrence or persistent disease in a preserved bladder treated with curative intent
- metastatic or local recurrence postcystectomy treated with curative intent

Upper Genitourinary (GU) Tract Tumors

- Therapy for metastatic disease for:
 - second-line systemic therapy if a first-line therapy containing both platinum chemotherapy and an immune checkpoint inhibitor was used, including maintenance checkpoint inhibitor
 - subsequent-line systemic therapy for individuals who received a platinum-containing chemotherapy and a checkpoint inhibitor, if eligible

Urothelial Carcinoma of the Prostate

Therapy for metastatic disease for one of the following:

- second-line systemic therapy if a first-line therapy containing both platinum chemotherapy and an immune checkpoint inhibitor was used, including maintenance checkpoint inhibitor
- subsequent-line systemic therapy for individuals who received a platinum-containing chemotherapy and a checkpoint inhibitor, if eligible
- locally advanced or metastatic urothelial cancer (mUC) who have previously received a platinum-containing chemotherapy and either programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor

Primary Carcinoma of the Urethra

- For recurrent or metastatic disease as one of the following (except for recurrence of clinical stage T3-4 disease or palpable inguinal lymph nodes):

- second-line systemic therapy for individuals who received first-line therapy containing both platinum-containing chemotherapy and a checkpoint inhibitor was used, including maintenance checkpoint inhibitor
- subsequent-line systemic therapy for individuals who already received a platinum and a checkpoint inhibitor, if eligible

National Comprehensive Cancer Network (NCCN) note: Chemotherapy regimen based on histology. See Non-Urothelial and Urothelial with Variant Histology (BL-D) if appropriate.

Invasive or Inflammatory Breast Cancer

Sacituzumab govitecan-hziy (Trodelyv) injection is considered medically necessary and, therefore, covered as monotherapy for the indication(s) identified below, in individuals who meet the applicable criteria, and whose tumors have human epidermal growth factor receptor 2 (HER2) protein overexpression verified by one of the following US Food and Drug Administration (FDA)–approved diagnostic tests and dosing and frequency requirements when any of the following criteria are met:

- The individual has locally advanced or metastatic triple-negative (mTNBC) and has received two or more prior therapies, at least one of them for metastatic disease.
- The individual has unresectable locally advanced or metastatic hormone receptor (HR)–positive, HER2-negative (IHC 0, IHC 1+ or IHC 2+/ISH–) breast cancer and has received endocrine-based therapy and at least two additional systemic therapies in the metastatic setting
- As second-line therapy or a later line for recurrent unresectable (local or regional) or stage IV (M1) HR-positive and HER2-negative cancers in an individual who has received prior treatment including endocrine therapy, a CDK4/6 inhibitor, and at least two lines of chemotherapy (including a taxane), at least one of which was in the metastatic setting, and is not a candidate for fam-trastuzumab deruxtecan-nxki (NCCN-preferred regimen)
- As second-line therapy or a later line for recurrent unresectable (local or regional) or stage IV (M1) triple-negative breast cancer (TNBC) in individuals who have received at least one prior therapy, with at least one line for in metastatic setting disease (NCCN-preferred regimen)

NOT MEDICALLY NECESSARY

When FDA-approved diagnostic tests do not reveal triple-negative (ER–/PR–/HER2–) breast cancer, sacituzumab govitecan-hziy (Trodelyv) is considered not medically necessary and, therefore, not covered because the available published peer-reviewed literature does not support their use in the treatment of those diseases.

EXPERIMENTAL/INVESTIGATIONAL

All other uses for sacituzumab govitecan-hziy (Trodelyv) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

MANDATES

PENNSYLVANIA MEMBERS

In accordance with the Commonwealth of Pennsylvania's Act 6 of 2020 or Fair Access to Cancer Treatment Act, for members who are enrolled in Pennsylvania commercial products who have Stage 4, advanced metastatic cancer, refer to the Medical Policy titled "Coverage of Anticancer Prescription Oral and Injectable Drugs and Biologics and Supportive Agents" (08.01.08) for additional information regarding the applicable coverage of drugs and biologics.

DOSING AND FREQUENCY REQUIREMENTS

The Company reserves the right to modify the Dosing and Frequency Requirements listed in this Policy to ensure consistency with the most recently published recommendations for the use of sacituzumab govitecan-hziy (Trodelyv). Changes to these guidelines are based on a consensus of information obtained from resources such as, but not limited to: the FDA, Company-recognized authoritative pharmacology compendia, or published peer-reviewed clinical research. The professional provider must supply supporting documentation (i.e., published peer-reviewed literature) in order to request coverage for an amount of sacituzumab govitecan-hziy (Trodelyv) outside of the Dosing and Frequency Requirements listed in this Policy. For a list of Company-recognized pharmacology compendia, view the policy on off-label coverage for prescription drugs and biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of this drug. If the member's dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider must submit those changes to the Company for a new approval based on those changes as part of the precertification process. The Company reserves the right to conduct postpayment review and audit procedures for any claims submitted for sacituzumab govitecan-hziy (Trodelyv).

For sacituzumab govitecan-hziy (Trodelyv) is 10 mg/kg once weekly on days 1 and 8 of continuous 21-day treatment cycles.

ION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Guidelines

BLACK BOX WARNINGS

Refer to the specific manufacturer's prescribing information for any applicable Black Box Warnings.

HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR-2 (HER2) PROTEIN OVEREXPRESSION TESTING

Coverage of sacituzumab govitecan-hziy (Trodelyv) requires that HER2 protein expression is verified as a negative result by one of the following FDA-approved diagnostic tests:

- Immunohistochemical (IHC) assay with a result of 0 to 1+

- Fluorescence in situ hybridization (FISH) test (lower than 1.8)
- Single-probe in situ hybridization (ISH) test with average HER2 copy number less than 4.0 signals/cell
- Dual-probe ISH test HER2/CEP17 (chromosome enumeration probe 17) ratio less than 2.0 AND average HER2 copy number less than 4.0 signals/cell

Confirmatory tests should be performed for borderline results as follows:

- If IHC assay has a result of 2+, confirm with ISH test of the same sample or a new test with IHC or ISH (if new sample available).
- If FISH test has a HER2 gene/chromosome 17 ratio of 1.8 to 2.0, confirm with FISH re-test, additional cell counting and recalculation of the ratio, or IHC assay.
- If single-probe ISH assay has an average HER2 copy number result of 4.0 to less than 6.0 signals/cell, confirm with dual-probe ISH or with IHC (if same sample), or with a new ISH or IHC (if new sample available).
- If dual-probe ISH assay has a HER2/CEP17 ratio less than 2.0 and an average HER2 copy number result of 4.0 to less than 6.0 signals/cell, confirm with one of the following: IHC (if same sample), alternative ISH chromosome 17 probe, or order a new test with ISH or IHC (if new sample available).

DRUG INFORMATION

In accordance with US Food and Drug Administration (FDA) prescribing information, sacituzumab govitecan-hziy (Trodelvy) is administered 10 mg/kg intravenously on days 1 and 8 of continuous 21-day treatment cycles.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, sacituzumab govitecan-hziy (Trodelvy) is covered under the medical benefits of the Company's products when the medical necessity criteria are listed in this medical policy are met.

US FOOD AND DRUG ADMINISTRATION (FDA) STATUS

On April 13, 2021, the FDA granted accelerated approval to sacituzumab govitecan-hziy (Trodelvy, Immunomedics Inc.) for individuals with locally advanced or metastatic urothelial cancer (mUC) who previously received platinum-containing chemotherapy and either a programmed death receptor-1 (PD-1) or a programmed death-ligand 1 (PD-L1) inhibitor.

On April 22, 2020, sacituzumab govitecan-hziy (Trodelvy) was approved by the FDA on April 22, 2020, for the treatment of adult individuals with metastatic triple-negative breast cancer (mTNBC) who have received at least two prior therapies for metastatic disease. The safety and effectiveness have not been established in pediatric individuals.

Description

Sacituzumab govitecan-hziy (Trodelvy) is a trophoblast cell-surface antigen-2 (Trop-2)–directed antibody and topoisomerase inhibitor conjugate, composed of the following three components: the humanized monoclonal antibody, hRS7 IgG1 (also called sacituzumab), which binds to Trop-2 (the trophoblast cell-surface antigen-2); the drug SN-38, a topoisomerase inhibitor; a hydrolyzable linker (called CL2A), which links the humanized monoclonal antibody to SN-38. The cytotoxic component of sacituzumab govitecan-hziy (Trodelvy) is SN-38, a highly potent topoisomerase I inhibitor and metabolite of irinotecan. The cytotoxic activity of SN-38 delivered through sacituzumab govitecan-hziy (Trodelvy) is 100 to 1000 times as high as that of irinotecan. The recombinant monoclonal antibody is produced by mammalian (murine myeloma) cells, while the small molecule components SN-38 and CL2A are produced by chemical synthesis. Sacituzumab govitecan-hziy (Trodelvy) contains on average seven to eight molecules of SN-38 per antibody molecule. Sacituzumab govitecan-hziy (Trodelvy) enables delivery of high concentrations of SN-38 to tumors. Triple-negative breast cancers (TNBC) account for about 10% to 15% of all breast cancers. TNBC lack receptors for estrogen, progesterone, and HER2, and do not respond to drugs that target estrogen, progesterone, or HER2 receptors. TNBC differ from other types of invasive breast cancer in that they grow and spread faster, have limited treatment options, and a worse prognosis. These cancers tend to be more common in women younger than age 40, who are African-American, or who have a BRCA1 mutation.

DIAGNOSTIC TESTS FOR HER2 PROTEIN EXPRESSION TESTING

HER2 protein overexpression is detected either by immunohistochemical (IHC) assay that measures the amount of HER2 receptor protein on the surface of cells in a breast cancer tissue sample or with a type of in situ hybridization (ISH) test for gene amplification (e.g., fluorescence in situ hybridization [FISH], chromogenic in situ hybridization [CISH], dual in situ hybridization [DISH]). The US Food and Drug Administration (FDA) has approved several commercially available tests to aid in the selection of individuals with breast cancer for fam-trastuzumab

deruxtecan-nxki (Enhertu) therapy. The National Comprehensive Cancer Network (NCCN) and American Society of Clinical Oncology (ASCO) guidelines (2018) further recommend that IHC assay and ISH testing should only be done at laboratories that are accredited to perform HER2 testing.

- An IHC test result is reported as 0 or 1+ (negative), 2+ (borderline), or 3+ (positive).
- A FISH test result is reported as a HER2 gene/chromosome 17 ratio less than 1.8 (negative), a ratio of 1.8 to less than 2.0 (borderline), or a ratio of 2.0 or greater (positive).
- A single-probe ISH test result is reported as: average HER2 copy number less than 4.0 signals/cell (negative); 4.0 to less than 6.0 signals/cell (borderline); 6.0 or greater signals/cell (positive).
- A dual-probe ISH test result is reported as HER2/CEP17 (chromosome enumeration probe 17) ratio 2.0 or greater (positive); HER2/CEP17 ratio less than 2.0 AND average HER2 copy number less than 4.0 signals/cell (negative); HER2/CEP17 ratio less than 2.0 AND average HER2 copy number 4.0 to less than 6.0 signals/cell (borderline); HER2/CEP17 ratio less than 2.0 AND average HER2 copy number 6.0 signals/cell or greater (positive).

The NCCN and ASCO both have issued guidelines for HER2 testing in invasive breast cancer that call for confirming a borderline or equivocal result:

- IHC assay result of 2+: confirm with ISH test (if same sample), or with a new IHC or ISH test (if new sample available).
- FISH assay: confirm with either a repeat FISH test or an additional cell counting and recalculation of the ratio. If a repeat FISH test remains equivocal, an IHC assay is recommended for confirmation.
- Single-probe ISH assay: confirm with dual-probe ISH or with IHC (if same sample), or with a new ISH or IHC (if new sample available).
- Dual-probe ISH assay: confirm with one of the following: IHC (if same sample), alternative ISH chromosome 17 probe, or order a new test with ISH or IHC (if new sample available).

PEER-REVIEWED LITERATURE

SUMMARY

Sacituzumab govitecan-hziy (Trodelyv) was evaluated in a phase 1/2 open label, single-group, multicenter trial involving individuals with advanced epithelial cancers. A total of 108 individuals received sacituzumab govitecan-hziy (Trodelyv) at a dose of 10 mg per kilogram of body weight after receiving at least two previous anticancer therapies for metastatic TNBC. The primary

efficacy endpoint was the objective response rate. The secondary endpoints were the time to response and the duration of response and progression-free and overall survival. Safety evaluations included assessments of adverse events, changes in laboratory values, vital signs, physical examination, and 12-lead electrocardiography (ECG). The response rate was 33.3% (36 of 108 individuals), including complete responses in three individuals (2.8%). The clinical benefit rate (including stable disease for at least 6 months) was 45.4% (49 of 108 individuals). At the time of data cutoff, 94 individuals (87.0%) had disease progression and 77 individuals (71.3%) had died. The median progression-free survival was 5.5 months (95% CI, 4.1 to 6.3); the estimated probability of progression-free survival was 41.9% at 6 months and 15.1% at 12 months. The median overall survival was 13.0 months (95% CI, 11.2–13.7); the estimated probability of survival was 78.5% at 6 months and 51.3% at 12 months. Among individuals with metastatic TNBC who had received at least two previous therapies for metastatic disease (median, three) and who received treatment with sacituzumab govitecan-hziy (Trodelyv), the response rate was 33.3%, the median duration of response was 7.7 months, the median progression-free survival was 5.5 months, and the median overall survival was 13.0 months. The duration of treatment with sacituzumab govitecan-hziy (Trodelyv) was longer than with the immediate previous antitumor therapy (5.1 months vs. 2.5 months). The most common adverse events were nausea, diarrhea, fatigue, neutropenia, and anemia, and the most common adverse events of grade 3 or higher (>5% incidence) included neutropenia, anemia, and a decreased white-cell count.

The efficacy of sacituzumab govitecan-hziy (Trodelyv) was evaluated in TROPHY (IMMU-132-06; NCT03547973), a single-arm, multicenter trial that enrolled 112 individuals with locally advanced or metastatic urothelial cancer (mUC) who have received prior treatment with a platinum-containing chemotherapy and either PD-1 or PD-L1 inhibitor. Individuals were administered sacituzumab govitecan-hziy (Trodelyv) 10 mg/kg as an intravenous infusion on Days 1 and 8 of a 21-day treatment cycle. Individuals were treated until disease progression or unacceptable toxicity. All individuals had a baseline Eastern Cooperative Oncology Group (ECOG) performance status of 0 (28%) or 1 (72%). Ninety-six percent of individuals had metastatic disease; 67% percent of individuals had visceral metastases, including 34% with liver metastases. The median number of prior systemic therapies was 3 (range, 1–8). Sixty-five percent of individuals received prior cisplatin, 21% received prior carboplatin, 13% received both prior cisplatin and carboplatin, and 100% received prior PD1 or PD-L1 inhibitor. For 34% of individuals, the platinum-containing chemotherapy was received in the neoadjuvant/adjuvant setting only. Nine percent of individuals received prior enfortumab vedotin. The major efficacy outcome measures were the objective response rate (ORR) and duration of response (DOR). The most common adverse reactions (incidence >25%) in individuals receiving sacituzumab govitecan-hziy (Trodelyv) are neutropenia, nausea, diarrhea, fatigue, alopecia, anemia, vomiting, constipation, decreased appetite, rash, and abdominal pain. This indication is

approved under accelerated approval based on tumor response rate and duration of response.

CLINICAL TRIAL

Efficacy was evaluated in a multicenter, open-label, randomized trial (ASCENT; NCT02574455) conducted in 529 individuals with unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC) who had relapsed after at least two prior lines of chemotherapy for breast cancer (one of which could be in the neoadjuvant or adjuvant setting provided progression occurred within a 12-month period). All individuals received previous taxane treatment in either the adjuvant, neoadjuvant, or advanced stage unless there was a contraindication or intolerance to taxanes during or at the end of the first taxane cycle.

The major efficacy outcome was progression-free survival (PFS) in individuals without brain metastases at baseline (i.e., BMNeg) as measured by a blinded, independent, centralized review assessed using Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 criteria. Additional efficacy measures included PFS for the full population (all individuals with and without brain metastases) and overall survival (OS).

An exploratory analysis of PFS in individuals with previously treated, stable brain metastases showed a stratified HR of 0.65 (95% CI, 0.35–1.22). The median PFS in the sacituzumab govitecan-hziy (Trodely) arm was 2.8 months (95% CI, 1.5–3.9) and the median PFS with single-agent chemotherapy was 1.6 months (95% CI, 1.3–2.9). Exploratory OS analysis in the same population showed a stratified HR of 0.87 (95% CI, 0.47–1.63). The median OS in the sacituzumab govitecan-hziy (Trodely) arm was 6.8 months (95% CI, 4.7–14.1) and the median OS with single-agent chemotherapy was 7.4 months (95% CI, 4.7–11.1).

OFF-LABEL INDICATION

There may be additional indications contained in the Policy section of this document due to evaluation of criteria highlighted in the Company's off-label policy, and/or review of clinical guidelines issued by leading professional organizations and government entities.

Duration of authorization: 12 months

Version Effective Date: 10/07/2024

Attachment A: [Sacituzumab govitecan-hziy \(Trodelvy™\)](#)

Description: Diagnosis list

Policy Attachment

Attachment to Policy # 08.01.60f

Attachment: A

Policy #: 08.01.60f

Description: Diagnosis list

Title: Sacituzumab govitecan-hziy (Trodelvy™)

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

Diagnosis Codes

C50.011 Malignant neoplasm of nipple and areola, right female breast

C50.012 Malignant neoplasm of nipple and areola, left female breast

C50.021 Malignant neoplasm of nipple and areola, right male breast

C50.022 Malignant neoplasm of nipple and areola, left male breast

C50.111 Malignant neoplasm of central portion of right female breast

C50.112 Malignant neoplasm of central portion of left female breast
C50.121 Malignant neoplasm of central portion of right male breast
C50.122 Malignant neoplasm of central portion of left male breast
C50.211 Malignant neoplasm of upper-inner quadrant of right female breast
C50.212 Malignant neoplasm of upper-inner quadrant of left female breast
C50.221 Malignant neoplasm of upper-inner quadrant of right male breast
C50.222 Malignant neoplasm of upper-inner quadrant of left male breast
C50.311 Malignant neoplasm of lower-inner quadrant of right female breast
C50.312 Malignant neoplasm of lower-inner quadrant of left female breast
C50.321 Malignant neoplasm of lower-inner quadrant of right male breast
C50.322 Malignant neoplasm of lower-inner quadrant of left male breast
C50.411 Malignant neoplasm of upper-outer quadrant of right female breast
C50.412 Malignant neoplasm of upper-outer quadrant of left female breast
C50.421 Malignant neoplasm of upper-outer quadrant of right male breast
C50.422 Malignant neoplasm of upper-outer quadrant of left male breast
C50.511 Malignant neoplasm of lower-outer quadrant of right female breast
C50.512 Malignant neoplasm of lower-outer quadrant of left female breast
C50.521 Malignant neoplasm of lower-outer quadrant of right male breast
C50.522 Malignant neoplasm of lower-outer quadrant of left male breast
C50.611 Malignant neoplasm of axillary tail of right female breast
C50.612 Malignant neoplasm of axillary tail of left female breast
C50.621 Malignant neoplasm of axillary tail of right male breast
C50.622 Malignant neoplasm of axillary tail of left male breast
C50.811 Malignant neoplasm of overlapping sites of right female breast
C50.812 Malignant neoplasm of overlapping sites of left female breast
C50.821 Malignant neoplasm of overlapping sites of right male breast
C50.822 Malignant neoplasm of overlapping sites of left male breast
C50.911 Malignant neoplasm of unspecified site of right female breast
C50.912 Malignant neoplasm of unspecified site of left female breast

C50.921 Malignant neoplasm of unspecified site of right male breast

C50.922 Malignant neoplasm of unspecified site of left male breast

C61 Malignant neoplasm of prostate

C65.1 Malignant neoplasm of right renal pelvis

C65.2 Malignant neoplasm of left renal pelvis

C66.1 Malignant neoplasm of right ureter

C66.2 Malignant neoplasm of left ureter

C67.0 Malignant neoplasm of trigone of bladder

C67.1 Malignant neoplasm of dome of bladder

C67.2 Malignant neoplasm of lateral wall of bladder

C67.3 Malignant neoplasm of anterior wall of bladder

C67.4 Malignant neoplasm of posterior wall of bladder

C67.5 Malignant neoplasm of bladder neck

C67.6 Malignant neoplasm of ureteric orifice

C67.7 Malignant neoplasm of urachus

C67.8 Malignant neoplasm of overlapping sites of bladder

C67.9 Malignant neoplasm of bladder, unspecified

C68.0 Malignant neoplasm of urethra

D09.0 Carcinoma in situ of bladder

Version Effective Date: 10/07/2024

Title: Sebelipase alfa (Kanuma®)

MEDICALLY NECESSARY

INFANTS WITH RAPIDLY PROGRESSIVE LYSOSOMAL ACID LIPASE (LAL) DEFICIENCY PRESENTING WITHIN THE FIRST 6 MONTHS OF LIFE

Sebelipase alfa (Kanuma) is considered medically necessary and, therefore, covered for infants with rapidly progressive lysosomal acid lipase (LAL) deficiency presenting within the first 6 months of life when **all** the following criteria, including Dosing and Frequency Requirements, are met:

- Diagnosis of LAL deficiency is confirmed by **either** of the following:
 - Confirmation of the absence or deficiency of LAL resulting from dried blood spot (DBS) testing
 - Confirmation of molecular genetic testing that reveals pathogenic variation(s) in the lipase A, lysosomal acid type (LIPA) gene, which results in reduction of functionality of LAL enzyme activity
- Documented presence of clinical signs and symptoms of the disease (e.g., diarrhea, vomiting, marked failure to thrive [e.g., weight decreasing across two or more major centiles on a standard World Health Organization {WHO} weight-for-age {WFA} chart; body weight below the 10th centile on a standard WHO WFA chart and no weight gain during the 2 weeks before screening; loss of greater than 5 percent of birth weight after 2 weeks of age], abdominal distension, hepatomegaly, splenomegaly, rapidly progressive liver failure, adrenal calcifications, anemia)

Dosing and Frequency Requirements

The following dosing and frequency information, and definitions of suboptimal clinical responses, were taken from the Prescribing Information for this product and specific reliable evidence including peer-reviewed literature:

Infants with rapidly progressive LAL deficiency presenting within the first six months of life: 1 mg/kg intravenously (IV) once weekly. If optimal clinical response is not achieved, increase to 3 mg/kg once weekly. For continued suboptimal clinical response on 3 mg/kg once weekly dosage, further increase the dosage to 5 mg/kg once weekly.

A suboptimal clinical response within the first 3 months of treatment is defined as **all** of the following:

- Absence of other potential causes of any observed clinical manifestations
- Absence of missed infusions
- Absence of acute cholecystitis
- Absence of the initiation of a potentially hepatotoxic concomitant medication
- Absence of a concomitant illness that could cause any of the observed lack of clinical responsiveness to the drug
- **Two or more** of the following after receiving at least 4 infusions of the current dose:
 - Poor growth (i.e., failure to gain an average of 5 g/kg body weight per day **AND** the presence of either WHO weight-for-length or weight-for-height z score less than -2, or WHO length-for-age or height-for-age z score less than -2)
 - Albumin less than 3.5 g/dl
 - ALT more than twice the upper limit of normal (ULN)
 - Ongoing requirement for blood and/or platelet transfusion
 - Presence of anti-drug, anti-enzyme, or anti-uptake antibodies

A suboptimal clinical response after the first 3 months of treatment is defined as lack of improvement from a minimum of 3 assessments or failure to normalize within 12 months of treatment in **all** of the following:

- Absence of other potential causes of any observed clinical manifestations
- Absence of missed infusions
- Absence of acute cholecystitis
- Absence of the initiation of a potentially hepatotoxic concomitant medication
- Absence of a concomitant illness that could cause any of the observed lack of clinical responsiveness to the drug
- **One or more** of the following (not an all-inclusive list of the clinically important manifestations of LAL deficiency):
 - Decrease in weight-for-age crossing at least 2 major centiles
 - Albumin less than 3.5 g/dl

- ALT more than twice the ULN
- Persistent or worsening hepatomegaly, splenomegaly, or lymphadenopathy
- Presence of anti-drug, anti-enzyme, or anti-uptake antibodies

PEDIATRIC AND ADULT INDIVIDUALS WITH LAL DEFICIENCY

Initial Therapy

Sebelipase alfa (Kanuma) is considered medically necessary and, therefore, covered for pediatric and adult individuals with lysosomal acid lipase (LAL) deficiency when **all** the following criteria, including Dosing and Frequency Requirements, are met:

- Diagnosis of LAL deficiency is confirmed by **either** of the following:
 - Confirmation of the absence or deficiency of LAL resulting from dried blood spot (DBS) testing
 - Confirmation of molecular genetic testing that reveals pathogenic variation(s) in the lipase A, lysosomal acid type (LIPA) gene, which results in reduction of functionality of LAL enzyme activity
- Documented presence of clinical signs and symptoms of the disease (e.g., hepatomegaly, dyslipidemia, increased serum transaminases [ALT, aspartate aminotransferase {AST}], evidence of advanced liver disease [i.e., cirrhosis, fibrosis, steatosis], histologically-confirmed disease recurrence in individuals with past liver or hematopoietic transplant more than 2 years prior)

Continuation Therapy

Sebelipase alfa (Kanuma) is considered medically necessary and, therefore, covered for continuation therapy of LAL deficiency in individuals who have improvement from baseline (for the initial request for continuation therapy), or maintenance of previous improvements, as evidenced by at least **two** of the following:

- Improvement in any **one** of the following symptoms:
 - For pediatric individuals: increase in growth and/or weight parameters (based on expected anthropometric parameters)
 - Decrease in diarrhea/vomiting (i.e., decrease in frequency and/or volume)

- Improvement in liver volume (normal liver volume in liters is defined as 2.5 percent of body weight in kg)
- Improvement in liver fat content (i.e., decrease of >5 percent in the liver fat content from baseline as measured by magnetic resonance imaging [MRI]; the normal fat content of the liver is considered to be <5 percent)
- Improvement in liver histopathology (e.g., cirrhosis, fibrosis)
- Improvement in any **one** component of a lipid panels:
 - Improvement in low-density lipoprotein-cholesterol (LDL-c) (based on clinical comparisons with baseline and/or previous results)
 - Improvement in high-density lipoprotein-cholesterol (HDL-c) (based on clinical comparisons with baseline and/or previous results)
 - Improvement in triglycerides (TG) (based on clinical comparisons with baseline and/or previous results)
- Improvement in any **one** serum transaminases
 - Improvement in ALT (based on clinical comparisons with baseline and/or previous results)
 - Improvement in AST (based on clinical comparisons with baseline and/or previous results)

If the individual does not demonstrate continued improvement, or maintenance of previous improvement, from baseline in **two** of the above after 8 consecutive infusions, and is on a higher dosage of sebelipase alfa (Kanuma), then the dosage will be decreased to the previous dosage that demonstrated a level of efficacy for the individual.

Dosing and Frequency Requirements

The following dosing and frequency information, and definitions of suboptimal clinical response/significant clinical progression, were taken from the Prescribing Information for this product and specific reliable evidence including peer-reviewed literature:

Pediatric and Adult Individuals with LAL Deficiency: 1 mg/kg IV once every other week. For individuals with a suboptimal clinical response or significant clinical progression, increase the dosage to 3 mg/kg once every other week.

A suboptimal clinical response is defined as **all** of the following after at least 8 consecutive infusions:

- Absence of other potential causes of any observed clinical manifestations (e.g., initiation of a potentially hepatotoxic concomitant medication in an individual with abnormal AST or ALT; missed infusions; development of viral or autoimmune hepatitis; development of another alternative etiology of liver disease)
- Presence of **one** of the following:
 - ALT or AST remain abnormal and either have not improved from baseline or have worsened from the previously achieved lowest value over the preceding 8 consecutive infusions
 - LDL-c or TG remain abnormal and either have not improved or have worsened over the preceding 8 consecutive infusions
 - The individual is <18 years of age at the time of the assessment and has a WFA z-score that is 2 standard deviations below the mean and either did not improve or worsened during the preceding 6 months and the individual did not miss more than 20 percent of infusions in the preceding 6 months

A significant clinical progression is defined as **all** of the following after at least 5 consecutive infusions:

- Absence of other potential causes of any observed clinical manifestations (e.g., initiation of a potentially hepatotoxic concomitant medication in an individual with abnormal AST or ALT; missed infusions; development of viral or autoimmune hepatitis; development of another alternative etiology of liver disease)
- Confirmed elevation of ALT or AST to >5x ULN and at least twice the highest pre-treatment value **AND** the presence of **one** of the following:
 - Increase of total bilirubin to >3x ULN and at least twice the highest pre-treatment value
 - Prolongation of prothrombin time (PT) 4 seconds or greater above baseline
 - Development or worsening of ascites
 - Development of encephalopathy

Subject to the terms and conditions of the applicable benefit contract, sebelipase alfa (Kanuma) is covered under the medical benefits of the Company's products when the medical necessity criteria and Dosing and Frequency Requirements listed in this medical policy are met.

The Company reserves the right to modify the Dosing and Frequency Requirements listed in this policy to ensure consistency with the most recently published recommendations for the use of

sebelipase alfa (Kanuma). Changes to these guidelines are based on a consensus of information obtained from resources such as, but not limited to: the US Food and Drug Administration (FDA); Company-recognized authoritative pharmacology compendia; or published peer-reviewed clinical research. The professional provider must supply supporting documentation (i.e., published peer-reviewed literature) in order to request coverage for an amount of sebelipase alfa (Kanuma) outside of the Dosing and Frequency Requirements listed in this policy. For a list of Company-recognized pharmacology compendia, view our policy on Off-Label Coverage for Prescription Drugs and/or Biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of this drug. If the member's dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider must submit those changes to the Company for a new approval based on those changes as part of the utilization management activities. The Company reserves the right to conduct post-payment review and audit procedures for any claims submitted for sebelipase alfa (Kanuma).

NOT MEDICALLY NECESSARY

When molecular genetic testing reveals established benign variation(s) or wild-type genotype in the lipase A, lysosomal acid type (LIPA) gene, sebelipase alfa (Kanuma) is considered not medically necessary and, therefore, not covered because the available published peer-reviewed literature does not support its use in the treatment of this disease.

EXPERIMENTAL/INVESTIGATIONAL

All other uses for sebelipase alfa (Kanuma) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

When molecular genetic testing reveals likely pathogenic or variations of unknown significance (VUS) in the lipase A, lysosomal acid type (LIPA) gene, the use of sebelipase alfa (Kanuma) is considered experimental/investigational and, therefore, not covered because the safety and/or effectiveness of this service cannot be established by review of the available published peer-reviewed literature.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's

office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

When coverage of sebelipase alfa (Kanuma) is requested outside of the Dosing and Frequency Requirements listed in this policy, the prescribing professional provider must supply documentation (i.e., published peer-reviewed literature) to the Company that supports this request.

Duration of authorization: 12 months

Version Effective Date: 08/21/2024

Title: Secukinumab (Cosentyx®) for Intravenous Use

MEDICALLY NECESSARY

INITIAL THERAPY

Secukinumab (Cosentyx) for intravenous (IV) infusion is considered medically necessary and, therefore, covered for the following indications when, for each individual indication, all of the associated criteria are met:

Note: Secukinumab (Cosentyx) for IV infusion is only eligible for coverage when the individual has a documented contraindication, intolerance to or there is a clinical reason that a trial of Secukinumab (Cosentyx) for subcutaneous (SC) injection would be otherwise inappropriate for the member.

Psoriatic Arthritis (PsA)

Secukinumab (Cosentyx) for IV infusion may be covered as monotherapy or concomitantly with non-biologic DMARDs when **all** of the following inclusion criteria are met:

- The individual is 18 years of age or older.
- The individual has had an inadequate response after at least 3 months of one or more DMARDs (e.g., methotrexate, hydroxychloroquine, leflunomide, azathioprine, sulfasalazine), or the use of all DMARDs is contraindicated in the individual.
- The individual has a documented failure, contraindication, or intolerance to **two** anti-TNFs such as infliximab (Remicade) **and** golimumab (Simponi Aria), unless there was a primary non-response of an anti-TNF or a serious adverse event associated with an anti-TNF (in which case no additional anti-TNF trial is needed).
- Active or latent tuberculosis (TB) has been ruled out.
- Secukinumab (Cosentyx) will not be used in combination with other biologic DMARDs or Janus kinase inhibitor (JAK) inhibitors.

Ankylosing Spondylitis (AS)

- The individual is at least 18 years old.
- Documentation of failure, contraindication, or intolerance to the following:
 - At least a 4-week trial of two nonsteroidal anti-inflammatory drugs (NSAIDs) at maximum recommended or tolerated anti-inflammatory dose

- The individual has a documented failure, contraindication, or intolerance to **two** anti-TNFs such as infliximab (Remicade) **and** golimumab (Simponi Aria), unless there was a primary non-response of an anti-TNF or a serious adverse event associated with an anti-TNF (in which case no additional anti-TNF trial is needed).
- Active or latent TB has been ruled out.

Axial spondyloarthritis (nonradiographic):

- When all of the following criteria are met:
 - The individual is over 18 years of age with evidence of active disease (increasing inflammation, pain, disability, and decreased function)
 - Documentation of an adequate therapeutic trial* of at least two NSAIDs that have failed to control symptoms

*An adequate therapeutic trial is defined as: Treatment with NSAIDs for at least 3 months at maximum recommended or tolerated anti-inflammatory dose unless treatment is discontinued due to lack of response, intolerance, toxicity or contraindication.

- Individual has a documented failure, contraindication, or intolerance to TWO anti-TNF's such as infliximab (Remicade) AND golimumab (Simponi Aria), unless there was a primary non-response of an anti-TNF or a serious adverse event associated with an anti-TNF (in which case no additional anti-TNF trial is needed).
- If the above criteria are not met, there must be documentation both of very severe disease and that the clinician considers infliximab or related biosimilars the best initial drug of choice with appropriate justification (severe pain, disability, and inability to perform activities of daily living [ADLs], or severe impact on quality of life)
- Active or latent tuberculosis (TB) has been ruled out.

**Primary non-response: Lack of response within the first 6 months of treatment. Secondary non-response: Loss of response after having sustained a positive effectiveness outcome for ≥12 months from treatment initiation, or after two consecutive positive measurements with a minimum time interval.*

CONTINUATION THERAPY

Secukinumab (Cosentyx) for IV infusion is considered medically necessary and, therefore, covered for continuation therapy when the individual meets all of the following:

- There is documentation of a positive clinical response or stabilization to therapy (e.g., improvement in total active [swollen and tender] joint count from baseline, improvement in symptoms [e.g., pain, stiffness, inflammation, fever, fatigue, nonproductive cough] from baseline)

EXPERIMENTAL/INVESTIGATIONAL

All other uses for secukinumab (Cosentyx) for IV use are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the service.

Duration of authorization: 12 months

Version Effective Date: 05/28/2025

Title: Self-Administered Drugs and Biologics

Policy

Coverage is subject to the terms, conditions, and limitations of the member's contract.

The Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition.

For most of the Company's commercial products, self-administered drugs and biologics are not covered under the member's medical benefit and, therefore, are not eligible for reimbursement under the member's medical benefit. Coverage may be available under the pharmacy benefit or through a pharmacy vendor. Individual benefits must be verified.

The codes listed in Attachment A of this policy represent the products that the Company considers to meet the definition of self-administered drugs and biologics. These drugs are not eligible for reimbursement consideration under the member's medical benefit even if the drugs are provided or administered by a professional provider (for some products, there may be exceptions relating to coagulation factors for hemophilia and other bleeding conditions [please refer to the medical policy titled "Coagulation Factors", policy number 08.00.92]). Additionally, drugs may be considered self-administered by the Company even in circumstances where initial medical supervision and/or instruction is required prior to patient self-administration.

The self-administered designation does not apply to prescription drugs and biologics that are: (a) mandated to be covered by law under the medical benefit (e.g., insulin or any drug required for the treatment of diabetes); or (b) required for treatment of an emergency condition that requires the use of a Company-determined self-administered drug (e.g., epinephrine).

When the member or caregiver is unable to administer a self-administered drug, the drug can be administered by an eligible professional provider (e.g., a professional provider may administer the drug when a caregiver is unable to provide treatment due to a prolonged trip or absence). In this situation, the drug remains ineligible for coverage under the medical benefit; however, the administration fee for the professional provider is covered and eligible for reimbursement under the member's medical benefit.

Injection therapy services (represented by "S" codes listed in the coding table of this policy) must not be utilized by the eligible professional provider when reporting the administration of a self-administered drug because these services encompass more than the administration of the drug (e.g., pharmacy services, care coordination). Therefore, they are not covered and not eligible for reimbursement under the medical benefit of the Company. Coverage may be available under the pharmacy benefit or through a pharmacy vendor. For members enrolled in

commercial plans in New Jersey, self-administered coagulation factors may be available under the applicable medical or pharmacy benefit. Individual benefits must be verified.

MAINTENANCE OF DRUG/BIOLOGICS LIST

The drugs and biologics listed in Attachment A of this policy are considered by the Company to be self-administered and are subject to change as new medications come to market or new determinations are made by the Company.

BILLING REQUIREMENTS

For drugs and biologics that have more than one method of administration, application of an appropriate modifier is required to indicate the route of administration.

- To report the subcutaneous route of administration, append the following modifier: JB Administered Subcutaneously

Inclusion of a code in this policy does not imply reimbursement. Eligibility, benefits, limitations, exclusions, utilization management/referral requirements, provider contracts, and Company policies apply.

Duration of authorization: 12 months

Version Effective Date: 01/01/2025

Attachment A: [Self-Administered Drugs and Biologics](#)

Description: Prescription drugs and biologics that are considered by the Company to be self-administered.

Policy Attachment

Attachment to Policy #08.00.78at

Attachment: A

Policy #: 08.00.78at

Description: Prescription drugs and biologics that are considered by the Company to be self-administered.

Title: Self-Administered Drugs and Biologics

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

Self-Administered Drugs and Biologics

For most of the Company's commercial products, self-administered drugs and biologics are not covered under the member's medical benefit and, therefore, are not eligible for reimbursement under the member's medical benefit. Self-administered drugs are only covered under the member's pharmacy benefit, if one exists, unless an exception by product or group exists. Therefore, individual benefits must be verified, as coverage may vary by product and/or group. Providers should work directly with the member's Pharmacy Benefit Administrator on options to obtain a self-administered drug through specialty pharmacy distribution under the member's pharmacy benefit.

The Company-determined, self-administered drugs and biologics listed in this Attachment are subject to change as new medications come to market or new determinations are made by the Company. This list contains only those drugs and biologics that are determined by the Company to be self-administered. Any FDA-approved biosimilar products will be managed the same way as their reference product, already listed in this Table.

Note: Drug/Biologic codes that must use modifier JB when the subcutaneous form of the drug/biologic is administered are listed with an asterisk * in this Coding Table.

Brand Name	Generic Name	USC Class	Code	Date Drug or Biologic Classifi

				ed as Self-Administered
N/A	concizumab	Coagulants, Other	J3590	Upon FDA-approval
N/A	dihydroergotamine (DHE) (prefilled autoinject or for self-administered administration)	Anti-Migraine, Other	J3490	Upon FDA-approval
N/A	garadacimab	Clotting Factor inhibitor	J3590	Upon FDA-approval
N/A	glepaglutide	Gastrointestinal	J3590	Upon FDA-approval
N/A	naloxone hydrochloride	Opioid antagonist	J2310	10/05/2020
N/A	volanesorsen sodium	Antihyperlipidemia Agents	J3490	01/01/2019
Abrilada	adalimumab-afzb	Antiarthritic, Syst. Bio. Response Modifier	Q5145	10/21/2019
Actemra (for subcutaneous use) <i>Note: For Intravenous use of Actemra covered under the medical benefit, please refer to policy 08.00.85 Tocilizumab (Actemra®) and related biosimilars for Intravenous Infusion</i>	tocilizumab	Monoclonal Antibodies	J3590	10/22/2013
Actimmune	interferon gamma-1b	Interferons	J9216	1/1/2010

Adbry	tralokinumab-ldrm	Monoclonal Antibodies	J3590	06/07/2021
Advate	antihemophilic factor VIII	Clotting Factor	J7192	1/1/2014
Adynovate	antihemophilic factor VIII	Clotting Factor	J7207	1/01/2016
Afstyla	antihemophilic factor VIII	Factor VIII	J7210	12/12/2016
Aimovig	erenumab-aooe	Monoclonal Antibodies	J3590	05/28/2018
Ajovy	fremanezumab-vfrm	Monoclonal Antibodies	J3031 J3590	01/01/2019
Alphanate	antihemophilic factor VIII/von Willebrand factor complex (human)	Clotting Factor	J7186	1/1/2014
Alphanine SD	coagulation factor IX (human)	Clotting Factor	J7193	1/1/2014
Alprolix	coagulation factor IX (recombinant)	Clotting Factor	J7201	7/30/2014
Altuviio	antihemophilic factor (recombinant), Fc-VWF-XTEN fusion protein-ehtl	Clotting Factor VIII	J7214	02/23/2023
Amjevita	adalimumab-atto	Antiarthritic, Syst. Bio. Response Modifier	J3590	12/12/2016
Apokyn	apomorphine	Anti-Parkinson's, Others	J0364	1/1/2010

Arcalyst	rilonacept	Immunomodulators	J2793	01/01/2019
Arixtra	fondaparinux	Anticoagulants, Injectable, Other	J1652	1/1/2010
Avonex	interferon beta–1a	Interferons	J1826	1/1/2011
Benefix	coagulation factor IX (recombinant)	Clotting Factor	J7195	1/1/2014
Benlysta* (<i>for subcutaneous use</i>) <i>Note: For Intravenous use of Benlysta covered under the medical benefit, please refer to policy 08.00.99 Belimumab (Benlysta®)</i>	belimumab	Monoclonal Antibodies	J3590	09/28/2017
Berinert	C1 Esterase Inhibitor Subcutaneous (Human)	Biologicals, Other	J0597	01/01/2018
Besremi	ropeginterferon alfa-2b	Interferons	J3490	06/07/2021
Betaseron	interferon beta–1b	Interferons	J1830 J3490	1/1/2010
Bimzelx	bimekizumab-bkzx	Monoclonal Antibodies	J3590	10/17/2023
Bonsity	teriparatide	Bone Formation Agents	J3590	10/05/2020
Bravelle	urofollitropin	Gonadotropins	J3355	1/1/2010
Cablivi (<i>for subcutaneous use</i>)	caplacizumab-yhdp	Platelet Inhibitors, Other	J3590	10/21/2019

Caverject	alprostadil	Peripheral Vasodilators	J0270 J3490	1/1/2010
Cetrotide	cetrorelix acetate	Anabolic Hormones	J3490	1/1/2010
Cimzia	certolizumab pegol	Gastrointes- tinal anti- Inflammatory	J0717 J3590	1/1/2014
Cinryze	C1 Esterase Inhibitor Subcutaneous (Human)	Biologicals, Other	J0598	01/01/2018
Coagadex	coagulation factor X, (human)	Clotting Factor	J7175	1/01/2016
Copaxone	glatiramer acetate	Nervous System Disorders, Other	J1595	1/1/2010
Corifact	Factor XIII concentrate (Human)	Clotting Factor	J7180	12/01/2014
Cosentyx (<i>for subcutaneous use</i>)	secukinumab	Monoclonal Antibodies	J3590	03/25/2015
Cyltezo	adalimumab-adbm	Antiarthritic, Syst. Bio. Response Modifier	Q514 3	05/28/2018
Dupixent	dupilumab	Monoclonal Antibodies	J3590	05/31/2017
Ebglyss	lebrikizumab-lbkz	Monoclonal Antibodies	J3590	09/13/2024
Edex	alprostadil	Peripheral Vasodilators	J0270 J3490	1/1/2010

Egrifta SV	tesamorelin	Analog; growth hormone-releasing factor	J3490	01/01/2021
Eloctate	recombinant factor VIII Fc fusion protein	Clotting Factor	J7205	7/30/2014
Elonva	corifollitropin alfa	Modified follicle stimulating hormone	J3490	7/30/2014
Emgality	galcanezumab-gnlm	Monoclonal Antibodies	J3590	05/28/2018
Empaveli	pegcetacoplan	Hemolysis reduction	J3490	06/07/2021
Enbrel	etanercept	Antiarthritic, Syst. Bio. Response Modifier	J1438 J3590	1/1/2010
Enspryng	satralizumab	Monoclonal Antibodies	J3590	10/05/2020
Entyvio (<i>for subcutaneous use</i>) <i>Note: For Intravenous use of Entyvio covered under the medical benefit, please refer to policy 08.01.18 Vedolizumab (Entyvio®)</i>	vedolizumab	Monoclonal Antibodies	J3590	10/05/2020
Erelzi	etanercept-szsz	Antiarthritic, Syst. Bio. Response Modifier	J3590	12/12/2016
Esperoct	antihemophilic factor (recombinant), glycopegylated-exei	Clotting Factor	J7204	7/1/2020

Eticovo	etanercept-ykro	Antiarthritic, Syst. Bio. Response Modifier	J3590	10/21/2019
Extavia	interferon beta–1b	Interferons	J1830 J3490	1/1/2010
Feiba	anti-inhibitor coagulant complex	Hemostatic	J7198	1/1/2014
Fasenra	benralizumab	Monoclonal Antibodies	J0517	01/01/2021
Fibryga	fibrinogen concentrate (human)	Clotting Factor	J7177	09/28/2017
Firazyr	icatibant	Bradykinin B2 receptor antagonist	J1744	9/9/2011
Follistim AQ	follitropin beta	Gonadotropins	S0128	1/1/2010
Forteo	teriparatide	Bone Formation Agents	J3110	1/1/2010
Fragmin	dalteparin	Anticoagulants, Fractionated Heparins	J1645	1/1/2010
Furoscix (<i>for subcutaneous use</i>)	furosemide	Diuretics, Loop	J1941	10/07/2022
Fuzeon	enfuvirtide	HIV Entry/Fusion Inhibitor	J1324	1/1/2010
Ganirelix	ganirelix acetate	Gonadotropins	S0132	1/1/2010
Gattex	teduglutide	GLP Agonist	J3490	9/12/2012
Genotropin	somatropin	Anabolic Hormones	J2941	1/1/2010
Genotropin MiniQuick	somatropin	Anabolic Hormones	J2941	1/1/2010

Glatopa	glatiramer acetate	Nervous System Disorders, Other	J1595	1/01/2016
Gonal-f	follitropin alfa	Gonadotropins	S0126	1/1/2010
Gonal-f RFF	follitropin alfa	Gonadotropins	S0126	1/1/2010
Hadlima	adalimumab-bwwd	Antiarthritic, Syst. Bio. Response Modifier	J3590	10/21/2019
Haegarda	C1 Esterase Inhibitor Subcutaneous (Human)	Biologicals, Other	J0599	09/28/2017
Hemlibra	emicizumab-kxwh	Clotting Factor; Monoclonal Antibodies	J7170	05/28/2018
Hemofil-M	antihemophilic factor VIII	Clotting Factor	J7190	1/1/2014
Hepcludex	bulevirtide	Viral hepatitis products	J3490	Upon FDA-approval
Hulio	adalimumab-fkip	Antiarthritic, Syst. Bio. Response Modifier	Q5140	10/05/2020
Humate-P	antihemophilic factor VIII/Von Willebrand factor complex (human)	Clotting Factor	J7187	1/1/2014
Humatrope	somatropin	Anabolic Hormones	J2941	1/1/2010
Humira	adalimumab	Antiarthritic, Syst. Bio. Response Modifier	J0139	1/1/2010
Hypavzi	marstacimab-hncq	Clotting Factor; Monoclonal Antibodies	J3590	10/11/2024

Hyrimoz	adalimumab-adaz	Antiarthritic, Syst. Bio. Response Modifier	J3590	10/21/2019
Idacio	adalimumab-aacf	Antiarthritic, Syst. Bio. Response Modifier	Q5144	12/13/2022
Idelvion	coagulation Factor IX (recombinant)	Factor IX	J7202	3/09/2016
Imcivree	setmelanotide	Anti-obesity in rare disease	J3490	01/01/2021
Imitrex	sumatriptan	Serotonin 5HT-1 Receptor Agonists	J3030 J3490	1/1/2010
Increlex	mecasermin	Anabolic Hormones	J2170	1/1/2010
Infergen	interferon alfacon-1	Interferons	J9212	1/1/2010
Innohep	tinzaparin	Anticoagulants, Fractionated Heparins	J1655	1/1/2010
Ixinity	coagulation Factor IX (recombinant)	Factor IX	J7213	7/15/2015
Jivi	antihemophilic Factor VIII	Clotting Factor	J7208	01/01/2019
Kesimpta	ofatumumab	Monoclonal Antibodies	J3590	10/05/2020
Kevzara	sarilumab	Monoclonal Antibodies	J3590	12/12/2016
Kineret	anakinra	Antiarthritic, Syst. Bio. Response Modifier	J3490	1/1/2010
Koate-DVI	antihemophilic Factor VIII	Clotting Factor	J7190	1/1/2014

Kogenate FS	antihemophilic Factor VIII	Clotting Factor	J7192	1/1/2014
Kovaltry	antihemophilic Factor VIII	Clotting Factor	J7211	3/09/2016
Lovenox	enoxaparin	Anticoagulants, Fractionated Heparins	J1650	1/1/2010
Lupron (<i>2-week kit only</i>)	leuprolide	GRH Analogs	J9218	1/1/2010
Menopur	menotropins	Gonadotropins	S0122	1/1/2010
Miacalcin	calcitonin–salmon	Bone Density Regulators, Calcitonins	J0630	1/1/2010
Mononine	Coagulation Factor IX (human)	Clotting Factor	J7193	1/1/2014
Myalept	metreleptin	Leptin Analog	J3590	7/30/2014
Natpara	recombinant human parathyroid hormone (rhPTH 1-84)	Hormone	J3590	12/01/2014
Nemluvio	nemolizumab-ilto	Dermatologicals	J3590	08/12/2024
Ngenla	somatrogon-ghla	Anabolic Hormones	J2941	06/07/2021
Norditropin	somatropin	Anabolic Hormones	J2941	1/1/2010
Norditropin NordiFlex	somatropin	Anabolic Hormones	J2941	1/1/2010
Novarel	chorionic gonadotropin	Gonadotropins	J0725	1/1/2010
Novoeight	turotocog alfa	Clotting Factor	J7182	10/16/2013

NovosevenRT	recombinant Coagulation Factor VIIa (rFVIIa)	Clotting Factor	J7189	1/1/2014
Nucala	mepolizumab	Monoclonal Antibodies	J2182	01/01/2021
Nulibry	fosdenopterin	Nervous system disorders, Other	J3590	01/01/2021
Nutropin	somatropin	Anabolic Hormones	J2941	1/1/2010
Nutropin AQ	somatropin	Anabolic Hormones	J2941	1/1/2010
Nuwiq	Antihemophilic Factor VIII	Clotting Factor	J7209	1/01/2016
Obizur	recombinant antihemophilic porcine sequence factor VIII	Clotting Factor	J7188	12/01/2014
Oclaiz	octreotide	somatostatin analog	J3490	Upon FDA-approval
Omnitrope	somatropin	Anabolic Hormones	J2941	1/1/2010
OmvoH (<i>for subcutaneous use</i>)	mirikizumab-mrkz	Monoclonal Antibodies	J2267	10/26/2023
Orencia* (<i>for subcutaneous use</i>) <i>Note: for Intravenous use of Orencia covered under the medical benefit, please refer to policy 08.00.62 Abatacept (Orencia®)</i>	abatacept	Immunomodulators	J3590	9/9/2011
Otrexup	methotrexate	Folic Acid Antagonist	J3490	10/11/2013
Ovidrel	chorionic gonadotropin	Gonadotropins	J0725	1/1/2010

Palynziq	pegvaliase-pqpz	Enzymes, Systemic	J3590	05/28/2018
Pegasys	peginterferon alfa-2a	Interferons	S0145	1/1/2010
PEG-Intron	peginterferon alfa-2b	Interferons	S0148	10/1/2010
PEG-Intron Redi-Pen	peginterferon alfa-2b	Interferons	S0148	10/1/2010
Plegridy	PEG interferon beta-1A	Interferons	J3490	7/30/2014
Praluent	alriocumab	Monoclonal Antibodies	J3590	7/15/2015
Pregnyl	chorionic gonadotropin	Gonadotropins	J0725	1/1/2010
Profilnine	coagulation Factor IX complex (human)	Clotting Factor	J7194	10/25/2021
Proplex T	coagulation Factor IX complex (human)	Clotting Factor	J7194	1/1/2014
Protropin	somatrem	Anabolic Hormones	J2940	4/30/2010
Rasuvo	methotrexate	folic acid antagonist	J3490	7/30/2014
Rebif	interferon beta-1a	Interferons	J1826	1/1/2011
Rebif	interferon beta-1a	Interferons	Q3027	1/1/2014
Rebif	interferon beta-1a	Interferons	Q3028	1/1/2014
Rebinyn	coagulation Factor IX (recombinant)	Clotting Factor	J7203	09/28/2017
Recombinate	antihemophilic Factor VIII	Clotting Factor	J7192	1/1/2014

RediTrex	methotrexate	Folic acid antagonist	J3490	10/05/2020
Relistor	methylnaltrexone bromide acetate	MU-Opioid Receptor Antagonists	J2212	1/1/2010
Repatha	evolocumab	Monoclonal Antibodies	J3590	7/15/2015
Repronex	menotropins	Gonadotropins	S0122	1/1/2010
RiaSTAP	fibrinogen concentrate (human)	Clotting Factor	J7178	3/09/2016
Rivfloza	nedosiran	Genitourinary Tract, Other	J3590	09/29/2023
Rixubis	coagulation Factor IX (recombinant)	Clotting Factor	J7200	1/1/2014
Roferon-A	interferon alfa-2a	Interferons	J9213	4/30/2010
Ruconest	C1 Esterase Inhibitor Subcutaneous (Recombinant)	Biologicals, Other	J0596	01/01/2018
Saizen	somatropin	Anabolic Hormones	J2941	1/1/2010
Saxenda	liraglutide	Human GLP-1 Analog	J3490	1/01/2016
Serostim	somatropin	Anabolic Hormones	J2941	1/1/2010
Sevenfact	coagulation factor VIIa (recombinant)- jncw	Clotting Factor	J7212	10/05/2020
Signifor	pasireotide	somatostatin analog	J3490	1/31/2013
Siliq	brodalumab	Monoclonal Antibodies	J3590	12/12/2016

Simponi	golimumab	Antiarthritic, Syst.Bio. Response Modifier	J3490	1/1/2010
Skyrizi* (for subcutaneous use) <i>Note: for Intravenous use of Skyrizi covered under the medical benefit, please refer to policy 08.01.95 Risankizumab-rzaa (Skyrizi®) for Intravenous Use</i>	risankizumab-rzaa	Monoclonal Antibodies	J3590	10/21/2019
Simlandi	adalimumab-ryvk	Antiarthritic, Syst. Bio. Response Modifier	Q514 2	02/23/2024
Sogroya	somapacitan-beco	Analog; growth hormone	J3590	01/01/2021
Somavert	pegvisomant	Anabolic Hormones	J3490	1/1/2010
Skytrofa	lonapegsomatropin-tcgd	Anabolic Hormones	J3490	06/07/2021
Strensiq	asfotase alfa	Enzymes, Systemic	J3490	3/25/2015
Sumavel DosePro	sumatriptan	Serotonin 5HT-1 Receptor Agonists	J3030 J3490	1/1/2010
Supprelin	histrelin	Sex Hormones, Other	J1675	1/1/2010
Sylatron	peginterferon alfa-2b	Interferons	S0148	5/10/2011
Takhzyro	lanadelumab-flyo	Monoclonal Antibodies	J0593 J3590	01/01/2019

Taltz	ixekizumab	Monoclonal Antibodies	J3590	12/12/2016
Tegsedi	inotersen	Neuropathic Pain, Other	J3490	01/01/2019
Tev-Tropin	somatropin	Anabolic Hormones	J2941	1/1/2010
Tezspire (<i>for subcutaneous use</i>)	tezepelumab-ekko	Respiratory Other	J2356	01/01/2024
Tremfya (<i>for subcutaneous use</i>)	guselkumab	Monoclonal Antibodies	J1628	09/28/2017
Tretten	coagulation Factor XIII-A-subunit (recombinant)	Coagulation Factor	J7181	12/23/2013
Tyenne (<i>for subcutaneous use</i>)	tocilizumab-aazg	Monoclonal Antibodies	Q5135	03/05/2024
Tymlos	abaloparatide	Bone Formation Agents	J3490	05/31/2017
Tyvaso DPI (inhalation powder, for oral inhalation use)	treprostinil	Prostacyclin Mimetic	J3490	05/23/2022
Ultomiris* (<i>for subcutaneous use</i>) <i>Note: for Intravenous use of Ultomiris covered under the medical benefit, please refer to policy</i> <i>08.00.84 Eculizumab (Soliris®) and Related Biosimilars, Ravulizumab-cwvz (Ultomiris®) for intravenous use</i>	ravulizumab-cwvz	Paroxysmal Nocturnal Hemoglobinuria and Atypical Hemolytic Uremic Syndrome	J3590	07/22/2022
Vonvendi	Von Willebrand Factor (recombinant)	Coagulation Factor	J7179	3/09/2016

Voxzogo	vosoritide	Bone growth disorder	J3490	06/07/2021
Vyleesi	bremelanotide	Sexual Function Disorders	J3490	10/21/2019
Wainua	eplontersen	Neuropathic Pain, Other	J3490	12/21/2023
Wegovy	semaglutide	Anti-Obesity	J3490	06/04/2021
Wilate	Von Willebrand Factor/Factor VIII Complex (human)	Coagulation Factor Complex	J7183	1/1/2014
Winrevair	sotatercept-csrk	Cardiac agents, others	J3590	03/26/2024
Xolair (prefilled syringe for self-administered administration) <i>Note: For administration by a professional provider, covered under the medical benefit, please refer to policy 08.00.55 Omalizumab (Xolair®)</i>	omalizumab	Respiratory, Other	J3590	04/09/2021
Xyntha	antihemophilic Factor (recombinant)	Clotting Factor	J7185	1/1/2014
Xyosted	testosterone enanthate	Sex Hormones, Other	J3121	05/28/2018
Yorvipath	palopegteriparatide	Parathyroid agent	J3490	08/09/2024
Yuflyma	adalimumab-aaty	Antiarthritic, Syst. Bio. Response Modifier	Q5141	05/24/2023

Yusimry	adalimumab-aqvh	Antiarthritic, Syst. Bio. Response Modifier	J3590	12/17/2021
Zegalogue	dasiglucagon	Diabetes	J3490	06/07/2021
Zembrace SymTouch	sumatriptan succinate	Serotonin 5HT-1 Receptor Agonists	J3490	3/09/2016
Zepbound	tirzepatide	Human GLP-1 Analogs	J3490	11/08/2023
Zilbrysc	zilucoplan	Nervous System Disorders, Other	J3490	10/17/2023
Zimhi	naloxone hydrochloride	Opioid antagonist	J2311	01/01/2023
Zomacton	somatropin	Anabolic Hormones	J2941	09/28/2017
Zorbtive	somatropin	Anabolic Hormones	J2941	1/1/2010
Zurnai	nalmefene	Opioid antagonist	J3490	08/07/2024
Zymfentra (<i>for subcutaneous use</i>) <i>Note: For Intravenous use of Infliximab covered under the medical benefit, please refer to policy 08.00.34 Intravenous Infliximab and Related Biosimilars</i>	infliximab-dyyb	Monoclonal Antibodies	J1748	10/20/2023

Version Effective Date: 01/01/2025

Title: Spesolimab--sbzo (Spevigo®)

MEDICALLY NECESSARY

Spesolimab-sbzo (Spevigo) is considered medically necessary and, therefore, covered as a single-dose intravenous infusion for the treatment of individuals ages 12 years and older with generalized pustular psoriasis (GPP) flare when all of the following criteria are met:

- The individual has been diagnosed with generalized pustular psoriasis (GPP) and is currently experiencing a flare with all of the following:
 - The individual weighs 40 kg or more
 - The individual has at least 5% of body surface area (BSA) covered with erythema and the presence of pustules (new appearance or worsening of pustules)
 - The individual has a flare of GPP of moderate-to-severe intensity, as defined by the Generalized Pustular Psoriasis Physician Global Assessment (GPPPGA) total score of 3 (moderate) to 4 (severe) [the total GPPPGA score ranges from 0 (clear) to 4 (severe)]
- Prescribed by or in consultation with a dermatologist
- The individual does not have any of the following:
 - Synovitis-acne-pustulosis-hyperostosis-osteitis (SAPHO) syndrome.
 - Primary erythrodermic psoriasis vulgaris.
 - Primary plaque psoriasis vulgaris without the presence of pustules or with pustules that are restricted to psoriatic plaques.
 - Drug-triggered Acute Generalized Exanthematous Pustulosis (AGEP)
 - An immediate life-threatening flare of GPP or requiring intensive care treatment (e.g., cardiovascular/cytokine-driven shock, pulmonary distress)

syndrome, or renal failure)

- Severe, progressive, or uncontrolled hepatic disease, defined as >3- fold Upper Limit of Normal (ULN) elevation in AST or ALT or alkaline phosphatase, or >2-fold ULN elevation in total bilirubin.

NOTE: If flare symptoms persist, may administer an additional intravenous 900 mg dose one week after the initial dose.

EXPERIMENTAL/INVESTIGATIONAL

All other uses of Spesolimab-sbzo (Spevigo) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Duration of authorization: 12 months

Version Effective Date: 05/28/2025

Title: Sutimlimab-jome (Enjaymo)

MEDICALLY NECESSARY

SUTIMLIMAB-JOME (ENJAYMO)

Sutimlimab-jome (Enjaymo) is considered medically necessary and, therefore, covered for the treatment of hemolysis in adult individuals with cold agglutinin disease (CAD) when all of the following criteria are met:

- The individual confirmed diagnosis of primary cold agglutinin disease (CAD) based on all of the following criteria:
 - Chronic hemolysis
 - Polyspecific direct antiglobulin test (DAT) positive
 - Monospecific DAT is strongly positive for C3d
 - Cold agglutinin titer ≥ 64 at 4 degrees Celsius
 - Immunoglobulin G (IgG) DAT less than or equal to ($\leq$) 1+
 - No overt malignant disease (e. i., an aggressive or malignant disease that is easily observable; clinically obvious; symptomatic, and often rapid organ damage)
- History of at least one documented blood transfusion within six months of treatment
- Hemoglobin level ≤ 10.0 gram per deciliter (g/dL)
- Bilirubin level above the normal reference range, including individuals with Gilbert's Syndrome
- The individual has a bodyweight of greater than or equal to ($\geq$) 39 kilogram (kg) at the initiation of the treatment
- The individual does **not** have any of the following conditions:
 - Cold agglutinin syndrome secondary to an infection, rheumatologic disease, or active hematologic malignancy
 - Clinically relevant infection of any kind within the month preceding treatment (eg, active hepatitis C, pneumonia)
 - Clinical diagnosis of systemic lupus erythematosus (SLE) or other autoimmune disorders with anti-nuclear antibodies at the initiation of the treatment.

- The individual has all of the following:
 - Negative hepatitis panel (including hepatitis B surface antigen and/or hepatitis C virus antibody) prior to or at the initiation of the treatment
 - Negative human immunodeficiency virus (HIV) antibody at the initiation of the treatment
 - Vaccination against encapsulated bacteria at least two weeks prior to the treatment

EXPERIMENTAL/INVESTIGATIONAL

All other uses for sutimlimab-jome (Enjaymo), are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

An Individual's medical record must reflect the medical necessity for the care provided. These medical records may include but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the service.

Duration of authorization: 12 months

Version Effective Date: 10/30/2024

Title: Tafasitamab-cxix (Monjuvi®)

MEDICALLY NECESSARY

Tafasitamab-cxix (Monjuvi) is considered medically necessary and, therefore, covered as a single agent in adult individuals for the following B-cell lymphomas:

- **Human Immunodeficiency Virus (HIV)–Related B-Cell Lymphomas**
 - Second-line and subsequent therapy in combination with lenalidomide (Revlimid) for HIV-related diffuse large B-cell lymphoma, primary effusion lymphoma, and human herpesvirus 8+ (HHV8+) diffuse large B-cell lymphoma, not otherwise specified, or for HIV-related plasmablastic lymphoma if no intention to proceed to transplant for:
 - relapsed or disease >12 months after completion of first-line therapy
 - primary refractory disease (partial response, no response, or progression) or relapsed disease <12 months after completion of first-line therapy in noncandidates for chimeric antigen receptor (CAR) T-cell therapy
 - alternative systemic therapy (if not previously used) for relapsed/refractory disease in noncandidates for CAR T-cell therapy
- **High-Grade B-Cell Lymphomas**
 - Second-line and subsequent therapy in combination with lenalidomide (Revlimid) if no intention to proceed to transplant for:
 - relapsed or refractory disease >12 months after completion of first-line therapy
 - primary refractory disease (partial response, no response, or progression) or relapsed disease <12 months after completion of first-line therapy in noncandidates for CAR T-cell therapy
 - alternative systemic therapy (if not previously used) for relapsed/refractory disease in noncandidates for CAR T-cell therapy
- **Post-Transplant Lymphoproliferative Disorders (PTLDs)**
 - Second-line and subsequent in combination with lenalidomide (Revlimid) in individuals with monomorphic PTLD (B-cell type) if no intention to proceed

to transplant for:

- relapsed or refractory disease >12 months after completion of initial treatment with chemoimmunotherapy
 - primary refractory disease (partial response, no response, or progression) or relapsed disease <12 months after completion of initial treatment with chemoimmunotherapy in noncandidates for CAR T-cell therapy
 - alternative systemic therapy (if not previously used) for relapsed/refractory disease in noncandidates for CAR T-cell therapy
- **Histologic Transformation of Indolent Lymphoma to Diffuse Large B-Cell Lymphoma**
 - In combination with lenalidomide (Revlimid) if previously treated with an anthracycline-based regimen if no intention to proceed to transplant and any of the following (National Comprehensive Cancer Network [NCCN]-preferred regimen):
 - as additional therapy for partial response, no response, relapsed or progressive disease following chemoimmunotherapy in individuals with histologic transformation of follicular or marginal zone lymphomas after minimal or no prior treatment
 - for histologic transformation of follicular or marginal zone lymphomas after multiple lines of prior therapies including ≥ 2 chemoimmunotherapy regimens for indolent or transformed disease
- **Diffuse Large B-Cell Lymphoma**
 - As a second-line and subsequent therapy (NCCN preferred regimen) in combination with lenalidomide (Revlimid) in non-candidates if no intention to proceed to for transplant for the following indications:
 - relapsed >12 months after completion of first-line therapy
 - primary refractory disease (partial response, no response, or progression) or relapsed disease <12 months after completion of first-line therapy in non-candidates for CAR T-cell therapy
 - alternative systemic therapy (if not previously used) for relapsed/refractory disease in non-candidates for CAR T-cell therapy

- In combination with lenalidomide (Revlimid) for the treatment of individuals with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) not otherwise specified, including DLBCL arising from low-grade lymphoma, and who are not eligible for autologous stem cell transplant (ASCT).

MANDATES

PENNSYLVANIA MEMBERS

In accordance with the Commonwealth of Pennsylvania's Act 6 of 2020 or Fair Access to Cancer Treatment Act, for members who are enrolled in Pennsylvania commercial products who have stage 4, advanced metastatic cancer, refer to the Medical Policy titled "Coverage of Anticancer Prescription Oral and Injectable Drugs and Biologics and Supportive agents (08.01.08)" for additional information regarding the applicable coverage of drugs and biologics.

EXPERIMENTAL/INVESTIGATIONAL

All other uses of tafasitamab-cxix (Monjuvi) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Duration of authorization: 12 months

Version Effective Date: 10/01/2024

Attachment A: [Tafasitamab-cxix \(Monjuvi®\)](#)

Description: ICD 10 Diagnosis Codes

Policy Attachment

Attachment to Policy # 08.01.81d

Attachment: A

Policy #: 08.01.81d

Description: ICD 10 Diagnosis Codes

Title: Tafasitamab-cxix (Monjuvi®)

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

ICD-10 CODES AND NARRATIVES

C83.30 Diffuse large B-cell lymphoma, unspecified site

C83.31 Diffuse large B-cell lymphoma, lymph nodes of head, face, and neck

C83.32 Diffuse large B-cell lymphoma, intrathoracic lymph nodes

C83.33 Diffuse large B-cell lymphoma, intra-abdominal lymph nodes

C83.34 Diffuse large B-cell lymphoma, lymph nodes of axilla and upper limb

C83.35 Diffuse large B-cell lymphoma, lymph nodes of inguinal region and lower limb

C83.36 Diffuse large B-cell lymphoma, intrapelvic lymph nodes

C83.37 Diffuse large B-cell lymphoma, spleen

C83.38 Diffuse large B-cell lymphoma, lymph nodes of multiple sites

C83.398 Diffuse large B-cell lymphoma of other extranodal and solid organ sites

C83.90 Non-follicular (diffuse) lymphoma, unspecified, unspecified site

C83.91 Non-follicular (diffuse) lymphoma, unspecified, lymph nodes of head, face, and neck

C83.92 Non-follicular (diffuse) lymphoma, unspecified, intrathoracic lymph nodes

C83.93 Non-follicular (diffuse) lymphoma, unspecified, intra-abdominal lymph nodes

C83.94 Non-follicular (diffuse) lymphoma, unspecified, lymph nodes of axilla and upper limb

C83.95 Non-follicular (diffuse) lymphoma, unspecified, lymph nodes of inguinal region and lower limb

C83.96 Non-follicular (diffuse) lymphoma, unspecified, intrapelvic lymph nodes

C83.97 Non-follicular (diffuse) lymphoma, unspecified, spleen

C83.98 Non-follicular (diffuse) lymphoma, unspecified, lymph nodes of multiple sites

C83.99 Non-follicular (diffuse) lymphoma, unspecified, extranodal and solid organ sites

C85.10 Unspecified B-cell lymphoma, unspecified site

C85.11 Unspecified B-cell lymphoma, lymph nodes of head, face, and neck

C85.12 Unspecified B-cell lymphoma, intrathoracic lymph nodes

C85.13 Unspecified B-cell lymphoma, intra-abdominal lymph nodes

C85.14 Unspecified B-cell lymphoma, lymph nodes of axilla and upper limb

C85.15 Unspecified B-cell lymphoma, lymph nodes of inguinal region and lower limb

C85.16 Unspecified B-cell lymphoma, intrapelvic lymph nodes

C85.17 Unspecified B-cell lymphoma, spleen

C85.18 Unspecified B-cell lymphoma, lymph nodes of multiple sites

C85.19 Unspecified B-cell lymphoma, extranodal and solid organ sites

C85.20 Mediastinal (thymic) large B-cell lymphoma, unspecified site

C85.21 Mediastinal (thymic) large B-cell lymphoma, lymph nodes of head, face, and neck

C85.22 Mediastinal (thymic) large B-cell lymphoma, intrathoracic lymph nodes

C85.23 Mediastinal (thymic) large B-cell lymphoma, intra-abdominal lymph nodes

C85.24 Mediastinal (thymic) large B-cell lymphoma, lymph nodes of axilla and upper limb

C85.25 Mediastinal (thymic) large B-cell lymphoma, lymph nodes of inguinal region and lower limb

C85.26 Mediastinal (thymic) large B-cell lymphoma, intrapelvic lymph nodes

C85.27 Mediastinal (thymic) large B-cell lymphoma, spleen

C85.28 Mediastinal (thymic) large B-cell lymphoma, lymph nodes of multiple sites

C85.29 Mediastinal (thymic) large B-cell lymphoma, extranodal and solid organ sites

C85.80 Other specified types of non-Hodgkin lymphoma, unspecified site

C85.81 Other specified types of non-Hodgkin lymphoma, lymph nodes of head, face, and neck

C85.82 Other specified types of non-Hodgkin lymphoma, intrathoracic lymph nodes

C85.83 Other specified types of non-Hodgkin lymphoma, intra-abdominal lymph nodes

C85.84 Other specified types of non-Hodgkin lymphoma, lymph nodes of axilla and upper limb

C85.85 Other specified types of non-Hodgkin lymphoma, lymph nodes of inguinal region and lower limb

C85.86 Other specified types of non-Hodgkin lymphoma, intrapelvic lymph nodes

C85.87 Other specified types of non-Hodgkin lymphoma, spleen

C85.88 Other specified types of non-Hodgkin lymphoma, lymph nodes of multiple sites

C85.89 Other specified types of non-Hodgkin lymphoma, extranodal and solid organ sites

D83.398 Diffuse large B-cell lymphoma of other extranodal and solid organ sites

D47.Z1 Post-transplant lymphoproliferative disorder (PTLD)

Version Effective Date: 10/01/2024

Title: Talquetamab-tgvs (Talvey™)

MEDICALLY NECESSARY

Talquetamab-tgvs (Talvey) is considered medically necessary and, therefore, covered as a single agent in adult individuals with refractory or relapsed multiple myeloma (RRMM) who have received at least four prior therapies, including a proteasome inhibitor (e.g., bortezomib, carfilzomib, ixazomib), an immunomodulatory agent (e.g., thalidomide, lenalidomide, pomalidomide), and an anti-CD38 monoclonal antibody (isatuximab-irfc, daratumumab) as National Comprehensive Cancer Network (NCCN)-preferred therapy.

INPATIENT ADMISSION FOR ADMINISTRATION

When the medical necessity criteria has been met, the inpatient admission for first cycle administration of talquetamab-tgvs (Talvey), as recommended by the US Food and Drug Administration (FDA), is covered in accordance with the following timeframes*:

- First Cycle (days 1, 4, 7, 10 of therapy): individuals should be hospitalized for 48 hours after administration of all doses within the step-up dosing schedule due to the risk of cytokine release syndrome (CRS) and immune effector cell–associated neurotoxicity syndrome (ICANS)

*Inpatient hospital stays that are longer than the preceding timeframes must be re-evaluated for medical necessity.

EXPERIMENTAL/INVESTIGATIONAL

All other uses for talquetamab-tgvs (Talvey) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These

medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the service.

Duration of authorization: 12 months

Version Effective Date: 03/05/2025

Title: Tarlatamab-dlle (Imdelltra™) for intravenous use

MEDICALLY NECESSARY

Tarlatamab-dlle (Imdelltra™) is considered medically necessary and, therefore, covered, as a single agent, for the treatment of adult individuals, age 18 years and older, with extensive stage small cell lung cancer (ES-SCLC) (i.e., Stage IV [T any, N any, M 1a/b/c], or T3-4 due to multiple lung nodules that are too extensive or have tumor/nodal volume that is too large to be encompassed in a tolerable radiation plan) who have experienced disease progression on or after platinum-based chemotherapy when **ALL** the following are met:

- Performance status 0 to 2
- One of the following:
 - Relapse following complete or partial response or stable disease with primary treatment
 - Primary progressive disease

EXPERIMENTAL/INVESTIGATIONAL

All other uses for tarlatamab-dlle (Imdelltra) are considered experimental/investigational and, therefore, not covered, unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

MANDATES

PENNSYLVANIA MEMBERS

In accordance with the Commonwealth of Pennsylvania's Act 6 of 2020 or Fair Access to Cancer Treatment Act, for members who are enrolled in Pennsylvania commercial products who have Stage 4, advanced metastatic cancer, refer to the Medical Policy titled "Coverage of Anticancer Prescription Oral and Injectable Drugs and Biologics and Supportive agents" (08.01.08) for additional information regarding the applicable coverage of drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the health care professional's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the

participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the service.

Duration of authorization: 12 months

Version Effective Date: 04/21/2025

Title: Tebentafusp-tebn (Kimmtrak®)

MEDICALLY NECESSARY

Tebentafusp-tebn (Kimmtrak®) is considered medically necessary and, therefore, covered as a first-line treatment for the treatment of HLA-A*02:01--positive uveal melanoma in adult individuals when both of the following criteria are met:

- The individual has unresectable or metastatic uveal melanoma.
- The individual did not receive prior systemic therapy for metastatic or advanced uveal melanoma or localized liver-directed therapy.

MANDATES

PENNSYLVANIA MEMBERS

In accordance with the Commonwealth of Pennsylvania's >Act 6 of 2020< or >Fair Access to Cancer Treatment Act, for members who are enrolled in Pennsylvania commercial products who have Stage 4, advanced metastatic cancer, refer to the Medical Policy titled "Coverage of Anticancer Prescription Oral and Injectable Drugs and Biologics and Supportive agents (08.01.08) for additional information regarding the applicable coverage of drugs and biologics.

EXPERIMENTAL/INVESTIGATIONAL

All other uses for tebentafusp-tebn (Kimmtrak®) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

An Individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the service.

When coverage of tebentafusp-tebn (Kimmtrak®) is requested outside of the Dosing and Frequency Requirements listed in this policy, the prescribing professional provider must supply documentation (i.e., published peer-reviewed literature) to the Company that supports this request.

Duration of authorization: 12 months

Version Effective Date: 04/03/2024

Title: Teclistamab-cqyv (Tecvayli®)

MEDICALLY NECESSARY

Teclistamab-cqyv (Tecvayli) injection is considered medically necessary and, therefore, covered as a single agent in adult individuals with refractory or relapsed multiple myeloma (RRMM) who have received at least four prior therapies, including a proteasome inhibitor (e.g., bortezomib, carfilzomib, ixazomib), an immunomodulatory agent (e.g., thalidomide, lenalidomide, pomalidomide), and an anti-CD38 monoclonal antibody (isatuximab-irfc, daratumumab) as National Comprehensive Cancer Network (NCCN) preferred therapy.

INPATIENT ADMISSION FOR ADMINISTRATION

When the medical necessity criteria has been met, the inpatient admission for first cycle administration of teclistamab-cqyv (Tecvayli), as recommended by the FDA, is covered in accordance with the following timeframes*:

- First cycle: individuals should be hospitalized for 48 hours after administration of all doses within the step-up dosing schedule (Days 1, 4, 7 of therapy) due to the risk of cytokine release syndrome (CRS) and immune effector cell–associated neurotoxicity syndrome (ICANS)

*Inpatient hospital stays that are longer than the preceding timeframes must be re-evaluated for medical necessity.

EXPERIMENTAL/INVESTIGATIONAL

All other uses for teclistamab-cqyv (Tecvayli) not identified in this policy are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Duration of authorization: 12 months

Version Effective Date: 04/02/2025

Title: Teplizumab-mzwv (Tzielid)

MEDICALLY NECESSARY

Teplizumab-mzwv (Tzielid) is considered medically necessary and, therefore, covered to delay the onset of Stage 3 type 1 diabetes (T1D) in adult and pediatric individuals eight years and older who currently have stage 2 type 1 diabetes when all of the following criteria are met, including dosing and frequency:

- Prescribed by or in consultation with endocrinologist
- The individual has abnormal oral glucose tolerance by OGTT defined by one of the following:
 - Fasting glucose 100 to 125 milligrams per deciliter (mg/dL) / 5.6 to 6.9 millimoles per liter (mmol/L)
 - Two-hour postprandial glucose 140 to 199 mg/dL / (7.8 to 11.1 mmol/L)
 - A1C 5.7 to 6.4 percent
- The individual has the presence of at least two confirmed diabetes autoantibodies detected in two samples obtained within 6 months before initiation of the treatment (e.g., glutamic acid decarboxylase 65 [GAD] autoantibodies, insulin autoantibody [IAA], insulinoma-associated antigen 2 autoantibody [IA-2A], zinc transporter 8 autoantibody [ZnT8A], islet cell autoantibody [ICA])
- The individual does NOT have any of the following:
 - Stage 3 type 1 diabetes (e.g., excessive hunger or thirst, blurry vision, severe fatigue, frequent urination, unexplained weight loss)
 - Clinical history consistent with type 2 diabetes
- Dosing and frequency for teplizumab-mzwv (Tzielid) intravenous infusion one treatment course (i.e., 14 doses) per lifetime:
 - Day one: 65 mcg/m²
 - Day two: 125 mcg/m²
 - Day three: 250 mcg/m²
 - Day four: 500 mcg/m²

- Days five through 14: 1,030 mcg/m²

EXPERIMENTAL/INVESTIGATIONAL

All other uses for teplizumab-mzwv (Tzield) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

DOSING AND FREQUENCY REQUIREMENTS

The Company reserves the right to modify the Dosing and Frequency Requirements listed in this policy to ensure consistency with the most recently published recommendations for the use of teplizumab-mzwv (Tzield). Changes to these guidelines are based on a consensus of information obtained from resources such as, but not limited to: the US Food and Drug Administration (FDA); Company-recognized authoritative pharmacology compendia; or published peer-reviewed clinical research. The professional provider must supply supporting documentation (i.e., published peer-reviewed literature) in order to request coverage for an amount of teplizumab-mzwv (Tzield) outside of the Dosing and Frequency Requirements listed in this policy. For a list of Company-recognized pharmacology compendia, view our policy on off-label coverage for prescription drugs and biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of this drug. If the member's dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider must submit those changes to the Company for a new approval based on those changes as part of the utilization management activities. The Company reserves the right to conduct postpayment review and audit procedures for any claims submitted for teplizumab-mzwv (Tzield).

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the service.

When coverage of teplizumab-mzwv (Tzield) is requested outside of the Dosing and Frequency Requirements listed in this policy, the prescribing professional provider must supply

documentation (i.e., published peer-reviewed literature) to the Company that supports this request.

Duration of authorization: 14 days

Version Effective Date: 05/28/2025

Title: Teprotumumab-trbw (Tepezza®)

MEDICALLY NECESSARY

Teprotumumab-trbw (Tepezza) is considered medically necessary and, therefore, covered for adult individuals with active or inactive thyroid eye disease who have a confirmed diagnosis of Graves' disease, when all of the following criteria listed below are met, including dosing and frequency:

- Individual has moderate to severe thyroid eye disease (TED) with documentation of one or more of the following:
 - lid retraction ≥ 2 mm
 - moderate or severe soft-tissue involvement
 - proptosis ≥ 3 mm above normal values, as determined by professional provider
 - periodic or constant diplopia
- Individual has documentation of symptomatic TED, characterized by one or more of the following symptoms:
 - dry eye
 - exposure keratitis
 - inflammation, pain, or redness of the eye/eyelids
 - lagophthalmos (incomplete or defective closure of the eyelids) with excessive lacrimation
 - strabismus
- Individual is euthyroid or with mild hypo- or hyperthyroidism defined as free thyroxine (FT4) and free tri-iodothyronine (FT3) levels less than 50% above or below the normal limits.
- Individual does not have planned surgical ophthalmological intervention for proptosis repair
- Prescribed by an ophthalmologist, or endocrinologist in consultation with an ophthalmologist

- Dosing and Frequency: 10 mg/kg for first infusion, followed by 20 mg/kg every 3 weeks for seven additional infusions (maximum of eight doses or one cycle)

EXPERIMENTAL/INVESTIGATIONAL

All other uses of teprotumumab-trbw (Tepezza), including subsequent treatment/retreatment therapy beyond a total of eight doses, are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the medical policy on off-label coverage for prescription drugs and biologics.

COSMETIC SERVICES

Requests for teprotumumab-trbw (Tepezza) that do not meet the medical necessity criteria listed in this policy (i.e., solely for the purpose of improving an individual's appearance) are considered cosmetic services. Services that are cosmetic are a benefit contract exclusion for all products of the Company. Therefore, they are not eligible for reimbursement consideration.

DOSING AND FREQUENCY REQUIREMENTS

The Company reserves the right to modify the Dosing and Frequency Requirements listed in this policy to ensure consistency with the most recently published recommendations for the use of teprotumumab-trbw (Tepezza). Changes to these guidelines are based on a consensus of information obtained from resources such as, but not limited to: the US Food and Drug Administration (FDA); Company-recognized authoritative pharmacology compendia; or published peer-reviewed clinical research. The professional provider must supply supporting documentation (i.e., published peer-reviewed literature) in order to request coverage for an amount of teprotumumab-trbw (Tepezza) outside of the Dosing and Frequency Requirements listed in this policy. For a list of Company-recognized pharmacology compendia, view our policy on off-label coverage for prescription drugs and biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of this drug. If the member's dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider must submit those changes to the Company for a new approval based on those changes as part of the utilization management process. The Company reserves the right to conduct post-payment review and audit procedures for any claims submitted for teprotumumab-trbw (Tepezza).

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

When coverage of teprotumumab-trbw (Tepezza) is requested outside of the Dosing and Frequency Requirements listed in this policy, the prescribing professional provider must supply documentation (i.e., published peer-reviewed literature) to the Company that supports this request.

Duration of authorization: 12 months

Version Effective Date: 01/06/2025

Title: Therapies for Spinal Muscular Atrophy Nusinersen (Spinraza®) and Onasemnogene abeparvovec-xioi (Zolgensma®)

MEDICALLY NECESSARY:

Initial Therapy

Nusinersen (Spinraza) is considered medically necessary and, therefore, covered when all of the following criteria, including Dosing and Frequency, are met:

- Diagnosis of spinal muscular atrophy type 1, 2, or 3, or presymptomatic types 1 or 2, confirmed by documentation of genetic testing for 5q-SMA by one of the following:
 - Homozygous gene deletion (e.g., homozygous deletion of exon 7 on chromosome 5)
 - Homozygous conversion mutation (e.g., conversion in allele 1 resulting in deletion of exon 7 or another pathogenic variation, as a result of pathogenicity [e.g., deletion of exon 7], present in the make-up of allele 2)
 - Compound heterozygote (e.g., deletion of SMN1 exon 7 on allele 1 and mutation of SMN1 on allele 2)
- Prescribed by a neurologist or a physiatrist with subspecialty certification in neuromuscular medicine
- Dosing and Frequency: Dose does not exceed 12 mg every 4 months after the loading doses. NOTE: The first three loading doses are 12 mg administered intrathecally at 14-day intervals. The fourth loading dose is administered 30 days after the third dose. A 12-mg maintenance dose is administered once every 4 months thereafter.

Continuation Therapy

Continuation of nusinersen (Spinraza) is considered medically necessary and, therefore, covered when all of the following criteria are met:

- All criteria under Initial Therapy as stated above are met. NOTE: Initial Therapy is defined as completion of the four loading doses followed by three maintenance doses administered 4 months apart.
- There is documented improvement in motor function, stability in motor function, or a slower rate of decline in motor function due to nusinersen (Spinraza) treatment based on a standard measurement scale in spinal muscular atrophy (SMA)-associated symptoms (e.g., Hammersmith Infant Neurological Examination (HINE), Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP-INTEND), and/or the Hammersmith Functional Motor Scale-Expanded [HFMSE] scores). It is expected that the same objective measurement scale will be used for both baseline and response to treatment.

DOSING AND FREQUENCY REQUIREMENTS FOR NUSINERSEN (SPINRAZA)

The Company reserves the right to modify the Dosing and Frequency Requirements listed in this policy to ensure consistency with the most recently published recommendations for the use of nusinersen (Spinraza). Changes to these guidelines are based on a consensus of information

obtained from resources such as, but not limited to: the US Food and Drug Administration (FDA); Company-recognized authoritative pharmacology compendia; or published peer-reviewed clinical research. The professional provider must supply supporting documentation (i.e., published peer-reviewed literature) in order to request coverage for an amount of nusinersen (Spinraza) outside of the Dosing and Frequency requirements listed in this policy. For a list of Company-recognized pharmacology compendia, view our policy on off-label coverage for prescription drugs and biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of this drug. If the member's dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider must submit those changes to the Company for a new approval based on those changes as part of the utilization management activities. The Company reserves the right to conduct postpayment review and audit procedures for any claims submitted for nusinersen (Spinraza).

ONASEMNOGENE ABEPARVOVEC-XIOI (ZOLGENSMA®)

MEDICALLY NECESSARY

Onasemnogene abeparvovec-xioi (Zolgensma) is considered medically necessary and, therefore, covered as a single-dose intravenous infusion for individuals of less than 2 years of age, when all of the following criteria are met:

- Diagnosis of SMA confirmed by genetic testing demonstrating biallelic mutations in the survival motor neuron 1 (*SMN1*) gene (examples below):
 - Deletion of both copies of the *SMN1* gene OR
 - compound heterozygous mutations of the *SMN1* gene (defined below):
 - Pathogenic variant(s) in both copies of the *SMN1* gene
 - Pathogenic variant(s) in one copy and deletion of the second copy of the *SMN1* gene
- Documentation of a genetic test confirms no more than two copies of the *SMN2* gene.
- Individuals have baseline antiadeno-associated virus serotype 9 (AAV9) antibody titers $\leq 1:50$
- Individual does not have advanced SMA (e.g., complete paralysis of limbs, permanent ventilator dependence).
- The medication is prescribed by a neurologist, who specializes in treatment of SMA

Duration of authorization: 12 months

Version Effective Date: 10/02/2024

Title: Tildrakizumab-asmn (Ilumya®)

MEDICALLY NECESSARY

Tildrakizumab-asmn (Ilumya) is considered medically necessary and, therefore, covered for adult individuals with moderate-to-severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy, when the following criteria listed below are met:

- Individual has been diagnosed with moderate-to-severe plaque psoriasis for at least 6 months
- There is documentation of failure, contraindication, or intolerance to a trial of at least one of the following:
 - Systemic agent (e.g., immunosuppressives, retinoic acid derivatives, and/or methotrexate)
 - Phototherapy (i.e., psoralens with UVA light (PUVA) OR UVB with coal tar or dithranol)
 - Topical agents (e.g., anthralin, coal tar preparations, corticosteroids, emollients, immunosuppressives, keratolytics, retinoic acid derivatives, and/or vitamin D analogues)
- Active or latent tuberculosis (TB) has been ruled out
- Individuals will not be treated with live vaccine(s) during treatment with tildrakizumab-asmn (Ilumya)

EXPERIMENTAL/INVESTIGATIONAL

All other uses of tildrakizumab-asmn (Ilumya) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Duration of authorization: 12 months

Version Effective Date: 03/05/2025

Title: Tisotumab vedotin-tftv (Tivdak®)

MEDICALLY NECESSARY

CERVICAL CANCER

Tisotumab vedotin-tftv (Tivdak) is considered medically necessary and, therefore, covered for the treatment of adult individuals with recurrent or metastatic cervical cancer when **any** of the following criteria are met:

- Second-line or subsequent therapy as a single agent for one of the following (National Comprehensive Cancer Network [NCCN]-preferred therapy):
 - locoregional recurrence
 - stage IVB or recurrence with distant metastases
- Second-line or subsequent therapy in combination with pembrolizumab for PD-L1 positive tumors (combined positive score [CPS] ≥ 1) if no prior immuno-oncology therapy received for one of the following:
 - locoregional recurrence
 - stage IVB or recurrence with distant metastases

VAGINAL CANCER

Tisotumab vedotin-tftv (Tivdak) is considered medically necessary and, therefore, covered for the treatment of adult individuals with vaginal cancer, when the following criteria are met:

- Second-line or subsequent therapy as a single agent for one of the following:
 - locoregional recurrence
 - stage IVB or recurrent distant metastases

Duration of authorization: 12 months

Version Effective Date: 06/16/2025

Title: Tocilizumab (Actemra®) and Related Biosimilars for Intravenous Infusion

MEDICALLY NECESSARYf

INITIAL THERAPY

Tocilizumab (Actemra) and related biosimilars for intravenous infusion are considered medically necessary and, therefore, covered for the following indications when, for each individual indication, all of the associated criteria are met:

Castleman disease (CD)

- In one of the following conditions, as a single agent:
 - Multicentric CD: Subsequent therapy for multicentric CD that has progressed following treatment of relapsed/refractory or progressive disease
 - Unicentric CD: Second-line therapy for individuals with relapsed or refractory disease who are human immunodeficiency virus–negative and human herpesvirus-8–negative
- Active or latent tuberculosis (TB) has been ruled out

Coronavirus disease 2019 (COVID-19)

- In individuals 18 years of age or older who are hospitalized with coronavirus disease 2019 (COVID-19)
- In conjunction with systemic corticosteroids and require supplemental oxygen, noninvasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO)
- Active or latent TB has been ruled out

Cytokine release syndrome (CRS) caused by chimeric antigen receptor (CAR) T-cell therapy (e.g., axicabtagene ciloleucel [Yescarta], brexucabtagene autoleucel [Tecartus], lisocabtagene maraleucel [Breyanzi], tisagenlecleucel [Kymriah])

- In individuals 2 years of age or older
- When used alone or in combination with corticosteroids
- When used for the following grades, per National Cancer Institute's Common Terminology criteria for Adverse Events (CTCAE v5.0) Grading System*:
 - CRS Grades 2–4

- CRS symptoms that persist for more than 24 hours in individuals treated with axicabtagene ciloleucel (Yescarta) or brexucabtagene autoleucel (Tecartus)
- For prolonged (>3 days) Grade 1 CRS in individuals with significant symptoms, comorbidities, and/or in elderly individuals
- Grade 1 CRS that develops less than 72 hours after infusion in those treated with lisocabtagene maraleucel (Breyanzi); for CRS that develops more than 72 hours after infusion, treat symptomatically
- Active or latent TB has been ruled out
- When used up to a maximum of four doses

Cytokine release syndrome (CRS), caused by blinatumomab (Blincyto) therapy in individuals with acute lymphoblastic leukemia

- In individuals 2 years of age or older
- Active or latent TB has been ruled out
- When used up to a maximum of four doses

Giant cell arteritis (GCA)

- In individuals 18 years of age or older
- Documented diagnosis of active GCA demonstrated by signs and symptoms associated with GCA (e.g., new-onset localized headache, scalp tenderness, ischemia-related vision loss, unexplained mouth or jaw pain upon mastication, or shoulder and/or hip girdle pain associated with inflammatory morning stiffness) AND one of the following:
 - Acute-phase reactant elevation (e.g., C-reactive protein ≥ 1 mg/L or erythrocyte sedimentation rate ≥ 30 mm/h)
 - Temporal artery biopsy or cross-sectional imaging
- There is documentation of inadequate response, intolerance, or contraindication to systemic corticosteroids
- Active or latent TB has been ruled out

Graft-versus-host disease (GVHD), acute, after hematopoietic cell transplantation

- In conjunction with systemic corticosteroids and/or immunosuppressive agent following no response (steroid-refractory disease) to first-line therapy options

- Active or latent TB has been ruled out

Immunotherapy-related toxicities caused by immune checkpoint inhibitors (e.g., ipilimumab [Yervoy], nivolumab [Opdivo], pembrolizumab [Keytruda])

- There is documentation of one of the following:
 - Moderate to severe inflammatory arthritis if no improvement after holding immunotherapy and treating with oral corticosteroids or if unable to taper corticosteroids
 - Polymyalgia rheumatica if unable to taper prednisone or no improvement in symptoms
 - Giant cell arteritis (urgent referral to rheumatology even in mild cases)
 - G2 elevated alanine transaminase/aspartate transaminase (ALT/AST) if liver enzymes suggest worsening or no improvement after 3 to 7 days of prednisone
 - G3 or G4 elevated ALT/AST if no improvement after 1 to 2 days of prednisone/methylprednisolone
 - G2 elevated alkaline phosphatase (predominant) with or without bilirubin/AST/ALT elevations if alkaline phosphatase worsens or does not improve within 3 days after initiating corticosteroids
 - G3 or G4 elevated alkaline phosphatase (predominant) with or without bilirubin/AST/ALT elevations if no improvement after 1 to 2 days of prednisone/methylprednisolone
- Active or latent TB has been ruled out

Neurotoxicity caused by CAR T-cell therapy (e.g., axicabtagene ciloleucel [Yescarta], lisocabtagene maraleucel [Breyanzi], tisagenlecleucel [Kymriah])

- Grades* 1–4 neurotoxicity as additional single-dose therapy if individual has concurrent CRS
- When used up to a maximum of four doses
- Active or latent TB has been ruled out

Polyarticular juvenile idiopathic arthritis (pJIA), active

- For individuals who have not previously received a biologic disease-modifying antirheumatic drug (DMARD) to treat pJIA, tocilizumab (Actemra) and related biosimilars for intravenous infusion are only eligible for coverage when the individual has

a documented failure, contraindication, or intolerance to golimumab (Simponi Aria), or there is a clinical reason that a trial of golimumab (Simponi Aria) would be otherwise inappropriate for the individual.

- In individuals 2 years of age or older
- Active or latent TB has been ruled out
- When used alone or in combination with methotrexate
- There is documentation of inadequate response, intolerance, or contraindication to nonbiologic DMARDs (e.g., methotrexate)

Rheumatoid arthritis

- For individuals who have not previously received a biologic DMARD to treat adult rheumatoid arthritis, tocilizumab (Actemra) and related biosimilars for intravenous infusion are only eligible for coverage when the individual has a documented failure, contraindication, or intolerance to infliximab (Remicade) or golimumab (Simponi Aria), or there is a clinical reason that a trial of infliximab (Remicade) or golimumab (Simponi Aria) would be otherwise inappropriate for the individual.
- Moderately to severely active disease
- In individuals 18 years of age or older
- Active or latent TB has been ruled out
- When used alone or in combination with methotrexate or other nonbiologic DMARDs
- There is documentation of inadequate response, intolerance, or contraindication to a 3-month trial of one or more DMARDs

Systemic juvenile idiopathic arthritis (SJIA), active

- In individuals 2 years of age or older
- Active or TB has been ruled out
- When used alone or in combination with methotrexate
- There is documentation of inadequate response, intolerance, or contraindication to nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, or DMARDs (e.g., leflunomide, methotrexate)

*See Guidelines Section for Grading Tables for CRS and neurotoxicity.

CONTINUATION THERAPY

Tocilizumab (Actemra) and related biosimilars are considered medically necessary and, therefore, covered for continuation therapy when the individual meets all of the following:

- The individual has met the medical necessity criteria for Initial Therapy
- There is documentation of a positive clinical response or stabilization to therapy (e.g., improvement in total active [swollen and tender] joint count from baseline, improvement in symptoms [e.g., pain, stiffness, inflammation, fever, fatigue, nonproductive cough] from baseline)

EXPERIMENTAL/INVESTIGATIONAL

All other uses for tocilizumab (Actemra) and related biosimilars for intravenous infusion are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

BILLING REQUIREMENTS

For drugs that have more than one method of administration, application of the JA modifier is required to indicate the route of administration.

- To report the intravenous route of administration, append the following modifier:
JA Administered Intravenously

Inclusion of a code in this policy does not imply reimbursement. Eligibility, benefits, limitations, exclusions, utilization management/referral requirements, provider contracts, and Company policies apply.

Duration of authorization: 12 months

Version Effective Date: 10/01/2024

Attachment A: [Tocilizumab \(Actemra®\) and Related Biosimilars for Intravenous Infusion](#)

Description: ICD-10 CODES AND NARRATIVES

Policy Attachment

Attachment to Policy # 08.00.85p

Attachment: A

Policy #: 08.00.85p

Description: ICD-10 CODES AND NARRATIVES

Title: Tocilizumab (Actemra®) and Related Biosimilars for Intravenous Infusion

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

THIS IS NOT AN ALL INCLUSIVE LIST

ICD-10 Codes and Narratives

C91.00 Acute lymphoblastic leukemia not having achieved remission

C91.01 Acute lymphoblastic leukemia, in remission

C91.02 Acute lymphoblastic leukemia, in relapse

D47.Z2 Castleman disease

D89.43 Secondary mast cell activation

D89.810 Acute graft-versus-host disease

D89.831 Cytokine release syndrome, grade 1

D89.832 Cytokine release syndrome, grade 2

D89.833 Cytokine release syndrome, grade 3

D89.834 Cytokine release syndrome, grade 4

G92.01 Immune effector cell-associated neurotoxicity syndrome, grade 1

G92.02 Immune effector cell-associated neurotoxicity syndrome, grade 2

G92.03 Immune effector cell-associated neurotoxicity syndrome, grade 3

G92.04 Immune effector cell-associated neurotoxicity syndrome, grade 4

M05.00 Felty's syndrome, unspecified site

M05.011 Felty's syndrome, right shoulder

M05.012 Felty's syndrome, left shoulder

M05.021 Felty's syndrome, right elbow

M05.022 Felty's syndrome, left elbow

M05.031 Felty's syndrome, right wrist

M05.032 Felty's syndrome, left wrist

M05.041 Felty's syndrome, right hand

M05.042 Felty's syndrome, left hand

M05.051 Felty's syndrome, right hip

M05.052 Felty's syndrome, left hip

M05.061 Felty's syndrome, right knee

M05.062 Felty's syndrome, left knee

M05.071 Felty's syndrome, right ankle and foot

M05.072 Felty's syndrome, left ankle and foot

M05.09 Felty's syndrome, multiple sites

M05.10 Rheumatoid lung disease with rheumatoid arthritis of unspecified site

M05.111 Rheumatoid lung disease with rheumatoid arthritis of right shoulder

M05.112 Rheumatoid lung disease with rheumatoid arthritis of left shoulder

M05.121 Rheumatoid lung disease with rheumatoid arthritis of right elbow

M05.122 Rheumatoid lung disease with rheumatoid arthritis of left elbow

M05.131 Rheumatoid lung disease with rheumatoid arthritis of right wrist

M05.132 Rheumatoid lung disease with rheumatoid arthritis of left wrist

M05.141 Rheumatoid lung disease with rheumatoid arthritis of right hand

M05.142 Rheumatoid lung disease with rheumatoid arthritis of left hand

M05.151 Rheumatoid lung disease with rheumatoid arthritis of right hip

M05.152 Rheumatoid lung disease with rheumatoid arthritis of left hip

M05.161 Rheumatoid lung disease with rheumatoid arthritis of right knee

M05.162 Rheumatoid lung disease with rheumatoid arthritis of left knee

M05.171 Rheumatoid lung disease with rheumatoid arthritis of right ankle and foot

M05.172 Rheumatoid lung disease with rheumatoid arthritis of left ankle and foot

M05.19 Rheumatoid lung disease with rheumatoid arthritis of multiple sites

M05.20 Rheumatoid vasculitis with rheumatoid arthritis of unspecified site

M05.211 Rheumatoid vasculitis with rheumatoid arthritis of right shoulder

M05.212 Rheumatoid vasculitis with rheumatoid arthritis of left shoulder

M05.221 Rheumatoid vasculitis with rheumatoid arthritis of right elbow

M05.222 Rheumatoid vasculitis with rheumatoid arthritis of left elbow

M05.231 Rheumatoid vasculitis with rheumatoid arthritis of right wrist

M05.232 Rheumatoid vasculitis with rheumatoid arthritis of left wrist

M05.241 Rheumatoid vasculitis with rheumatoid arthritis of right hand

M05.242 Rheumatoid vasculitis with rheumatoid arthritis of left hand

M05.251 Rheumatoid vasculitis with rheumatoid arthritis of right hip

M05.252 Rheumatoid vasculitis with rheumatoid arthritis of left hip

M05.261 Rheumatoid vasculitis with rheumatoid arthritis of right knee

M05.262 Rheumatoid vasculitis with rheumatoid arthritis of left knee

M05.271 Rheumatoid vasculitis with rheumatoid arthritis of right ankle and foot

M05.272 Rheumatoid vasculitis with rheumatoid arthritis of left ankle and foot

M05.29 Rheumatoid vasculitis with rheumatoid arthritis of multiple sites

M05.30 Rheumatoid heart disease with rheumatoid arthritis of unspecified site

M05.311 Rheumatoid heart disease with rheumatoid arthritis of right shoulder

M05.312 Rheumatoid heart disease with rheumatoid arthritis of left shoulder

M05.321 Rheumatoid heart disease with rheumatoid arthritis of right elbow

M05.322 Rheumatoid heart disease with rheumatoid arthritis of left elbow

M05.331 Rheumatoid heart disease with rheumatoid arthritis of right wrist

M05.332 Rheumatoid heart disease with rheumatoid arthritis of left wrist

M05.341 Rheumatoid heart disease with rheumatoid arthritis of right hand

M05.342 Rheumatoid heart disease with rheumatoid arthritis of left hand

M05.351 Rheumatoid heart disease with rheumatoid arthritis of right hip

M05.352 Rheumatoid heart disease with rheumatoid arthritis of left hip

M05.361 Rheumatoid heart disease with rheumatoid arthritis of right knee

M05.362 Rheumatoid heart disease with rheumatoid arthritis of left knee

M05.371 Rheumatoid heart disease with rheumatoid arthritis of right ankle and foot

M05.372 Rheumatoid heart disease with rheumatoid arthritis of left ankle and foot

M05.39 Rheumatoid heart disease with rheumatoid arthritis of multiple sites

M05.40 Rheumatoid myopathy with rheumatoid arthritis of unspecified site

M05.411 Rheumatoid myopathy with rheumatoid arthritis of right shoulder

M05.412 Rheumatoid myopathy with rheumatoid arthritis of left shoulder

M05.421 Rheumatoid myopathy with rheumatoid arthritis of right elbow

M05.422 Rheumatoid myopathy with rheumatoid arthritis of left elbow

M05.431 Rheumatoid myopathy with rheumatoid arthritis of right wrist

M05.432 Rheumatoid myopathy with rheumatoid arthritis of left wrist

M05.441 Rheumatoid myopathy with rheumatoid arthritis of right hand

M05.442 Rheumatoid myopathy with rheumatoid arthritis of left hand

M05.451 Rheumatoid myopathy with rheumatoid arthritis of right hip

M05.452 Rheumatoid myopathy with rheumatoid arthritis of left hip

M05.461 Rheumatoid myopathy with rheumatoid arthritis of right knee

M05.462 Rheumatoid myopathy with rheumatoid arthritis of left knee

M05.471 Rheumatoid myopathy with rheumatoid arthritis of right ankle and foot

M05.472 Rheumatoid myopathy with rheumatoid arthritis of left ankle and foot

M05.49 Rheumatoid myopathy with rheumatoid arthritis of multiple sites

M05.50 Rheumatoid polyneuropathy with rheumatoid arthritis of unspecified site

M05.511 Rheumatoid polyneuropathy with rheumatoid arthritis of right shoulder

M05.512 Rheumatoid polyneuropathy with rheumatoid arthritis of left shoulder

M05.521 Rheumatoid polyneuropathy with rheumatoid arthritis of right elbow

M05.522 Rheumatoid polyneuropathy with rheumatoid arthritis of left elbow

M05.531 Rheumatoid polyneuropathy with rheumatoid arthritis of right wrist

M05.532 Rheumatoid polyneuropathy with rheumatoid arthritis of left wrist

M05.541 Rheumatoid polyneuropathy with rheumatoid arthritis of right hand

M05.542 Rheumatoid polyneuropathy with rheumatoid arthritis of left hand

M05.551 Rheumatoid polyneuropathy with rheumatoid arthritis of right hip

M05.552 Rheumatoid polyneuropathy with rheumatoid arthritis of left hip

M05.561 Rheumatoid polyneuropathy with rheumatoid arthritis of right knee

M05.562 Rheumatoid polyneuropathy with rheumatoid arthritis of left knee

M05.571 Rheumatoid polyneuropathy with rheumatoid arthritis of right ankle and foot

M05.572 Rheumatoid polyneuropathy with rheumatoid arthritis of left ankle and foot

M05.59 Rheumatoid polyneuropathy with rheumatoid arthritis of multiple sites

M05.60 Rheumatoid arthritis of unspecified site with involvement of other organs and systems

M05.611 Rheumatoid arthritis of right shoulder with involvement of other organs and systems

M05.612 Rheumatoid arthritis of left shoulder with involvement of other organs and systems

M05.621 Rheumatoid arthritis of right elbow with involvement of other organs and systems

M05.622 Rheumatoid arthritis of left elbow with involvement of other organs and systems

M05.631 Rheumatoid arthritis of right wrist with involvement of other organs and systems

M05.632 Rheumatoid arthritis of left wrist with involvement of other organs and systems

M05.641 Rheumatoid arthritis of right hand with involvement of other organs and systems

M05.642 Rheumatoid arthritis of left hand with involvement of other organs and systems

M05.651 Rheumatoid arthritis of right hip with involvement of other organs and systems

M05.652 Rheumatoid arthritis of left hip with involvement of other organs and systems

M05.661 Rheumatoid arthritis of right knee with involvement of other organs and systems

M05.662 Rheumatoid arthritis of left knee with involvement of other organs and systems

M05.671 Rheumatoid arthritis of right ankle and foot with involvement of other organs and systems

M05.672 Rheumatoid arthritis of left ankle and foot with involvement of other organs and systems

M05.69 Rheumatoid arthritis of multiple sites with involvement of other organs and systems

M05.7A Rheumatoid arthritis with rheumatoid factor of other specified site without organ or systems involvement

M05.8A Other rheumatoid arthritis with rheumatoid factor of other specified site

M05.70 Rheumatoid arthritis with rheumatoid factor of unspecified site without organ or systems involvement

M05.711 Rheumatoid arthritis with rheumatoid factor of right shoulder without organ or systems involvement

M05.712 Rheumatoid arthritis with rheumatoid factor of left shoulder without organ or systems involvement

M05.721 Rheumatoid arthritis with rheumatoid factor of right elbow without organ or systems involvement

M05.722 Rheumatoid arthritis with rheumatoid factor of left elbow without organ or systems involvement

M05.731 Rheumatoid arthritis with rheumatoid factor of right wrist without organ or systems involvement

M05.732 Rheumatoid arthritis with rheumatoid factor of left wrist without organ or systems involvement

M05.741 Rheumatoid arthritis with rheumatoid factor of right hand without organ or systems involvement

M05.742 Rheumatoid arthritis with rheumatoid factor of left hand without organ or systems involvement

M05.751 Rheumatoid arthritis with rheumatoid factor of right hip without organ or systems involvement

M05.752 Rheumatoid arthritis with rheumatoid factor of left hip without organ or systems involvement

M05.761 Rheumatoid arthritis with rheumatoid factor of right knee without organ or systems involvement

M05.762 Rheumatoid arthritis with rheumatoid factor of left knee without organ or systems involvement

M05.771 Rheumatoid arthritis with rheumatoid factor of right ankle and foot without organ or systems involvement

M05.772 Rheumatoid arthritis with rheumatoid factor of left ankle and foot without organ or systems involvement

M05.79 Rheumatoid arthritis with rheumatoid factor of multiple sites without organ or systems involvement

M05.80 Other rheumatoid arthritis with rheumatoid factor of unspecified site

M05.811 Other rheumatoid arthritis with rheumatoid factor of right shoulder

M05.812 Other rheumatoid arthritis with rheumatoid factor of left shoulder

M05.821 Other rheumatoid arthritis with rheumatoid factor of right elbow

M05.822 Other rheumatoid arthritis with rheumatoid factor of left elbow

M05.831 Other rheumatoid arthritis with rheumatoid factor of right wrist

M05.832 Other rheumatoid arthritis with rheumatoid factor of left wrist

M05.841 Other rheumatoid arthritis with rheumatoid factor of right hand

M05.842 Other rheumatoid arthritis with rheumatoid factor of left hand

M05.851 Other rheumatoid arthritis with rheumatoid factor of right hip

M05.852 Other rheumatoid arthritis with rheumatoid factor of left hip

M05.861 Other rheumatoid arthritis with rheumatoid factor of right knee

M05.862 Other rheumatoid arthritis with rheumatoid factor of left knee

M05.871 Other rheumatoid arthritis with rheumatoid factor of right ankle and foot

M05.872 Other rheumatoid arthritis with rheumatoid factor of left ankle and foot

M05.89 Other rheumatoid arthritis with rheumatoid factor of multiple sites

M05.9 Rheumatoid arthritis with rheumatoid factor, unspecified

M06.0A Rheumatoid arthritis without rheumatoid factor, other specified site

M06.8A Other specified rheumatoid arthritis, other specified site

M06.00 Rheumatoid arthritis without rheumatoid factor, unspecified site

M06.011 Rheumatoid arthritis without rheumatoid factor, right shoulder

M06.012 Rheumatoid arthritis without rheumatoid factor, left shoulder

M06.021 Rheumatoid arthritis without rheumatoid factor, right elbow

M06.022 Rheumatoid arthritis without rheumatoid factor, left elbow

M06.031 Rheumatoid arthritis without rheumatoid factor, right wrist

M06.032 Rheumatoid arthritis without rheumatoid factor, left wrist

M06.041 Rheumatoid arthritis without rheumatoid factor, right hand

M06.042 Rheumatoid arthritis without rheumatoid factor, left hand

M06.051 Rheumatoid arthritis without rheumatoid factor, right hip

M06.052 Rheumatoid arthritis without rheumatoid factor, left hip

M06.061 Rheumatoid arthritis without rheumatoid factor, right knee

M06.062 Rheumatoid arthritis without rheumatoid factor, left knee

M06.071 Rheumatoid arthritis without rheumatoid factor, right ankle and foot

M06.072 Rheumatoid arthritis without rheumatoid factor, left ankle and foot

M06.08 Rheumatoid arthritis without rheumatoid factor, vertebrae

M06.09 Rheumatoid arthritis without rheumatoid factor, multiple sites

M06.4 Inflammatory polyarthropathy

M06.80 Other specified rheumatoid arthritis, unspecified site

M06.811 Other specified rheumatoid arthritis, right shoulder

M06.812 Other specified rheumatoid arthritis, left shoulder

M06.821 Other specified rheumatoid arthritis, right elbow

M06.822 Other specified rheumatoid arthritis, left elbow

M06.831 Other specified rheumatoid arthritis, right wrist

M06.832 Other specified rheumatoid arthritis, left wrist

M06.841 Other specified rheumatoid arthritis, right hand

M06.842 Other specified rheumatoid arthritis, left hand

M06.851 Other specified rheumatoid arthritis, right hip

M06.852 Other specified rheumatoid arthritis, left hip

M06.861 Other specified rheumatoid arthritis, right knee

M06.862 Other specified rheumatoid arthritis, left knee

M06.871 Other specified rheumatoid arthritis, right ankle and foot

M06.872 Other specified rheumatoid arthritis, left ankle and foot

M06.88 Other specified rheumatoid arthritis, vertebrae

M06.89 Other specified rheumatoid arthritis, multiple sites

M06.9 Rheumatoid arthritis, unspecified

M08.2A Juvenile rheumatoid arthritis with systemic onset, other specified site

M08.00 Unspecified juvenile rheumatoid arthritis of unspecified site

M08.011 Unspecified juvenile rheumatoid arthritis, right shoulder

M08.012 Unspecified juvenile rheumatoid arthritis, left shoulder

M08.021 Unspecified juvenile rheumatoid arthritis, right elbow

M08.022 Unspecified juvenile rheumatoid arthritis, left elbow

M08.031 Unspecified juvenile rheumatoid arthritis, right wrist

M08.032 Unspecified juvenile rheumatoid arthritis, left wrist

M08.041 Unspecified juvenile rheumatoid arthritis, right hand

M08.042 Unspecified juvenile rheumatoid arthritis, left hand

M08.051 Unspecified juvenile rheumatoid arthritis, right hip

M08.052 Unspecified juvenile rheumatoid arthritis, left hip

M08.061 Unspecified juvenile rheumatoid arthritis, right knee

M08.062 Unspecified juvenile rheumatoid arthritis, left knee

M08.071 Unspecified juvenile rheumatoid arthritis, right ankle and foot

M08.072 Unspecified juvenile rheumatoid arthritis, left ankle and foot

M08.08 Unspecified juvenile rheumatoid arthritis, vertebrae

M08.09 Unspecified juvenile rheumatoid arthritis, multiple sites

M08.20 Juvenile rheumatoid arthritis with systemic onset, unspecified site

M08.211 Juvenile rheumatoid arthritis with systemic onset, right shoulder

M08.212 Juvenile rheumatoid arthritis with systemic onset, left shoulder

M08.221 Juvenile rheumatoid arthritis with systemic onset, right elbow

M08.222 Juvenile rheumatoid arthritis with systemic onset, left elbow

M08.231 Juvenile rheumatoid arthritis with systemic onset, right wrist

M08.232 Juvenile rheumatoid arthritis with systemic onset, left wrist

M08.241 Juvenile rheumatoid arthritis with systemic onset, right hand

M08.242 Juvenile rheumatoid arthritis with systemic onset, left hand

M08.251 Juvenile rheumatoid arthritis with systemic onset, right hip

M08.252 Juvenile rheumatoid arthritis with systemic onset, left hip

M08.261 Juvenile rheumatoid arthritis with systemic onset, right knee

M08.262 Juvenile rheumatoid arthritis with systemic onset, left knee

M08.271 Juvenile rheumatoid arthritis with systemic onset, right ankle and foot

M08.272 Juvenile rheumatoid arthritis with systemic onset, left ankle and foot

M08.28 Juvenile rheumatoid arthritis with systemic onset, vertebrae

M08.29 Juvenile rheumatoid arthritis with systemic onset, multiple sites

M08.3 Juvenile rheumatoid polyarthritis (seronegative)

M08.80 Other juvenile arthritis, unspecified site

M08.811 Other juvenile arthritis, right shoulder

M08.812 Other juvenile arthritis, left shoulder

M08.821 Other juvenile arthritis, right elbow

M08.822 Other juvenile arthritis, left elbow

M08.831 Other juvenile arthritis, right wrist

M08.832 Other juvenile arthritis, left wrist

M08.841 Other juvenile arthritis, right hand

M08.842 Other juvenile arthritis, left hand

M08.851 Other juvenile arthritis, right hip

M08.852 Other juvenile arthritis, left hip

M08.861 Other juvenile arthritis, right knee

M08.862 Other juvenile arthritis, left knee

M08.871 Other juvenile arthritis, right ankle and foot

M08.872 Other juvenile arthritis, left ankle and foot

M08.88 Other juvenile arthritis, other specified site

M08.89 Other juvenile arthritis, multiple sites

M08.90 Juvenile arthritis, unspecified, unspecified site

M08.911 Juvenile arthritis, unspecified, right shoulder

M08.912 Juvenile arthritis, unspecified, left shoulder

M08.921 Juvenile arthritis, unspecified, right elbow

M08.922 Juvenile arthritis, unspecified, left elbow

M08.931 Juvenile arthritis, unspecified, right wrist

M08.932 Juvenile arthritis, unspecified, left wrist

M08.941 Juvenile arthritis, unspecified, right hand

M08.942 Juvenile arthritis, unspecified, left hand

M08.951 Juvenile arthritis, unspecified, right hip

M08.952 Juvenile arthritis, unspecified, left hip

M08.961 Juvenile arthritis, unspecified, right knee

M08.962 Juvenile arthritis, unspecified, left knee

M08.971 Juvenile arthritis, unspecified, right ankle and foot

M08.972 Juvenile arthritis, unspecified, left ankle and foot

M08.98 Juvenile arthritis, unspecified, vertebrae

M08.99 Juvenile arthritis, unspecified, multiple sites

M31.5 Giant cell arteritis with polymyalgia rheumatica

M31.6 Other giant cell arteritis

M34.81 Systemic sclerosis with lung involvement

M35.3 Polymyalgia rheumatica

R74.01 Elevation of levels of liver transaminase levels

T80.82XA Complication of immune effector cellular therapy, initial encounter

T80.82XD Complication of immune effector cellular therapy, subsequent encounter

T80.89XA Other complications following infusion, transfusion and therapeutic injection, initial encounter

T80.89XD Other complications following infusion, transfusion and therapeutic injection, subsequent encounter

U07.1 COVID-19

Version Effective Date: 10/07/2024

Title: Toripalimab-tpzi (LOQTORZI™)

MEDICALLY NECESSARY

HEAD AND NECK CANCERS

Cancer of the Nasopharynx (Squamous cell Carcinoma with Mixed Subtypes)

Toripalimab-tpzi (Loqtorzi) as single agent is considered medically necessary and, therefore, covered in the following regimens:

- Subsequent therapy for the treatment of recurrent or metastatic nasopharyngeal carcinoma (NPC) of the head and neck with disease progression on or after a platinum-based therapy
- Subsequent therapy for T1-4, N0-3, M1 disease as a therapy preferred by the National Comprehensive Cancer Network for:
 - Oligometastatic disease and performance status (PS) 0-2
 - Widely metastatic disease and good PS (0-2)

Toripalimab-tpzi (Loqtorzi) in combination with cisplatin and gemcitabine is considered medically necessary and, therefore, covered in the following regimens:

- First-line systemic therapy for the treatment of metastatic or recurrent locally advanced NPC
- First-line systemic therapy for T1-4, N0-3, M1 disease for (NCCN-preferred regimen):
 - Oligometastatic disease and PS 0-2
 - Widely metastatic disease and good PS (0-2)
- Subsequent-line systemic therapy, if not previously used for T1-4, N0-3, M1 disease for:
 - Oligometastatic disease and PS 0-2
 - Widely metastatic disease and good PS (0-2)

Very Advanced Head and Neck Cancer (Squamous Cell Carcinoma with Mixed Subtypes)

Toripalimab-tpzi (Loqtorzi) is considered medically necessary and, therefore, covered in the following regimens:

- First-line (NCCN-preferred regimen) or subsequent-line option (note: if not previously used, may be considered in subsequent lines) in combination with cisplatin and gemcitabine for NPC in individuals with PS 0-1 for:
 - unresectable locoregional recurrence with prior radiation therapy (RT)
 - unresectable second primary with prior RT
 - unresectable persistent disease with prior RT, or
 - recurrent/persistent disease with distant metastases

- Subsequent-line therapy as a preferred alternate single agent option, for NPC if disease progression on or after platinum therapy and PS 0-3 in:
 - unresectable locoregional recurrence with prior radiation therapy (RT)
 - unresectable second primary with prior RT
 - unresectable persistent disease with prior RT, or recurrent/persistent disease with distant metastases

NON-SMALL CELL LUNG CANCER (NSCLC)

Toripalimab-tpzi (Loqtorzi) is considered medically necessary and, therefore, covered in the following regimens:

- First-line therapy in combination with platinum-containing doublet chemotherapy (for four to six cycles) for advanced disease (with pemetrexed for nonsquamous cell disease) followed by toripalimab-tpzi maintenance therapy
- Neoadjuvant therapy in combination with platinum-containing doublet chemotherapy, followed by one adjuvant cycle with combination therapy then continued as toripalimab-tpzi maintenance therapy

EXPERIMENTAL/INVESTIGATIONAL

All other uses for toripalimab-tpzi (Loqtorzi) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

MANDATES

PENNSYLVANIA MEMBERS

In accordance with the Commonwealth of Pennsylvania's Act 6 of 2020 or Fair Access to Cancer Treatment Act, for members who are enrolled in Pennsylvania commercial products who have Stage 4, advanced metastatic cancer, refer to the Medical Policy titled "Coverage of Anticancer Prescription Oral and Injectable Drugs and Biologics and Supportive Agents" (08.01.08) for additional information regarding the applicable coverage of drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Duration of authorization: 12 months

Version Effective Date: 07/15/2024

Title: Total Parenteral Nutrition (TPN) / Intradialytic Parenteral Nutrition (IDPN) / Intraperitoneal Parenteral Nutrition (IPN)

MEDICALLY NECESSARY

TOTAL PARENTERAL NUTRITION (TPN)

Initial Therapy for Malnutrition

Total parenteral nutrition (TPN), for initial therapy, is considered medically necessary and, therefore, covered when **all** of the following are met:

- The individual is not able to maintain weight and strength commensurate with the individual's general condition
- The individual has been screened for malnutrition by a professional provider with appropriate skills and training
- The individual meets **one** of the following:
 - Currently having malnutrition based on **both** of the following:
 - Individual has **one** of the following:
 1. A body mass index (BMI) of less than 20 kg/m²
 2. Unintentional weight loss >5 percent within the past 6 months or >10 percent beyond 6 months
 3. Reduced muscle mass assessed by a validated body composition measuring technique (e.g., dual-energy absorptiometry, bioelectrical impedance, ultrasound computed tomography, magnetic resonance imaging, anthropometric measurements)
 - Individual has **one** of the following:
 1. Reduced food intake or assimilation of less than or equal to 50 percent of the individual's energy requirements for >1 week or any reduction for >2 weeks
 2. Individual has any chronic gastrointestinal (GI) condition (e.g., dysphagia, diarrhea, nausea/vomiting, pancreatic insufficiency, gastroparesis) that adversely impacts food assimilation or absorption
 3. Individual has inflammation caused by acute disease/injury (e.g., major infection, burns, trauma, closed head injury) or related to chronic disease (e.g., malignancy, renal disease, heart failure, obstructive lung disease)
 - Adult currently at risk for malnutrition based on **one** of the following:
 - The individual is eating little or nothing for more than 5 days and/or is likely to eat little or nothing for 5 days or longer

- The individual has a poor absorptive capacity and/or high nutrient losses and/or increased nutritional needs from causes such as catabolism
 - The individual has experienced severe trauma or is experiencing severe acute illness that will contribute to the rapid development of malnutrition if left untreated
- Child currently at risk for malnutrition based on **one** of the following:
 - Weight for length, weight for height, or sex less than 10th percentile
 - BMI for age or sex less than 5th percentile
 - Increased metabolic requirements that are unable to be adequately met either through the oral or enteral (EN) route
 - Impaired ability to ingest or tolerate oral feeding
 - Inadequate weight gain or a significant decrease in usual growth percentile
- Neonate currently at risk for malnutrition based on **one** of the following:
- Documented inadequate provision of or tolerance to nutrients
 - Preterm less than 28 weeks at birth (high risk) or 28–31 weeks (moderate risk)
 - Low birth weight less than 1000 g (high risk) or 1000–1500 g (moderate risk)
 - Infant establishing feeds after episode of necrotizing enterocolitis or GI perforation (high risk)
 - Infants with severe congenital GI malformations (high risk)
 - Intrauterine growth restriction (weight less than 9th percentile) (moderate risk)
 - Illness or congenital anomaly that may compromise feeding (moderate risk)
- The individual's provider documents **one** of the following:
 - EN has been considered and ruled out
 - EN has been tried and been found ineffective
 - EN exacerbates GI tract dysfunction
- The individual has **one** of the following:
 - A condition involving the small intestine and/or its exocrine glands that significantly impairs the absorption of nutrients
 - A disease of the stomach and/or intestine that is a motility disorder and impairs the ability of nutrients to be transported through and absorbed by the GI system
 - A postoperative complication or condition that would require complete bowel rest (e.g., post-operative gastrointestinal anastomotic leak, gastrointestinal fistula)
- The GI impairment or other cause of malnutrition is permanent*

*For an impairment to be considered to be permanent does not require a determination that there is no possibility that the individual's condition may improve sometime in the future. If, in the judgement of the provider, the impairment will be of long and indefinite duration, the test of permanence is considered met.

Continuation Therapy for Malnutrition

TPN continuation is considered medically necessary and, therefore, covered if the individual's evidence for malnutrition has stabilized or improved after the initial period of therapy based on screening by a professional provider and documented in the medical record. Weaning of TPN can begin when the individual is able to meet 50–75 percent of their caloric, protein, and micronutrient needs through oral and/or EN intake unless there is an underlying condition that will preclude the individual from ever meeting 100 percent of their nutritional needs through oral and/or EN intake (e.g., impaired GI function).

Therapy for Hyperemesis Gravidarum (HG)

TPN is considered medically necessary and, therefore, covered when the individual has severe hyperemesis gravidarum (HG) when **all** of the following are met:

- Weight loss of more than 5 percent
- Other causes of nausea and/or vomiting have been ruled out (e.g., cholecystitis, gastroenteritis, gastroesophageal reflux, migraines, molar pregnancy)
- Inability to adequately control nausea and/or vomiting with the administration of pharmaceutical agents, unless deemed unsafe for the individual or fetus by the professional provider or the individual (e.g., antiemetics, vitamin B6, antihistamines, promotility agents, steroids)
- Inability to maintain or gain weight with the administration of oral or EN nutrition (unless contraindicated or deemed unsafe for the individual by the professional provider due to an underlying comorbidity)

INTRADIALYTIC PARENTERAL NUTRITION (IDPN)

Intradialytic parenteral nutrition (IDPN) is considered medically necessary and, therefore, covered when it is infused as an alternative to a regularly scheduled regimen of TPN in individuals who meet the medical necessity criteria for TPN, not in addition to a regularly scheduled infusion of TPN.

INTRAPERITONEAL NUTRITION (IPN)

Total Parenteral Nutrition (TPN) for individuals on continuous ambulatory peritoneal dialysis (CAPD) is considered medically necessary and, therefore, covered in individuals who meet the medical necessity criteria for TPN.

SPECIAL FORMULATIONS OF PARENTERAL NUTRITION

Special nutrient formulas are produced to meet the unique nutrient needs for specific disease

conditions. The individual's medical record must adequately document the specific condition and the necessity for the special nutrient.

ASSOCIATED SERVICE

When an infusion therapy service is covered, all associated services (e.g., solutions, additives, equipment and/or supplies, nursing) are considered covered and eligible for reimbursement.

When an infusion therapy service is not covered, all associated services (e.g., solutions, equipment and/or supplies, nursing) are considered not covered, and, therefore, not eligible for reimbursement.

REQUIRED DOCUMENTATION

For individuals who meet the criteria for TPN, a total daily caloric intake of 20–35 kcal/kg/day is considered sufficient to achieve or maintain appropriate body weight. A total daily protein intake of 0.8–2.0 g/kg/day is considered sufficient. The ordering professional provider must document the medical necessity for orders outside of these ranges. If the individual is at a high risk of developing refeeding issues, the TPN may need to be initiated at 50 percent of the target caloric and protein intake and be titrated up over the course of the first few days to weeks. A total fluid intake of 30–40 mL fluid/kg/d (account for extra output from drains or fistulas and additional input from other sources such as intravenous drugs) will be needed to maintain hydration status. If appropriate, electrolytes, minerals, and micronutrients may need to be added but should be individualized based on the individual's specific needs and comorbidities.

The ordering professional provider is required to evaluate the individual within 30 days prior to initiation of TPN. If the professional provider does not see the beneficiary within this timeframe, they must document the reason why and describe what other monitoring methods were used to evaluate the individual's parenteral nutrition needs. There must be documentation in the medical record supporting the clinical diagnosis.

The Company may conduct reviews and audits of services to our members regardless of the participation status of the provider. Medical record documentation must be maintained on file to reflect the medical necessity of the care and services provided. These medical records may include but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

STANDARD WRITTEN ORDER REQUIREMENTS

Before submitting a claim to the Company, the supplier must have on file a timely, appropriate, and complete order for each item billed that is signed and dated by the professional provider who is treating the member. Requesting a provider to sign a retrospective order at the time of

an audit or after an audit for submission as an original order, reorder, or updated order will not satisfy the requirement to maintain a timely professional provider order on file.

PROOF OF DELIVERY REQUIREMENTS

Medical record documentation must include a contemporaneously prepared delivery confirmation or member's receipt of supplies and equipment. The medical record documentation must include a copy of delivery confirmation if delivered by a commercial carrier and a signed copy of delivery confirmation by member/caregiver if delivered by the durable medical equipment (DME) supplier/provider. All documentation is to be prepared contemporaneous with delivery and be available to the Company upon request.

CONSUMABLE SUPPLIES (WHEN APPLICABLE)

For items and supplies provided on a recurring basis, billing must be based on prospective, not retrospective use. For products that are supplied as refills to the original order, suppliers must contact the beneficiary, and document an affirmative response, prior to dispensing the refill and not automatically ship on a pre-determined basis, even if authorized by the beneficiary. This shall be done to ensure that the refilled item remains reasonable and necessary, existing supplies are expected to end, and to confirm any changes or modifications to the order. Contact with the beneficiary or designee regarding refills must take place no sooner than 30 calendar days prior to the expected end of the current supply. For delivery of refills, the supplier must deliver the product no sooner than 10 calendar days prior to the expected end of the current supply. This is regardless of which delivery method is utilized. Regardless of utilization, a supplier must not dispense more than a 1-month quantity at a time.

If required documentation is not available on file to support a claim at the time of an audit or record request, the DME supplier may be required to reimburse the Company for overpayments.

Guidelines

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, total parenteral nutrition (TPN), intradialytic parenteral nutrition (IDPN), and intraperitoneal nutrition (IPN) are covered under the medical benefits of the Company's products when the medical necessity criteria listed in this medical policy are met.

MACRONUTRIENTS

The following tables are examples of ranges for macronutrients for adult and pediatric individuals. The macronutrients for an individual should be determined based upon their clinical situation.

Macronutrients for Adult Individuals

Clinical State	Daily Protein Intake (g/kg)	Daily Energy Intake (kcal/kg)	Dextrose Intake (mg/kg/min)	Daily Fat Emulsions (g/kg)	Daily Fluid Intake (mL/kg)
Stable	0.8-1.5	20-35	4-5	1	30-40
Critically ill	1.2-2.5	12-25 in the early ICU stay	<3-4	<1	Minimal to provide adequate macronutrients
Burns	1.5-2.0	20-30	4-5	1	30-40
Open abdomen	Additional 15-30 g/L exudate	20-30	4-5	1	30-40
Acute kidney injury	0.8-2.0	20-30	4-5	1	30-40
Continuous renal replacement therapy	Additional 0.2 g/kg/d not to exceed 2.5 g/kg/d	25-35	4-5	1	30-40
Chronic kidney disease (CKD) stages 3-5 without diabetes	0.55-0.60	25-35	4-5	1	30-40
CKD stages 3-5 with diabetes	0.6-0.8	25-35	4-5	1	30-40
CKD 5D on maintenance hemodialysis or peritoneal dialysis	1.2-1.5	25-35	4-5	1	30-40
Hepatic failure	1.2-2.0 based on "dry" weight and tolerance	20-30	4-5	1	30-40

Obese	2.0-2.5 based on ideal body weight (IBW)	22-25 based on IBW	4-5	1	30-40

Macronutrients for Pediatric Individuals

Infants (<1yr)	Initiation		Advance by		Goals	
	Preterm	Term	Preterm	Term	Preterm	Term
Daily protein intake (g/kg) (use higher end of range for critically ill)	1.5	1.5	N/A	N/A	2.5-3.5	3.0
Dextrose intake (mg/kg/min)	4-8	2.5-5.0	Increase gradually over 2-3 days	Increase gradually over 2-3 days	8-10 (max 12)	5-10 (max 12)
Daily fat emulsions (g/kg)	0.5-1.0	0.5-1.0	0.5-1.0	0.5-1.0	3-4	2.5-4.0
Children (1 to 10 yrs) Stable (Critically ill-when different)						
Daily protein intake (g/kg)	1		N/A		1-2 (use higher end of range for critically ill)	
Dextrose intake (mg/kg/min)	3-6		1-2		8-10	
Daily fat emulsions (g/kg)	1-2		0.5-1.0		2-3 (2-4 with monitoring of triglycerides)	
Adolescents (11 to <18 yrs) Stable (Critically ill-when different)						
Daily protein intake (g/kg)	1		N/A		1-2 (use higher end of range for critically ill)	
Dextrose intake (mg/kg/min)	2.5-3.0		1-2		5-6	

Daily fat emulsions (g/kg)	1	1	1-2 (2-4 with monitoring of triglycerides)

Description

Malnutrition is defined in American Society for Parenteral and Enteral Nutrition (ASPEN) guidelines as: “an acute, subacute, or chronic state of nutrition in which a combination of varying degrees of overnutrition or undernutrition, with or without inflammatory activity, has led to a change in body composition and diminished function.” The malnutrition can have any number of causes including, but not limited to: anorexia, intestinal disease/failure, acute/chronic pancreatitis, burns, trauma, and sepsis. The malnutrition can be the result of inadequate intake of nutrients, increased requirements for nutrients, altered/impaired absorption of nutrients, altered/impaired transportation of the nutrients through the gastrointestinal (GI) tract, or altered/impaired utilization of the nutrients by the body.

TOTAL PARENTERAL NUTRITION

Malnutrition exists when there is a deficiency of nutrients such as protein, energy, and micronutrients that cause adverse effects on an individual's body function, body composition, or on the individual's clinical outcome or vulnerability to additional adverse effects or events. Strategies to improve or maintain adequate nutrition include the administration of oral nutritional supplements (ONS); enteral nutrition (EN), in which the nutrition is infused directly into the GI tract through a tube or catheter; or parenteral nutrition (PN). PN is the provision of nutritional requirements intravenously. PN is administered through a central intravenous line access or a peripherally inserted central catheter (PICC), often in the home. An infusion pump regulates the flow of the solution on either a continuous (24-hour) or intermittent schedule. PN consists of the optimal levels of glucose, amino acids, electrolytes, vitamins, minerals, and fats; the concentration of each component is calculated for the individual's specific metabolic need. The benefit of PN is that it is a life-sustaining source of nutrition for individuals who are unable to meet their nutritional needs through an oral or enteral route, usually due to impaired GI tract function. The use of PN may be temporary, such as an individual who experiences hyperemesis gravidarum (HG), or it may be permanent, such as an individual with intestinal failure. PN can be infused during hemodialysis or peritoneal dialysis, in certain circumstances. When nutritional support other than the oral route is necessary, EN is usually initially preferable to PN for the following reasons:

- In a fluid-restricted individual, EN permits delivery of all necessary nutrients in a more concentrated volume than PN

- EN allows for safer home delivery of nutrients
- EN lowers the risk of central line–associated bloodstream infections (CLABSI)
- Even small amounts of EN can help support and maintain intestinal function

INTRADIALYTIC PARENTERAL NUTRITION

Protein-energy wasting (PEW) is the term used for the loss of body protein mass and fuel reserves seen in chronic kidney disease (CKD). PEW is associated with increased morbidity and mortality among individuals with CKD. PEW can be diagnosed if certain characteristics are present in an individual. These include, but are not limited to, low serum albumin, reduced body mass (low/reduced body/fat mass or weight loss associated with the reduced intake of protein and/or energy), and reduced muscle mass (muscle wasting). According to the literature, the prevalence of PEW in individuals on chronic hemodialysis (HD) ranges from 20 percent to 70 percent. The prevalence increases with the individual's age and number of years on HD. It is estimated that the annual mortality rate is between 20 percent and 30 percent for individuals undergoing HD who are malnourished. The life expectancy for these individuals is 3 to 11 years shorter than individuals not on chronic HD.

Many factors associated with renal failure can contribute to PEW in individuals receiving chronic HD. These can include decreased oral intake/anorexia, dietary restrictions, loss of nutrients (including amino acids) during HD, loss of water-soluble vitamins during HD, loss of blood during HD, loss of electrolytes during HD, uremic toxicity, physical inactivity, metabolic acidosis, impaired lipolysis, GI issues (impaired absorption of nutrients, gastroparesis), endocrine issues (increased leptin levels, peripheral insulin resistance, hyperparathyroidism), protein catabolism, and chronic microinflammation. Feeding through the GI tract is the preferred route for nutritional intake, but if that is not possible, then parenteral nutrition is an alternative.

Intradialytic parenteral nutrition (IDPN) is the administration of PN while the individual is undergoing HD. The PN is infused three times a week through the venous line. Some benefits of IDPN include reduced protein catabolism, improved nutritional parameters (e.g., albumin, prealbumin), some parameters that improve quality of life for the individual, decreased PEW-related complications including mortality, and IDPN may reduce hospitalization rates. Some drawbacks to infusing IDPN during HD include that clinical studies have been unable to demonstrate an improvement in the individuals' overall nutritional status, an improvement in most quality-of-life parameters, or an overall increase in the 2-year survival of individuals receiving IDPN along with oral nutritional supplements (ONS) as well as the possibility of adverse effects occurring due to the rapid infusion of glucose and lipids during a HD session. It is therefore recommended that individuals on HD with severe PEW receive daily PN if their nutritional needs cannot be supplied by the oral or enteral route.

INTRAPERITONEAL NUTRITION

Many of the same factors contributing to PEW in individuals on chronic HD can also affect individuals receiving continuous abdominal peritoneal dialysis (CAPD). Usually, however, individuals on CAPD have better residual renal function, metabolic abnormalities are not as severe, and uremic toxicity is less pronounced. There are some unique issues associated with CAPD that can contribute to PEW, including significant losses of proteins and protein-bound nutrients during CAPD; the presence of dialysate in the abdomen may cause the individual to feel full and lead to a decreased oral intake; there can be slow gastric emptying, which can decrease the appetite; and the absorption of glucose from the CAPD exchange solution can not only decrease the individual's appetite but it can also increase the percentage of body fat while masking the loss of lean body mass. The increased glucose levels can also induce or aggravate diabetes and hypertriglyceridemia, as well as increase low-density lipoprotein (LDL) and very low-density lipoprotein (VLDL) cholesterol levels. Intraperitoneal nutrition (IPN) is the substitution of a regular exchange with an exchange containing increased amino acids. This is usually done during one dialysate exchange daily into the peritoneal cavity. Studies have found that IPN does improve nutritional parameters in malnourished individuals. There are currently no commercially available amino acid–based solutions for intraperitoneal nutrition in the United States.

HYPEREMESIS GRAVIDARUM (HG)

HG is defined as vomiting during pregnancy that is so protracted and severe that the individual experiences some, or all, of the following: weight loss, dehydration, starvation acidosis, alkalosis from vomiting, and electrolyte derangement. The incidence in the United States is estimated to be about 0.5 percent of live births. Some of the risk factors for HG include a personal history of HG, fetal anomalies, a female fetus, a diet high in saturated fat prior to pregnancy, gestational trophoblastic disease, and multiple pregnancies. Some factors associated with HG include slow gastric emptying due to abnormal thyroid hormones during pregnancy, the size of the placental mass, a *Helicobacter pylori* infection, and high levels of human chorionic gonadotropin (hCG). Severe complications due to HG can include esophageal tears/rupture, retinal hemorrhage, intrauterine growth retardation/low fetal birth weight, pneumothorax/pneumomediastinum, Wernicke's encephalopathy, and maternal/fetal death.

Coding

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted

coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

CPT Procedure Code Number(s)

N/A

ICD - 10 Procedure Code Number(s)

N/A

ICD - 10 Diagnosis Code Number(s)

N/A

HCPCS Level II Code Number(s)

THE FOLLOWING CODES ARE USED TO REPRESENT HOME INFUSION THERAPY:

S9364	Home infusion therapy, total parenteral nutrition (TPN); administrative services, professional pharmacy services, care coordination, and all necessary supplies and equipment including standard TPN formula (lipids, specialty amino acid formulas, drugs other than in standard formula and nursing visits coded separately), per diem (do not use with home infusion codes S9365-S9368 using daily volume scales)
S9365	Home infusion therapy, total parenteral nutrition (TPN); 1 liter per day, administrative services, professional pharmacy services, care coordination, and all necessary supplies and equipment including standard TPN formula (lipids, specialty amino acid formulas, drugs other than in standard formula and nursing visits coded separately), per diem
S9366	Home infusion therapy, total parenteral nutrition (TPN); more than 1 liter but no more than 2 liters per day, administrative services, professional pharmacy services, care coordination, and all

necessary supplies and equipment including standard TPN formula (lipids, specialty amino acid formulas, drugs other than in standard formula and nursing visits coded separately), per diem

S9367 Home infusion therapy, total parenteral nutrition (TPN); more than 2 liters but no more than 3 liters per day, administrative services, professional pharmacy services, care coordination, and all necessary supplies and equipment including standard TPN formula (lipids, specialty amino acid formulas, drugs other than in standard formula and nursing visits coded separately), per diem

S9368 Home infusion therapy, total parenteral nutrition (TPN); more than 3 liters per day, administrative services, professional pharmacy services, care coordination, and all necessary supplies and equipment including standard TPN formula (lipids, specialty amino acid formulas, drugs other than in standard formula and nursing visits coded separately), per diem

THE FOLLOWING CODES ARE USED TO REPRESENT PARENTERAL NUTRITION SOLUTIONS:

B4164 Parenteral nutrition solution; carbohydrates (dextrose), 50 % or less (500 ml = 1 unit) - home mix

B4168 Parenteral nutrition solution; amino acid, 3.5 %, (500 ml = 1 unit) - home mix

B4172 Parenteral nutrition solution; amino acid, 5.5 % through 7 %, (500 ml = 1 unit) - home mix

B4176 Parenteral nutrition solution; amino acid, 7 % through 8.5 %, (500 ml = 1 unit) - home mix

B4178 Parenteral nutrition solution; amino acid, greater than 8.5 % (500 ml = 1 unit) - home mix

B4180 Parenteral nutrition solution; carbohydrates (dextrose), greater than 50 % (500 ml = 1 unit) - home mix

B4185 Parenteral nutrition solution, not otherwise specified, 10 grams lipids

B4187 Omegaven, 10 g lipids

B4189 Parenteral nutrition solution; compounded amino acid and carbohydrates with electrolytes, trace elements, and vitamins, including preparation, any strength, 10 to 51 grams of protein-premix

B4193 Parenteral nutrition solution; compounded amino acid and carbohydrates with electrolytes, trace elements and vitamins, including preparation, any strength, 52 to 73 grams of protein-premix

B4197 Parenteral nutrition solution; compounded amino acid and carbohydrates with electrolytes, trace elements and vitamins, including preparation, any strength 74 to 100 grams of protein-premix

B4199 Parenteral nutrition solution; compounded amino acid and carbohydrates with electrolytes, trace elements and vitamins, including preparation, any strength, over 100 grams of protein - premix

B4216 Parenteral nutrition; additives (vitamins, trace elements, heparin, electrolytes) - home mix, per day

THE FOLLOWING CODES ARE USED TO REPRESENT SPECIALIZED NUTRITION SOLUTIONS:

B5000 Parenteral nutrition solution compounded amino acid and carbohydrates with electrolytes, trace elements, and vitamins, including preparation, any strength, renal-aminosyn-rf, nephramine, renamine-premix

B5100 Parenteral nutrition solution compounded amino acid and carbohydrates with electrolytes, trace elements, and vitamins, including preparation, any strength, hepatic, hepatamine-premix

B5200 Parenteral nutrition solution compounded amino acid and carbohydrates with electrolytes, trace elements, and vitamins, including preparation, any strength, stress-branch chain amino acids-freamine-hbc-premix

THE FOLLOWING CODE IS USED TO REPRESENT PARENTERAL NUTRITION SOLUTIONS CONTAINING LESS THAN 10 GRAMS OF PROTEIN PER DAY:

B9999 NOC for parenteral supplies

THE FOLLOWING CODES ARE USED TO REPRESENT PARENTERAL NUTRITION EQUIPMENT AND SUPPLIES:

B4220 Parenteral nutrition supply kit; premix, per day

B4222 Parenteral nutrition supply kit; home mix, per day

B4224 Parenteral nutrition administration kit, per day

B9004 Parenteral nutrition infusion pump, portable

B9006 Parenteral nutrition infusion pump, stationary

E0776 IV Pole

Duration of authorization: 12 months

Version Effective Date: 01/02/2025

Title: Trastuzumab (Herceptin®) and Related Biosimilars, Trastuzumab and Hyaluronidase-oysk (Herceptin Hylecta)

MEDICALLY NECESSARY

COMPANY-DESIGNATED PREFERRED PRODUCTS

Although there are many trastuzumab products on the market (e.g., trastuzumab [Herceptin], trastuzumab-qyyp [Trazimera], trastuzumab-anns [Kanjinti], trastuzumab-dttb [Ontruzant], trastuzumab-pkrb [Herzuma], trastuzumab-dkst [Ogivri], trastuzumab-strf [Hercessi]) there is no reliable evidence of the superiority of any one product of trastuzumab compared with other products. The Company has designated the following trastuzumab biosimilar products as its preferred products: trastuzumab-qyyp [Trazimera] and trastuzumab-anns [Kanjinti].

These products are less costly and at least as likely to produce equivalent therapeutic results as the non-preferred products, which include, but are not limited to, trastuzumab (Herceptin) and any other non-preferred trastuzumab biosimilars.

According to the US Food and Drug Administration (FDA), “a biosimilar is a biological product that has no clinically meaningful differences from the existing FDA-approved reference product. All biosimilar products meet the FDA’s rigorous standards for approval for the indications described in the product labeling. Once a biosimilar has been approved by the FDA, the safety and effectiveness of these products have been established, just as they have been for the reference product.” Coverage of a biosimilar product as an alternate to a reference product is not considered a form of step therapy by the Company.

NON-PREFERRED PRODUCTS

Use of the non-preferred products trastuzumab (Herceptin) or any non-preferred biosimilar is considered medically necessary and, therefore, covered only for individuals who are currently receiving or have previously received a non-preferred product for the specified trastuzumab indication.

If the individual has not previously received trastuzumab (Herceptin) or a trastuzumab biosimilar to treat the specified indication, these non-preferred products are eligible for coverage when the individual has contraindication(s) or intolerance(s) to the Company-designated preferred products (e.g., as documented per the FDA labeling).

TRASTUZUMAB AND RELATED BIOSIMILARS

Trastuzumab and related biosimilars are considered medically necessary and, therefore, covered for individuals whose human epidermal growth factor receptor 2 (HER2) status has been verified by one of the FDA-approved diagnostic tests listed in the guideline section and the individual has a left ventricular ejection fraction of 50% or greater for the following indications and regimens when the requirements for COMPANY-DESIGNATED PREFERRED PRODUCTS and NON-PREFERRED PRODUCTS are met:

Adjuvant Breast Cancer

- As adjuvant therapy for HER2-overexpressing node-positive or node-negative (estrogen receptor/progesterone receptor [ER/PR] negative or with one high-risk feature) breast cancer as part of a treatment regimen containing:
 - Doxorubicin, cyclophosphamide, and either paclitaxel or docetaxel
 - Docetaxel and carboplatin
 - As a single agent following multimodality anthracycline-based therapy

Invasive Breast Cancer

- As adjuvant systemic therapy** for individuals with HER2-positive tumors and (pT1-3 and pN0 or pN+ tumors) disease for any of the following regimens:
 - In combination with paclitaxel following AC (doxorubicin and cyclophosphamide) regimen (dose-dense or every 3 weeks) (both useful in certain circumstances)*
 - As a component of TCH (docetaxel, carboplatin, and trastuzumab) regimen (NCCN-preferred regimen)
 - In combination with docetaxel following AC regimen*
 - In combination with paclitaxel, carboplatin, and pertuzumab for pT2-3 and pN0 or pN+ tumors only
 - In combination with docetaxel and cyclophosphamide
 - As a component of TCHP (docetaxel, carboplatin, trastuzumab, and pertuzumab) regimen (preferred regimen) for pT2-3 and pN0 or pN+ tumors only
 - In combination with pertuzumab and paclitaxel following AC regimen (dose-dense or every 3 weeks) (both useful in certain circumstances) for pT2-3 and pN0 or pN+ tumors only*
 - In combination with pertuzumab and docetaxel following AC regimen for pT2-3 and pN0 or pN+ tumors only*
 - In combination with paclitaxel and pertuzumab for pT2-3 and pN0 or pN+ tumors only
 - In combination with paclitaxel for low-risk T1, N0, M0, HER2-positive tumors particularly for individuals not eligible for other standard adjuvant regimens due to comorbidities (NCCN-preferred regimen)

NCCN notes: *It is acceptable to change administration sequence to taxane (with or without HER2-targeted therapy) followed by AC.

**If no residual disease after preoperative therapy or no preoperative therapy, complete up to 1 year of HER2-targeted therapy with trastuzumab with or without pertuzumab after completing planned chemotherapy regimen course. If residual disease is present after preoperative therapy and ado-trastuzumab emtansine is discontinued for toxicity, then trastuzumab with or without pertuzumab to complete 1 year of therapy can be used (preferred).

- As preoperative systemic therapy for individuals with HER2-positive tumors and locally advanced c≥T2 or cN+ and M0 disease (NCCN-preferred regimen), or cT1c, cN0 disease:
 - As a component of TCH (docetaxel, carboplatin, and trastuzumab) regimen (preferred regimen)
 - As a component of TCHP (docetaxel, carboplatin, trastuzumab, and pertuzumab) regimen (preferred regimen)
 - In combination with docetaxel with or without pertuzumab following AC regimen*
 - In combination with paclitaxel, carboplatin, and pertuzumab
 - In combination with paclitaxel following AC (doxorubicin and cyclophosphamide) regimen (dose-dense or every 3 weeks) (both useful in certain circumstances)*
 - In combination with paclitaxel and pertuzumab following AC regimen (dose-dense or every 3 weeks) (both useful in certain circumstances)*
 - In combination with docetaxel and cyclophosphamide (useful in certain circumstances)
 - In combination with paclitaxel and pertuzumab (useful in certain circumstances)

NCCN notes: *It is acceptable to change the administration sequence to taxane (with or without HER2-targeted therapy) followed by AC.

- For recurrent unresectable (local or regional) or stage IV (M1) HER2-positive disease that is either hormone receptor-negative, or hormone receptor-positive with or without endocrine therapy for any of the following:
 - As NCCN-preferred first-line therapy in combination with pertuzumab with either docetaxel or paclitaxel
 - As fourth-line therapy and beyond in combination with docetaxel, vinorelbine, or capecitabine, or with paclitaxel with or without carboplatin

- As fourth-line therapy and beyond in combination with cyclophosphamide, eribulin, gemcitabine, ixabepilone, lapatinib (without cytotoxic therapy), or albumin-bound paclitaxel
- In combination with pertuzumab with or without cytotoxic therapy (e.g., vinorelbine or taxane) for one line of therapy in individuals previously treated with chemotherapy and trastuzumab in the absence of pertuzumab
- In combination with tamoxifen, fulvestrant, or aromatase inhibition with or without lapatinib, for the treatment of recurrent unresectable (local or regional) or stage IV (M1) hormone receptor–positive HER2-positive disease in postmenopausal women* or premenopausal women treated with ovarian ablation/suppression
- Treatment for recurrent unresectable (local or regional) or stage IV (M1) hormone receptor–positive HER2-positive disease in combination with tamoxifen for premenopausal women without ovarian ablation/suppression

NCCN notes: *Men with breast cancer should be treated similarly to postmenopausal women, except that use of an aromatase inhibitor is ineffective without concomitant suppression of testicular steroidogenesis.

- As a third-line therapy and beyond (may also be given in the second-line setting) in combination with capecitabine and tucatinib (NCCN preferred in individuals with both systemic and central nervous system [CNS] progression in the third-line setting and beyond) for recurrent unresectable (local or regional) or stage IV (M1) HER2-positive disease that is:
 - Hormone receptor-negative
 - Hormone receptor-positive with or without endocrine therapy
- As NCCN-preferred adjuvant systemic therapy for individuals with HER2-positive tumors and locally advanced disease, following completion of planned chemotherapy and following mastectomy or breast-conserving surgery (BCS) with surgical axillary staging, for any of the following:
 - With or without pertuzumab if ypT0N0 or pCR
 - With or without pertuzumab ypT1-4N0 or ypN≥1 (if ado-trastuzumab discontinued for toxicity)
 - With pertuzumab if ypT1-4N0 or ypN≥1 and node positive at initial staging (if ado-trastuzumab discontinued for toxicity)
 - With pertuzumab if ypT0N0 or pCR and node positive at initial staging
- Stage IV (M1) disease with activity in emerging biomarkers (i.e., HER2 activating mutations*), in combination with neratinib and fulvestrant as third-line and beyond therapy for one of the following:
 - Hormone receptor–positive HER2-negative disease in individuals who have already received a CDK4/6 inhibitor therapy
 - Triple-negative disease

* See GUIDELINES Section for this mutation list.

Inflammatory Breast Cancer

- Preoperative systemic therapy for HER2-positive disease
 - As a component of TCH (docetaxel, carboplatin, and trastuzumab) regimen (NCCN-preferred regimen)
 - As a component of TCHP (docetaxel, carboplatin, trastuzumab, and pertuzumab) regimen (NCCN-preferred regimen)
 - In combination with docetaxel with or without pertuzumab following AC regimen*
 - In combination with paclitaxel, carboplatin, and pertuzumab
 - In combination with paclitaxel following AC (doxorubicin and cyclophosphamide) regimen (dose-dense or every 3 weeks) (both useful in certain circumstances)*

- In combination with paclitaxel and pertuzumab following AC regimen (dose-dense or every 3 weeks) (both useful in certain circumstances)*
- In combination with docetaxel and cyclophosphamide
- In combination with paclitaxel and pertuzumab

NCCN notes: *It is acceptable to change administration sequence to taxane (with or without HER2-targeted therapy) followed by AC.

- For the treatment of individuals with recurrent unresectable (local or regional) or stage IV (M1) hormone receptor–positive HER2-positive disease in postmenopausal women* or premenopausal women treated with ovarian ablation/suppression in combination with tamoxifen, fulvestrant, or aromatase inhibition with or without lapatinib.
- Used in combination with tamoxifen, fulvestrant, or aromatase inhibition with or without lapatinib, for the treatment of individuals with recurrent unresectable (local or regional) or stage IV (M1) hormone receptor–positive HER2-positive disease in postmenopausal women* or premenopausal women treated with ovarian ablation/suppression
- Treatment for recurrent unresectable (local or regional) or stage IV (M1) hormone receptor–positive HER2-positive disease in combination with tamoxifen for premenopausal women without ovarian ablation/suppression

NCCN notes: *Men with breast cancer should be treated similarly to postmenopausal women, except that use of an aromatase inhibitor is ineffective without concomitant suppression of testicular steroidogenesis.

- As a third-line therapy and beyond (may also be given in the second-line setting) in combination with capecitabine and tucatinib (NCCN preferred in individuals with both systemic and CNS progression in the third-line setting and beyond) for individuals with no response to preoperative systemic therapy, or recurrent unresectable (local or regional) or stage IV (M1) HER2-positive disease that is:
 - Hormone receptor-negative
 - Hormone receptor-positive with or without endocrine therapy

NCCN notes: *It is acceptable to change administration sequence to taxane (with or without HER2-targeted therapy) followed by AC

- For individuals with no response to preoperative systemic therapy, or recurrent unresectable (local or regional) or stage IV (M1) HER2-positive disease that is either hormone receptor-negative, or hormone receptor-positive with or without endocrine therapy for any of the following lines of therapy:
 - As NCCN-preferred first-line therapy in combination with pertuzumab with either docetaxel or paclitaxel
 - As fourth-line therapy and beyond in combination with docetaxel, vinorelbine, or capecitabine, or with paclitaxel with or without carboplatin
 - As fourth-line therapy and beyond in combination with cyclophosphamide, eribulin, gemcitabine, ixabepilone, lapatinib (without cytotoxic therapy), or albumin-bound paclitaxel
 - May be considered in combination with pertuzumab with or without cytotoxic therapy (e.g., vinorelbine or taxane) for one line of therapy in individuals previously treated with chemotherapy and trastuzumab in the absence of pertuzumab
- Adjuvant systemic therapy** for individuals who had a response to preoperative systemic therapy, followed by surgery, and need to complete planned chemotherapy, for individuals with HER2-positive tumors for any of the following regimens:
 - In combination with paclitaxel following AC (doxorubicin and cyclophosphamide) regimen (dose-dense or every 3 weeks)*
 - As a component of TCH (docetaxel, carboplatin, and trastuzumab) regimen (NCCN-preferred regimen)
 - In combination with docetaxel following AC regimen*

- In combination with paclitaxel, carboplatin, and pertuzumab for node-positive pT2-3 and pN0 or pN+ tumors only
- In combination with docetaxel and cyclophosphamide
- As a component of TCHP (docetaxel, carboplatin, trastuzumab, and pertuzumab) regimen (NCCN-preferred regimen) for pT2-3 and pN0 or pN+ tumors only
- In combination with pertuzumab and paclitaxel following AC regimen (dose-dense or every 3 weeks) for node-positive pT2-3 and pN0 or pN+ tumors only*
- In combination with pertuzumab and docetaxel following AC regimen for pT2-3 and pN0 or pN+ tumors only*
- In combination with paclitaxel, carboplatin, and pertuzumab for pT2-3 and pN0 or pN+ tumors
- In combination with paclitaxel for low-risk T1, N0, M0, HER2-positive tumors particularly for individuals not eligible for other standard adjuvant regimens due to comorbidities (NCCN-preferred regimen)

NCCN notes: *It is acceptable to change administration sequence to taxane (with or without HER2-targeted therapy) followed by AC.

**If no residual disease after preoperative therapy or no preoperative therapy, complete up to 1 year of HER2-targeted therapy with trastuzumab with or without pertuzumab after completing planned chemotherapy regimen course. If residual disease is present after preoperative therapy and ado-trastuzumab emtansine is discontinued for toxicity, then trastuzumab with or without pertuzumab to complete 1 year of therapy can be used (NCCN preferred).

Metastatic Breast Cancer

- As first-line therapy for HER2-overexpressing metastatic breast cancer in combination with paclitaxel
- As a single agent for the treatment of HER2-overexpressing breast cancer in individuals who have received one or more chemotherapy regimens for metastatic disease

Central Nervous System Metastases

- Intra-cerebrospinal fluid (CSF) treatment for leptomeningeal metastases from HER2-positive breast cancer, as part of the following treatment options:
 - Primary treatment of individuals with good risk status (Karnofsky performance score [KPS] ≥ 60 , no major neurologic deficits, minimal systemic disease, and reasonable systemic treatment options if needed)
 - As a maintenance therapy for individuals with negative CSF cytology or for clinically stable individuals with persistently positive CSF cytology
- As NCCN-preferred regimen for limited brain metastases treatment, in combination with capecitabine and tucatinib as a treatment in individuals with HER2-positive breast cancer, if previously treated with one or more anti-HER2-based regimens:
 - As initial treatment in select individuals (e.g., individuals with small asymptomatic brain metastases)
 - Treatment for recurrent brain metastases
 - Treatment of a relapsed disease with either stable systemic disease or reasonable systemic treatment options
- As NCCN-preferred regimen for treatment of extensive brain metastases in combination with capecitabine and tucatinib as treatment of extensive brain metastases in individuals with HER2-positive breast cancer if previously treated with one or more anti-HER2-based regimens:
 - As primary treatment in select individuals (e.g., individuals with small asymptomatic brain metastases)
 - Treatment for recurrent disease with either stable systemic disease or reasonable systemic treatment options
- For extensive brain metastases in high doses in combination with pertuzumab as treatment in individuals with HER2-positive breast cancer for any of the following indications:

- As primary treatment in select individuals (e.g., individuals with small asymptomatic brain metastases)
 - As a treatment for a recurrent disease with stable systemic disease or reasonable systemic treatment options
- For limited brain metastases in high doses in combination with pertuzumab as treatment in individuals with HER2 positive breast cancer for any of the following indications:
 - As initial treatment in select individuals (e.g., individuals with small asymptomatic brain metastases)
 - As a treatment for recurrent brain metastases
 - As a treatment of relapsed disease with either stable systemic disease or reasonable systemic treatment options

Appendiceal Adenocarcinoma

- As initial systemic therapy for individuals with advanced or metastatic disease (proficient mismatch repair/microsatellite-stable (pMMR/MSS) or ineligible for or progressed on checkpoint inhibitor immunotherapy for deficient mismatch repair/microsatellite instability-high (dMMR/MSI-H) or polymerase epsilon/delta [POLE/POLD1] mutation with ultrahypermutated phenotype [e.g., TMB >50 mut/Mb]) (with HER2-amplified and RAS and BRAF wild-type) tumors in combination with pertuzumab, or lapatinib or tucatinib if intensive therapy is not recommended and no previous treatment with a HER2 inhibitor.
- Second-line and subsequent therapy (biomarker-directed) in combination with pertuzumab, lapatinib, or tucatinib for progression of advanced or metastatic disease (pMMR/MSS) or ineligible for or progressed on checkpoint inhibitor immunotherapy for dMMR/MSI-H or POLE/POLD1 mutation with ultrahypermutated phenotype [e.g., TMB >50 mut/Mb] (HER2-amplified and RAS and BRAF wild type) not previously treated with HER2 inhibitor

Colon Cancer

- Second-line and subsequent therapy (biomarker-directed) in combination with pertuzumab, lapatinib, or tucatinib for progression of advanced or metastatic disease (HER2-amplified and RAS and BRAF wild type) pMMR/MSS or ineligible for or progressed on checkpoint inhibitor immunotherapy for dMMR/MSI-H or POLE/POLD1 mutation with ultrahypermutated phenotype (e.g., TMB >50 mut/Mb) not previously treated with HER2 inhibitor
- Initial treatment in combination with pertuzumab, lapatinib, or tucatinib in individuals (HER2-amplified and RAS and BRAF wild-type) deficient mismatch repair/microsatellite instability-high [dMMR/MSI-H] or polymerase epsilon/delta (POLE/POLD1) mutation with ultrahypermutated phenotype (e.g., TMB >50 mut/Mb and individual is not a candidate for immunotherapy) for individuals with unresectable metachronous metastases and previous FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or CAPEOX (capecitabine and oxaliplatin) within the past 12 months
- Therapy in combination with pertuzumab or lapatinib in individuals (HER2-amplified and RAS and BRAF wild-type) (pMMR/MSS) or ineligible for or progressed on checkpoint inhibitor immunotherapy for dMMR/MSI-H or POLE/POLD1 mutation with ultra-hypermutated phenotype (e.g., TMB >50 mut/Mb) if intensive therapy not recommended and no previous treatment with a HER2 inhibitor if intensive therapy not recommended for any of the following conditions:
 - As primary treatment for locally unresectable or medically inoperable disease
 - As primary treatment for synchronous abdominal/peritoneal metastases that are nonobstructing, or following local therapy for individuals with existing or imminent obstruction
 - For synchronous unresectable metastases of other sites
 - As initial treatment for unresectable metachronous metastases in individuals who have not received previous adjuvant FOLFOX or CapeOX within the past 12 months, who have received previous fluorouracil/leucovorin (5-FU/LV) or capecitabine therapy, or who have not received any previous chemotherapy

Esophageal, Esophagogastric Junction

- As palliative therapy for individuals who are not surgical candidates or have an unresectable locally advanced, recurrent, or metastatic disease with HER2-overexpressing metastatic esophageal, esophagogastric junction and gastric cancers adenocarcinoma and KPS of 60% or greater, or Eastern Cooperative Oncology Group (ECOG) performance score of two or less, as first-line therapy in combination with systemic chemotherapy.
 - Fluorouracil or capecitabine and oxaliplatin or cisplatin (NCCN preferred)
 - Fluorouracil and irinotecan
 - Paclitaxel with or without carboplatin or cisplatin
 - Docetaxel with or without cisplatin
 - Fluorouracil
 - Capecitabine
 - Docetaxel, cisplatin or oxaliplatin, and fluorouracil
- As NCCN-preferred palliative therapy for HER2-overexpression–positive adenocarcinoma in individuals who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease and KPS 60% or greater or ECOG performance score 2 or less as first-line therapy in combination with one of the following:
 - Fluorouracil, cisplatin or oxaliplatin, and pembrolizumab (if no prior tumor progression while on therapy with a checkpoint inhibitor)
 - Capecitabine, cisplatin or oxaliplatin, and pembrolizumab (if no prior tumor progression while on therapy with a checkpoint inhibitor)

Gastric Cancers

- Primary treatment in combination with systemic chemotherapy for individuals who are medically fit for surgery but with surgically unresectable locoregional HER2 overexpression–positive adenocarcinoma in combination with any of the following regimens:
 - Fluorouracil or capecitabine and oxaliplatin or cisplatin (NCCN preferred)
 - Fluorouracil and irinotecan
 - Paclitaxel with or without carboplatin or cisplatin
 - Docetaxel with or without cisplatin
 - Fluorouracil
 - Capecitabine
 - Docetaxel, cisplatin or oxaliplatin, and fluorouracil
- As palliative therapy for individuals who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease (including peritoneal only metastatic disease, including positive cytology) with HER2 overexpression–positive adenocarcinoma with PD-L1 CPS ≥ 1 and KPS $\geq 60\%$ or ECOG performance score ≤ 2 as first-line therapy in combination with any of the following:
 - Cisplatin, pembrolizumab, and fluorouracil or capecitabine (if no prior tumor progression while on therapy with a checkpoint inhibitor) (NCCN preferred)
 - Oxaliplatin, pembrolizumab, and fluorouracil or capecitabine (if no prior tumor progression while on therapy with a checkpoint inhibitor) (NCCN preferred)
- As primary treatment (NCCN preferred) for medically fit individuals with surgically unresectable locoregional HER2 overexpression–positive adenocarcinoma and PD-L1 CPS ≥ 1 is given in combination with one of the following:
 - Cisplatin, pembrolizumab, and fluorouracil or capecitabine
 - Oxaliplatin, pembrolizumab, and fluorouracil or capecitabine
- Palliative therapy for individuals who are not surgical candidates or have unresectable locally advanced, recurrent, or metastatic disease (including peritoneal only metastatic disease, including positive cytology) with

HER2 overexpression—positive adenocarcinoma and KPS $\geq 60\%$ or ECOG performance score ≤ 2 as first-line therapy in combination with systemic chemotherapy listed below:

- Fluorouracil or capecitabine and oxaliplatin or cisplatin (NCCN preferred)
- Fluorouracil and irinotecan
- Paclitaxel with or without carboplatin or cisplatin
- Docetaxel with or without cisplatin
- Fluorouracil
- Capecitabine
- Docetaxel, cisplatin or oxaliplatin, and fluorouracil

Head and neck cancers

Salivary Gland Tumors

- As a single agent, in combination with docetaxel, or in combination with pertuzumab for HER2-positive recurrent disease with:
 - Distant metastases in individuals with a performance status (PS) of 0–3
 - Unresectable locoregional recurrence or second primary with prior radiation therapy

Biliary Tract Cancers

Gallbladder Cancer/Intrahepatic Cholangiocarcinoma/ Extrahepatic Cholangiocarcinoma

- As subsequent therapy in combination with pertuzumab or tucatinib for progression on or after systemic treatment for unresectable or resected gross residual (R2) or metastatic disease that is HER2-positive

Rectal Cancer

- Therapy in combination with pertuzumab or lapatinib in individuals (HER2-amplified and RAS and BRAF wild-type) (pMMR/MSS) or ineligible for or progressed on checkpoint inhibitor immunotherapy for dMMR/MSI-H or POLE/POLD1 mutation with ultrahypermutated phenotype (e.g., TMB >50 mut/Mb]) if intensive therapy not recommended and no previous treatment with a HER2 inhibitor for the following indications:
 - As primary treatment for synchronous abdominal/peritoneal metastases that are nonobstructing, or following local therapy for individuals with existing or imminent obstruction
 - As primary treatment for synchronous unresectable metastases of other sites
 - As primary treatment for unresectable isolated pelvic/anastomotic recurrence
 - As initial treatment for unresectable metachronous metastases in individuals who have not received previous FOLFOX or CapeOX within the past 12 months, who have received previous 5-FU/LV or capecitabine therapy, or who have not received any previous chemotherapy
- Initial treatment in combination with pertuzumab, lapatinib, or tucatinib for individuals (HER2-amplified and RAS and BRAF wild-type) with unresectable metachronous metastases (pMMR/MSS or dMMR/MSI-H) or polymerase epsilon/delta (POLE/POLD1) mutation with ultrahypermutated phenotype (e.g., TMB >50 mut/Mb and are not candidates for immunotherapy) and previous FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or CAPEOX (capecitabine and oxaliplatin) within the past 12 months
- As primary treatment for T3, N Any; T1-2, N1-2; T4, N Any; or locally unresectable or medically inoperable disease if resection is contraindicated following total neoadjuvant therapy (pMMR/MSS) or ineligible for or progressed on checkpoint inhibitor immunotherapy for dMMR/MSI-H or POLE/POLD1 mutation with ultrahypermutated phenotype (e.g., TMB >50 mut/Mb) or neoadjuvant/definitive immunotherapy (dMMR/MSI-H) if intensive therapy not recommended
- Second-line and subsequent therapy (biomarker-directed therapy) in combination with pertuzumab or lapatinib or tucatinib, if not previously given, for progression of advanced or metastatic disease (HER2-amplified and RAS and BRAF wild-type) (pMMR/MSS or ineligible for or progressed on checkpoint inhibitor immunotherapy for dMMR/MSI-H or POLE/POLD1 mutation with ultrahypermutated phenotype [e.g., TMB >50 mut/Mb]) not previously treated with HER2 inhibitor, in individuals previously treated:

- With oxaliplatin-based therapy without irinotecan
- With irinotecan-based therapy without oxaliplatin
- With oxaliplatin and irinotecan
- Without irinotecan or oxaliplatin

Uterine Neoplasms: Endometrial Carcinoma

- First-line therapy if no prior trastuzumab therapy (or second-line or subsequent therapy as clinically appropriate if no prior trastuzumab therapy) in combination with carboplatin and paclitaxel and continued as a single agent for maintenance therapy* (NCCN-preferred regimen) for recurrent HER2-positive uterine serous carcinoma or HER2-positive carcinosarcoma for any of the following:
 - For disseminated metastases with or without sequential palliative external-beam radiation therapy (EBRT)
 - With sequential EBRT and with or without brachytherapy for locoregional recurrence in individuals with no prior RT to site of recurrence, or previous vaginal brachytherapy only
 - After surgical exploration, with sequential EBRT for locoregional recurrence in individuals with disease confined to the vagina or paravaginal soft tissue, or in pelvic or para-aortic lymph nodes
 - After surgical exploration, with or without sequential EBRT for locoregional recurrence in individuals with upper abdominal or peritoneal disease
 - With or without sequential palliative EBRT or brachytherapy for locoregional recurrence in individuals who have received prior EBRT to site of recurrence
- In combination with carboplatin and paclitaxel and continued as a single agent for maintenance therapy* (NCCN-preferred regimen) for stage III/IV HER2-positive uterine serous carcinoma and stage III/IV HER2-positive for any of the following indications:
 - For a disease that is suitable for primary surgery as additional treatment with or without sequential EBRT and with or without vaginal brachytherapy after total hysterectomy/bilateral salpingo-oophorectomy (TH/BSO)
 - For a disease that is not suitable for primary surgery as primary treatment with or without sequential EBRT and with or without brachytherapy

NCCN note: *Trastuzumab may be continued as a maintenance therapy.

TRASTUZUMAB AND HYALURONIDASE-OYSK (HERCEPTIN HYLECTA)

Trastuzumab and hyaluronidase-oysk subcutaneous injection (Herceptin Hylecta) is considered medically necessary and, therefore, covered for the treatment of adult individuals whose HER2 status has been verified by one of the FDA-approved diagnostic tests and the individual has a left ventricular ejection fraction of 50% or greater for the following indications and regimens:

Invasive or Inflammatory Breast Cancer

- As a substitute for intravenous trastuzumab and used as a single agent or in combination with other systemic therapies.

Adjuvant Breast Cancer

- Adjuvant treatment of individuals with HER2-overexpressing node-positive or node-negative (ER/PR-negative or with one high-risk feature) breast cancer, as part of any of the following treatment regimens:
 - In combination with doxorubicin, cyclophosphamide, and either paclitaxel or docetaxel
 - With docetaxel and carboplatin
 - As a single agent following multimodality anthracycline-based therapy (e.g., AC=anthracycline (doxorubicin) plus cyclophosphamide)

- As a substitute for intravenous trastuzumab and used as a single agent or in combination with other systemic therapies. Do not substitute for or use with ado-trastuzumab emtansine (Kadcyla®) or fam-trastuzumab deruxtecan-nxki (Enhertu®).

Metastatic Breast Cancer

- Treatment of metastatic breast cancer as part of any of the following treatment regimens:
 - In combination with paclitaxel for the first-line treatment of HER2-overexpressing metastatic breast cancer
 - As a single agent for the treatment of HER2-overexpressing breast cancer in individuals who have received one or more chemotherapy regimens for metastatic disease
 - As a substitute for intravenous trastuzumab and used as a single agent or in combination with other systemic therapies. Do not substitute for or with ado-trastuzumab emtansine (Kadcyla®) or fam-trastuzumab deruxtecan-nxki (Enhertu®).

Duration of authorization: 12 months

Version Effective Date: 06/16/2025

Attachment A: [Trastuzumab \(Herceptin®\) and Related Biosimilars, Trastuzumab and Hyaluronidase-oysk \(Herceptin Hylecta\)](#)

Description: Dosing & Frequency Requirements for Trastuzumab (Herceptin®) and Related Biosimilars, Trastuzumab and Hyaluronidase-oysk (Herceptin Hylecta)

Attachment B: [Trastuzumab \(Herceptin®\) and Related Biosimilars, Trastuzumab and Hyaluronidase-oysk \(Herceptin Hylecta\)](#)

Description: ICD-10 CM Codes and Narratives

Policy Attachment

Attachment to Policy # 08.00.33s

Attachment: A

Policy #: 08.00.33s

Description: Dosing & Frequency Requirements for Trastuzumab (Herceptin®) and Related Biosimilars, Trastuzumab and Hyaluronidase-oysk (Herceptin Hylecta)

Title: Trastuzumab (Herceptin®) and Related Biosimilars, Trastuzumab and Hyaluronidase-oysk (Herceptin Hylecta)

DOSING AND FREQUENCY REQUIREMENTS FOR TRASTUZUMAB (HERCEPTIN®) and related biosimilars (e.g., trastuzumab-pkrb [Herzuma®], trastuzumab-dkst [Ogivri™], trastuzumab-dttb, [Ontruzant®], trastuzumab-qyyp [Trazimera™])

BREAST CANCER

Preoperative (Neoadjuvant) Chemotherapy	Preoperative (neoadjuvant) chemotherapy for individuals with HER2-positive breast cancer: • In those who have locally advanced, inflammatory, or early stage breast cancer (either greater than 2 cm in diameter or node positive): ○ In combination with (neoadjuvant) pertuzumab (Perjeta®) and chemotherapy⁵⁶ ▪ Trastuzumab (Herceptin®) and related biosimilars for a total of 52 weeks: Initial dose at 8 mg/kg; subsequent doses at 6 mg/kg every 3 weeks ▪ 1 dose 8 mg/kg ▪ 17 doses 6 mg/kg • In those who have stage IIA (T0, N1, M0 or T1, N1, M0 or T2, N0, M0), stage IIB (T2, N1, M0 or T3, N0, M0), or stage IIIA (T3, N1, M0) breast cancer who desire breast preservation and fulfill the criteria for breast-conserving surgery, except for tumor size, or for those who have node-positive disease likely to become node-negative with preoperative systemic therapy, or for individuals with locally advanced disease (stage IIIA (any T, N2, M0), IIIB, or IIIC): ○ Concurrently with paclitaxel following AC (doxorubicin and cyclophosphamide) with or without pertuzumab (Perjeta®) ^{6, 29, 37} ▪ Trastuzumab (Herceptin®) and related biosimilars for a total of 52 weeks: ▪ With weekly paclitaxel Initial dose of 4 mg/kg followed by 51 weekly doses of 2 mg/kg ○ 1 dose 4 mg/kg ○ 51 doses 2 mg/kg OR Initial dose of 4 mg/kg followed by 11 weekly doses of 2 mg/kg; subsequent 14 doses at 6 mg/kg every 3 weeks starting on week 13 through week 52 ○ 1 dose 4 mg/kg

	○ 11 doses 2 mg/kg ○ 14 doses 6 mg/kg ▪ With paclitaxel every 14 days following dose dense AC (doxorubicin and cyclophosphamide)^{6, 29} Initial dose of 4 mg/kg followed by 7 weekly doses of 2 mg/kg; subsequent 15 doses at 6 mg/kg every 3 weeks starting on week 9 through week 52 OR ▪ With paclitaxel and pertuzumab (Perjeta®) every 21 days following AC (doxorubicin and cyclophosphamide)^{6, 29} Initial dose at 8 mg/kg; subsequent doses at 6 mg/kg every 3 weeks ○ 1 dose 8 mg/kg ○ 17 doses 6 mg/kg • In TCH (docetaxel, carboplatin, and trastuzumab) regimen^{6, 29, 30, 60} ▪ Trastuzumab (Herceptin®) and related biosimilars for a total of 52 weeks: Initial dose of 4 mg/kg followed by 17 weekly doses of 2 mg/kg; subsequent 12 doses at 6 mg/kg every 3 weeks starting on week 19 through week 52 • In TCH (docetaxel, carboplatin, and trastuzumab) regimen with pertuzumab (Perjeta®)^{6, 29, 60} ▪ Trastuzumab (Herceptin®) and related biosimilars for a total of 52 weeks: Initial dose at 8 mg/kg; subsequent doses at 6 mg/kg every 3 weeks ▪ 1 dose 8 mg/kg ▪ 17 doses 6 mg/kg • In combination with docetaxel following AC regimen^{6, 29, 40, 42, 60}

	▪ Trastuzumab (Herceptin®) and related biosimilars : Initial dose of 4 mg/kg followed by 11 weekly doses of 2 mg/kg; subsequent 14 doses at 6 mg/kg every 3 weeks starting on week 13 through week 52 ▪ 1 dose 4 mg/kg ▪ 11 doses 2 mg/kg ▪ 14 doses 6 mg/kg • In combination with docetaxel and pertuzumab (Perjeta®) following AC regimen ^{6, 29} ▪ Trastuzumab (Herceptin®) and related biosimilars : Initial dose at 8 mg/kg; subsequent doses at 6 mg/kg every 3 weeks ▪ 1 dose 8 mg/kg ▪ 17 doses 6 mg/kg • In combination with docetaxel and cyclophosphamide ^{6, 29} ▪ Trastuzumab (Herceptin®) and related biosimilars for a total of 52 weeks: Initial dose of 4 mg/kg, then 11 weekly doses of 2 mg/kg, followed by 14 doses of 6 mg/kg administered every 21 days ▪ 1 dose 4 mg/kg ▪ 11 doses 2 mg/kg ▪ 14 doses 6 mg/kg OR Initial dose at 8 mg/kg; subsequent doses at 6 mg/kg every 3 weeks ▪ 1 dose 8 mg/kg ▪ 17 doses 6 mg/kg
Adjuvant Treatment	For adjuvant treatment of HER-2-overexpressing node-positive or node-negative breast cancer (ER/PR negative or with one high-risk feature) breast cancer as part of any of the following treatment regimens:

	• In combination with AC (doxorubicin and cyclophosphamide) and either paclitaxel or docetaxel ▪ Trastuzumab (Herceptin®) and related biosimilars for a total of 52 weeks: ▪ With weekly paclitaxel following AC (doxorubicin and cyclophosphamide)^{1, 6, 28, 29, 37, 52} Initial dose of 4 mg/kg followed by 11 weekly doses of 2 mg/kg; subsequent 14 doses at 6 mg/kg every 3 weeks starting on week 13 through week 52 ▪ With paclitaxel every 14 days following dose dense AC (doxorubicin and cyclophosphamide)^{6, 29, 61} Initial dose of 4 mg/kg followed by 7 weekly doses of 2 mg/kg; subsequent 15 doses at 6 mg/kg every 3 weeks starting on week 9 through week 52 ▪ With docetaxel every 21 days^{1, 6, 28, 29, 37, 40, 42, 52, 60} Initial dose of 4 mg/kg followed by 11 weekly doses of 2 mg/kg; subsequent 14 doses at 6 mg/kg every 3 weeks starting on week 13 through week 52 • In TCH (docetaxel, carboplatin, and trastuzumab) regimen^{1, 6, 28, 29, 30, 52, 60} ▪ Trastuzumab (Herceptin®) and related biosimilars (Herceptin®) for a total of 52 weeks: Initial dose of 4 mg/kg followed by 17 weekly doses of 2 mg/kg; subsequent 12 doses at 6 mg/kg every 3 weeks starting on week 19 through week 52 • As a single agent within 3 weeks following multi-modality anthracycline-based therapy^{1,28, 52} ▪ Trastuzumab (Herceptin®) and related biosimilars for a total of 52 weeks: Initial dose at 8 mg/kg; subsequent doses at 6 mg/kg every 3 weeks ▪ 1 dose 8 mg/kg ▪ 17 doses 6 mg/kg

- In combination with pertuzumab (Perjeta®) and either docetaxel or paclitaxel following AC regimen²⁹
 - Trastuzumab (Herceptin®) and related biosimilars for a total of 52 weeks:
Initial dose at 8 mg/kg; subsequent doses at 6 mg/kg every 3 weeks
 - 1 dose 8 mg/kg
 - 17 doses 6 mg/kg

Adjuvant treatment of individuals with HER2-positive stage I, IIA, IIB, or IIIA (T3, N1, M0) disease (ductal, lobular, mixed, or metaplastic histologies), or for locally advanced disease (stage IIIA (any T, N2, M0), IIIB, or IIIC).

- In combination with paclitaxel following AC (doxorubicin and cyclophosphamide) regimen as an NCCN-preferred regimen^{6, 29, 37}
 - Trastuzumab (Herceptin®) and related biosimilars for a total of 52 weeks:
Initial dose of 4 mg/kg, then 51 weekly doses of 2 mg/kg
 - 1 dose 4 mg/kg
 - 51 doses 2 mg/kg

OR

Initial dose of 4 mg/kg, then 11 weekly doses of 2 mg/kg, followed by 14 doses of 6 mg/kg administered every 21 days

- 1 dose 4 mg/kg
 - 11 doses 2 mg/kg
 - 14 doses 6 mg/kg
- In combination with paclitaxel following dose dense AC (doxorubicin and cyclophosphamide)^{6, 29, 61}
 - Trastuzumab (Herceptin®) and related biosimilars for a total of 52 weeks:
Initial dose of 4 mg/kg followed by 7 weekly doses of 2 mg/kg; subsequent 15 doses at 6 mg/kg every 3 weeks starting on week 9 through week 52

	▪ 1 dose 4 mg/kg ▪ 7 doses 2 mg/kg ▪ 15 doses 6 mg/kg • In TCH (docetaxel, carboplatin, and trastuzumab) regimen as an NCCN-preferred regimen ^{1, 6, 29, 60} ▪ Trastuzumab (Herceptin®) and related biosimilars for a total of 52 weeks: Initial dose of 4 mg/kg followed by 17 weekly doses of 2 mg/kg; subsequent 12 doses at 6 mg/kg every 3 weeks starting on week 19 through week 52 ▪ 1 dose 4 mg/kg ▪ 17 doses 2 mg/kg ▪ 12 doses 6 mg/kg • In combination with docetaxel following AC (doxorubicin and cyclophosphamide) regimen ^{6, 29, 40, 60} ▪ Trastuzumab (Herceptin®) and related biosimilars for a total of 52 weeks: Initial dose of 4 mg/kg, then 11 weekly doses of 2 mg/kg, followed by 14 doses of 6 mg/kg administered every 21 days ▪ 1 dose 4 mg/kg ▪ 11 doses 2 mg/kg ▪ 14 doses 6 mg/kg • In combination with docetaxel and cyclophosphamide ^{6, 29} ▪ Trastuzumab (Herceptin®) and related biosimilars for a total of 52 weeks: Initial dose at 8 mg/kg, then subsequent doses at 6 mg/kg every 3 weeks ▪ 1 dose 8 mg/kg ▪ 17 doses 6 mg/kg

OR

Initial dose of 4 mg/kg, then 11 weekly doses of 2 mg/kg, followed by 14 doses of 6 mg/kg administered every 21 days

- 1 dose 4 mg/kg
 - 11 doses 2 mg/kg
 - 14 doses 6 mg/kg
- In TCH regimen (as an NCCN-preferred regimen) with pertuzumab (Perjeta®)^{6, 29}
 - Trastuzumab (Herceptin®) and related biosimilars for a total of 52 weeks:
Initial dose at 8 mg/kg; subsequent doses at 6 mg/kg every 3 weeks
 - 1 dose 8 mg/kg
 - 17 doses 6 mg/kg
- In combination with pertuzumab (Perjeta®) and paclitaxel (as an NCCN-preferred regimen) or pertuzumab (Perjeta®) and docetaxel following AC regimen^{6, 29}
 - Trastuzumab (Herceptin®) and related biosimilars for a total of 52 weeks:
Initial dose at 8 mg/kg; subsequent doses at 6 mg/kg every 3 weeks
 - 1 dose 8 mg/kg
 - 17 doses 6 mg/kg

Adjuvant treatment of individuals with HER2-positive, low risk stage I breast cancer

- In combination with paclitaxel (particularly for individuals not eligible for other standard adjuvant regimens due to comorbidities)^{6, 29}
 - Trastuzumab (Herceptin®) and related biosimilars for a total of 52 weeks:
Initial dose of 4 mg/kg, then 51 weekly doses of 2 mg/kg
 - 1 dose 4 mg/kg

	▪ 51 doses 2 mg/kg OR Initial dose of 4 mg/kg, then 11 weekly doses of 2 mg/kg, followed by 6 mg/kg every 21 days for 14 doses. ▪ 1 dose 4 mg/kg ▪ 11 doses 2 mg/kg ▪ 14 doses 6 mg/kg Adjuvant treatment of individuals with HER2-positive early breast cancer at high risk of recurrence • In combination with pertuzumab (Perjeta®) and chemotherapy ▪ Trastuzumab (Herceptin®) and related biosimilars for a total of 52 weeks: Initial dose at 8 mg/kg; subsequent doses at 6 mg/kg every 3 weeks ▪ 1 dose 8 mg/kg ▪ 17 doses 6 mg/kg
Recurrent or Metastatic Breast Cancer	As a single agent for the treatment of HER2-overexpressing breast cancer in individuals who have received one or more chemotherapy regimens metastatic disease ▪ Trastuzumab (Herceptin®) and related biosimilars Initial dose of 4 mg/kg; subsequent doses at 2 mg/kg weekly until disease progression or unacceptable toxicity In combination with tamoxifen, fulvestrant, or aromatase inhibitors (e.g., anastrozole [Arimidex®], exemestane [Aromasin®], letrozole [Femara®] with or without lapatinib [Tykerb®] for the treatment of recurrent or stage IV estrogen receptor-positive, human epidermal growth factor receptor 2 (HER-2)-positive disease in postmenopausal women* 6, 29, 32 *Men with breast cancer should be treated similarly to postmenopausal women, except that use of an aromatase inhibitor is ineffective without concomitant suppression of testicular steroidogenesis

	▪ Trastuzumab (Herceptin®) and related biosimilars Initial dose of 8 mg/kg; subsequent doses at 6 mg/kg every 3 weeks until disease progression or unacceptable toxicity In combination with tamoxifen for the treatment of recurrent or stage IV estrogen receptor-positive, HER2-positive disease in premenopausal women* *Men with breast cancer should be treated similarly to postmenopausal women, except that use of an aromatase inhibitor is ineffective without concomitant suppression of testicular steroidogenesis ▪ Trastuzumab (Herceptin®) and related biosimilars Initial dose of 8 mg/kg; subsequent doses at 6 mg/kg every 3 weeks until disease progression or unacceptable toxicity In combination with pertuzumab (Perjeta) and docetaxel for the treatment of individuals with HER2-positive disease who have not received prior anti-HER2 therapy or chemotherapy ▪ Trastuzumab (Herceptin®) and related biosimilars Initial dose of 8 mg/kg; subsequent doses at 6 mg/kg every 3 weeks until disease progression or unacceptable toxicity OR Initial dose of 4 mg/kg; subsequent doses at 2 mg/kg weekly until disease progression or unacceptable toxicity For individuals with HER2-positive recurrent or metastatic breast cancer that is either hormone receptor-negative, hormone receptor-positive and endocrine therapy refractory, with symptomatic visceral disease, or visceral crisis: • First-line therapy in combination with pertuzumab (Perjeta®) with docetaxel or paclitaxel ▪ Trastuzumab (Herceptin®) and related biosimilars :

- With docetaxel^{16, 29,56,57}
Initial dose of 8 mg/kg; subsequent doses at 6 mg/kg every 3 weeks until disease progression or unacceptable toxicity
- With paclitaxel
Initial dose of 8 mg/kg; subsequent doses at 6 mg/kg every 3 weeks until disease progression or unacceptable toxicity
- In combination with docetaxel, vinorelbine, or capecitabine; or with paclitaxel with or without carboplatin
 - Trastuzumab (Herceptin®) and related biosimilars : ^{1, 6, 29, 41}
 - With docetaxel weekly or every 21 days^{6, 26, 29, 43, 44, 55}
Initial dose of 4 mg/kg followed by weekly doses of 2 mg/kg until disease progression or unacceptable toxicity

OR

Initial dose of 8 mg/kg; subsequent doses at 6 mg/kg every 3 weeks until disease progression or unacceptable toxicity

- With vinorelbine^{6, 29, 33, 36, 39, 45, 62}
Initial dose of 4 mg/kg followed by weekly doses of 2 mg/kg until disease progression or unacceptable toxicity

OR

Initial dose of 8 mg/kg; subsequent doses at 6 mg/kg every 3 weeks until disease progression or unacceptable toxicity

- With capecitabine^{6, 8, 26, 29, 33, 35, 36, 39, 50, 58}
Initial dose of 4 mg/kg followed by weekly

	doses of 2 mg/kg until disease progression or unacceptable toxicity OR Initial dose of 8 mg/kg; subsequent doses at 6 mg/kg every 3 weeks until disease progression or unacceptable toxicity ▪ With paclitaxel and carboplatin (weekly or every 21 days)^{6, 26, 29,46, 47} Initial dose of 4 mg/kg followed by weekly doses of 2 mg/kg until disease progression or unacceptable toxicity OR Initial dose of 8 mg/kg; subsequent doses at 6 mg/kg every 3 weeks until disease progression or unacceptable toxicity ▪ With Paclitaxel (weekly or every 21 days)^{1, 6, 8, 26, 29, 48} Initial dose of 4 mg/kg followed by weekly doses of 2 mg/kg until disease progression or unacceptable toxicity OR Initial dose of 8 mg/kg; subsequent doses at 6 mg/kg every 3 weeks until disease progression or unacceptable toxicity • As treatment for trastuzumab-exposed HER2-positive disease in combination with lapatinib (without cytotoxic therapy), capecitabine, carboplatin, cyclophosphamide, eribulin, gemcitabine, ixabepilone, paclitaxel, docetaxel, vinorelbine, or albumin-bound paclitaxel ▪ Trastuzumab (Herceptin®) and related biosimilars : Initial dose of 4 mg/kg followed by weekly doses of 2

	mg/kg until disease progression or unacceptable toxicity OR Initial dose of 8 mg/kg; subsequent doses at 6 mg/kg every 3 weeks until disease progression or unacceptable toxicity • In combination with pertuzumab (Perjeta®) with or without cytotoxic therapy (eg, vinorelbine or taxane) for one line of therapy beyond first-line therapy in patients previously treated with chemotherapy and trastuzumab in the absence of pertuzumab ▪ Trastuzumab (Herceptin®) and related biosimilars : ▪ With pertuzumab^{6, 29, 57, 59} Initial dose of 8 mg/kg; subsequent doses at 6 mg/kg every 3 weeks until disease progression or unacceptable toxicity

CENTRAL NERVOUS SYSTEM METASTASES

Leptomeningeal Metastases from Breast Cancer	• Primary treatment of individuals with normal CSF flow or no clinical evidence of abnormal flow • As maintenance therapy for individuals with negative CSF cytology or for clinically stable individuals with persistently positive CSF cytology • Therapy for individuals with positive CSF cytology ○ Trastuzumab (Herceptin®) and related biosimilars as intracerebrospinal fluid (CSF) treatment ^{6, 63, 64} Doses range from 20 - 100 mg weekly or every other week

COLON CANCER

Colon Cancer	Concurrent treatment with Lapatinib⁷²:

	Lapatinib 1000 mg PO daily on days 1-28⁷² - Trastuzumab (Herceptin®)⁷² and related biosimilars Initial dose of 4 mg/kg; subsequent doses at 2 mg/kg weekly until disease progression or unacceptable toxicity Concurrent treatment with Pertuzumab⁷²: Trastuzumab (Herceptin®)⁷² and related biosimilars - Initial dose of 8 mg/kg; subsequent doses at 6 mg/kg every 3 weeks until disease progression or unacceptable toxicity Pertuzumab (Prjeta)⁷² - Initial dose of 840 mg; subsequent doses at 420 mg/kg every 3 weeks until disease progression or unacceptable toxicity

GASTRIC, ESOPHAGEAL, OR ESOPHAGOGASTRIC JUNCTION CANCER

Metastatic Gastric, Esophageal, or Esophago-gastric Junction Cancer	For the palliative treatment of individuals with Karnofsky performance score of 60% or greater, or ECOG performance score of 2 or less who have advanced HER2 protein overexpressing gastric adenocarcinoma, esophageal adenocarcinoma, or esophagogastric junction adenocarcinoma, in combination with cisplatin and either fluorouracil or capecitabine as first-line therapy^{6, 9, 10, 11, 12, 31, 53, 65} - Trastuzumab (Herceptin®) and related biosimilars Initial dose of 8 mg/kg; subsequent doses at 6 mg/kg every 3 weeks until disease progression or unacceptable toxicity OR - Trastuzumab (Herceptin®) and related biosimilars Initial dose of 6 mg/kg; subsequent doses at 4 mg/kg every 2 weeks until disease progression or unacceptable toxicity

HEPATOBIILIARY CANCERS

Hepatobiliary Cancers	Pertuzumab + Trastuzumab⁷⁸ • Pertuzumab 840 mg IV over 60 minutes on Day 1 of Cycle 1 followed by 420 mg IV over 30 minutes on Day 1 beginning with Cycle 2 • Trastuzumab 8 mg/kg IV over 90 minutes on Day 1 of Cycle 1 followed by 6 mg/kg IV over 30 minutes on Day 1 beginning with Cycle 2
RECTAL CANCER	
Rectal Cancer	Concurrent treatment with Lapatinib⁷³: Lapatinib 1000 mg PO daily on days 1-28 ▪ Trastuzumab (Herceptin®) and related biosimilars Initial dose of 4mg/kg; subsequent doses at 2 mg/kg weekly until disease progression or unacceptable toxicity

SALIVARY GLAND TUMOR

Salivary Gland Tumors	Concurrent treatment with docetaxel or as a single agent ▪ Trastuzumab (Herceptin®)^{75,76,77} and related biosimilars The initial dose of 8 mg/kg; subsequent doses at 6 mg/kg every 3 weeks until disease progression or unacceptable toxicity

	▪ Docetaxel (Taxotere®)^{75,76,77} 70 mg/m² administered every 3 weeks until disease progression or unacceptable toxicity OR ▪ Trastuzumab (Herceptin®)^{75,76,77} and related biosimilars The initial dose of 4 mg/kg followed by 2 mg/kg weekly

UTERINE NEOPLASMS

Endometrial Carcinoma	For primary stage III or IV or recurrent HER2-positive disease with carboplatin (area under the curve [AUC] 5) and paclitaxel 175 mg/m² every 21 days for 6 cycles⁷¹ with ▪ trastuzumab at 8 mg/kg for the first dose and 6 mg/kg in subsequent cycles, followed by trastuzumab maintenance of 6 mg/kg every 3 weeks until disease progression or unacceptable toxicity

DOSING AND FREQUENCY REQUIREMENTS FOR TRASTUZUMAB (HERCEPTIN®) AND HYALURONIDASE-OYSK (HERCEPTIN HYLECTA™)

BREAST CANCER

Metastatic Breast Cancer	For adjuvant treatment with HER2 overexpression^{66,69,70} ▪ 600 mg trastuzumab/10,000 units hyaluronidase subQ every 3 weeks, for 52 weeks (1 year) or until disease recurrence, whichever occurs first; extending treatment beyond 1 year is not recommended. For metastatic breast cancer with HER2 overexpression as first-line treatment in combination with paclitaxel

	▪ 600 mg trastuzumab/10,000 units hyaluronidase subQ every 3 weeks until disease progression For metastatic breast cancer with HER2 overexpression as a monotherapy in individuals, who have received at least 1 prior chemotherapy regimen ▪ 600 mg trastuzumab/10,000 units hyaluronidase subQ every 3 weeks until disease progression

The Company reserves the right to modify the Dosing and Frequency Guidelines listed in this Policy to ensure consistency with the most recently published recommendations for the use of trastuzumab (Herceptin®) and related biosimilars . The professional provider must supply supporting documentation (ie, published peer-reviewed literature) in order to request coverage for an amount of trastuzumab (Herceptin®) and related biosimilars in excess of the Dosing and Frequency Guidelines listed in this Policy.

Changes to these guidelines are based on a consensus of information obtained from resources such as, but not limited to: the US Food and Drug Administration (FDA); drug manufacturer's guidelines; Company-recognized authoritative pharmacology compendia; or published peer-reviewed clinical research. For a list of Company-recognized pharmacology compendia and criteria for peer-reviewed clinical research, view our policy on off-label coverage for prescription drugs and biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of this drug. If the member's dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider **must** submit those changes to the Company for a new approval based on those changes as part of the precertification process. The Company reserves the right to conduct post-payment review and audit procedures for any claims submitted for trastuzumab (Herceptin®) and related biosimilar

Version Effective Date: 06/16/2025

Policy Attachment

Attachment to Policy # 08.00.33s

Attachment: B

Policy #: 08.00.33s

Description: ICD-10 CM Codes and Narratives

Title: Trastuzumab (Herceptin®) and Related Biosimilars, Trastuzumab and Hyaluronidase-oysk (Herceptin Hylecta)

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

ICD-10 CM CODES AND NARRATIVES

C06.9 Malignant neoplasm of mouth, unspecified

C07 Malignant neoplasm of parotid gland

C08.0 Malignant neoplasm of submandibular gland

C08.1 Malignant neoplasm of sublingual gland

C08.9 Malignant neoplasm of major salivary gland, unspecified

C15.3 Malignant neoplasm of upper third of esophagus

C15.4 Malignant neoplasm of middle third of esophagus

C15.5 Malignant neoplasm of lower third of esophagus

C15.8 Malignant neoplasm of overlapping sites of esophagus

C15.9 Malignant neoplasm of esophagus, unspecified

C16.0 Malignant neoplasm of cardia

C16.1 Malignant neoplasm of fundus of stomach

C16.2 Malignant neoplasm of body of stomach

C16.3 Malignant neoplasm of pyloric antrum

C16.4 Malignant neoplasm of pylorus

C16.5 Malignant neoplasm of lesser curvature of stomach, unspecified

C16.6 Malignant neoplasm of greater curvature of stomach, unspecified

C16.8 Malignant neoplasm of overlapping sites of stomach

C16.9 Malignant neoplasm of stomach, unspecified

C17.0 Malignant neoplasm of duodenum

C17.1 Malignant neoplasm of jejunum

C17.2 Malignant neoplasm of ileum

C17.3 Meckel's diverticulum, malignant

C17.8 Malignant neoplasm of overlapping sites of small intestine

C17.9 Malignant neoplasm of small intestine, unspecified

C18.0 Malignant neoplasm of cecum

C18.1 Malignant neoplasm of appendix

C18.2 Malignant neoplasm of ascending colon

C18.3 Malignant neoplasm of hepatic flexure

C18.4 Malignant neoplasm of transverse colon

C18.5 Malignant neoplasm of splenic flexure

C18.6 Malignant neoplasm of descending colon

C18.7 Malignant neoplasm of sigmoid colon

C18.8 Malignant neoplasm of overlapping sites of colon

C18.9 Malignant neoplasm of colon, unspecified

C19 Malignant neoplasm of rectosigmoid junction

C20 Malignant neoplasm of rectum

C21.8 Malignant neoplasm of overlapping sites of rectum, anus and anal canal

C22.1 Intrahepatic bile duct carcinoma

C23 Malignant neoplasm of gallbladder

C24.0 Malignant neoplasm of extrahepatic bile duct

C24.8 Malignant neoplasm of overlapping sites of biliary tract

C24.9 Malignant neoplasm of biliary tract, unspecified

C50.011 Malignant neoplasm of nipple and areola, right female breast

C50.012 Malignant neoplasm of nipple and areola, left female breast

C50.021 Malignant neoplasm of nipple and areola, right male breast

C50.022 Malignant neoplasm of nipple and areola, left male breast

C50.111 Malignant neoplasm of central portion of right female breast

C50.112 Malignant neoplasm of central portion of left female breast

C50.121 Malignant neoplasm of central portion of right male breast

C50.122 Malignant neoplasm of central portion of left male breast

C50.211 Malignant neoplasm of upper-inner quadrant of right female breast

C50.212 Malignant neoplasm of upper-inner quadrant of left female breast

C50.221 Malignant neoplasm of upper-inner quadrant of right male breast

C50.222 Malignant neoplasm of upper-inner quadrant of left male breast

C50.311 Malignant neoplasm of lower-inner quadrant of right female breast

C50.312 Malignant neoplasm of lower-inner quadrant of left female breast

C50.321 Malignant neoplasm of lower-inner quadrant of right male breast

C50.322 Malignant neoplasm of lower-inner quadrant of left male breast

C50.411 Malignant neoplasm of upper-outer quadrant of right female breast

C50.412 Malignant neoplasm of upper-outer quadrant of left female breast

C50.421 Malignant neoplasm of upper-outer quadrant of right male breast

C50.422 Malignant neoplasm of upper-outer quadrant of left male breast

C50.511 Malignant neoplasm of lower-outer quadrant of right female breast

C50.512 Malignant neoplasm of lower-outer quadrant of left female breast

C50.521 Malignant neoplasm of lower-outer quadrant of right male breast

C50.522 Malignant neoplasm of lower-outer quadrant of left male breast

C50.611 Malignant neoplasm of axillary tail of right female breast

C50.612 Malignant neoplasm of axillary tail of left female breast

C50.621 Malignant neoplasm of axillary tail of right male breast

C50.622 Malignant neoplasm of axillary tail of left male breast

C50.811 Malignant neoplasm of overlapping sites of right female breast

C50.812 Malignant neoplasm of overlapping sites of left female breast

C50.821 Malignant neoplasm of overlapping sites of right male breast

C50.822 Malignant neoplasm of overlapping sites of left male breast

C50.911 Malignant neoplasm of unspecified site of right female breast

C50.912 Malignant neoplasm of unspecified site of left female breast

C50.921 Malignant neoplasm of unspecified site of right male breast

C50.922 Malignant neoplasm of unspecified site of left male breast

C54.0 Malignant neoplasm of isthmus uteri

C54.1 Malignant neoplasm of endometrium

C54.2 Malignant neoplasm of myometrium

C54.3 Malignant neoplasm of fundus uteri

C54.8 Malignant neoplasm of overlapping sites of corpus uteri

C54.9 Malignant neoplasm of corpus uteri, unspecified

C55 Malignant neoplasm of uterus, part unspecified

C78.01 Secondary malignant neoplasm of right lung

C78.02 Secondary malignant neoplasm of left lung

C78.6 Secondary malignant neoplasm of retroperitoneum and peritoneum

C78.7 Secondary malignant neoplasm of liver and intrahepatic bile duct

C78.89 Secondary malignant neoplasm of other digestive organs

C79.31 Secondary malignant neoplasm of brain

C79.32 Secondary malignant neoplasm of cerebral meninges

C79.49 Secondary malignant neoplasm of other parts of nervous system

Version Effective Date: 06/16/2025

Title: Treatment of Pulmonary Artery Hypertension with Intravenous, Subcutaneous, and Inhaled Pharmacologic Agents

MEDICALLY NECESSARY

COMPANY-DESIGNATED PREFERRED PRODUCTS

Although there are many generic treprostinil sodium products on the market, there is no reliable evidence of the superiority of any one product of treprostinil sodium over another. The Company has designated the Sandoz treprostinil sodium product as its preferred product.

These products are less costly and at least as likely to produce equivalent therapeutic results as the non-preferred products, which include, but are not limited to, treprostinil sodium manufactured by other companies.

NON-PREFERRED PRODUCTS

Use of the non-preferred generic treprostinil sodium products that include, but are not limited to, manufacturers other than Sandoz, is considered medically necessary and, therefore, covered only for individuals who are currently receiving or have previously received a non-preferred product.

If the individual has not previously received Sandoz treprostinil sodium to treat the specified indication, these non-preferred products are only eligible for coverage when the individual has contraindication(s) or intolerance(s) to the Company-designated preferred product.

EPOPROSTENOL (FLOLAN®, VELETRI®)

Epoprostenol (Flolan, Veletri), IV (intravenous) infusion, is considered medically necessary and, therefore, covered when the dosing and frequency requirements listed in Attachment A and all of the following criteria are met:

- The individual has a confirmed diagnosis of pulmonary arterial hypertension (PAH), in accordance with the World Health Organization (WHO) Group 1 classification.
 - The diagnosis of PAH has been confirmed by a catheterization (right heart or Swan-Ganz) or echocardiography.

- Documentation all of the following:
 - Individual's mean pulmonary arterial pressure is greater than 20 mm Hg
 - Pulmonary artery wedge pressure (PAWP) of 15 mm Hg or less
 - Pulmonary vascular resistance (PVR) is greater than 2.0 Woods Units (WU)
- The individual meets the New York Heart Association (NYHA) Functional Classification requirement of Class III-IV.

TREPROSTINIL SODIUM (REMODULIN®)

Treprostinil sodium (Remodulin), IC or subcutaneous infusion, is considered medically necessary and, therefore, covered when the dosing and frequency requirements listed in Attachment A and all of the following criteria are met:

- The individual has a confirmed diagnosis of PAH, in accordance with the WHO Group 1 classification.
 - The diagnosis of PAH has been confirmed by a catheterization (right heart or Swan-Ganz) or echocardiography.
- Documentation of all of the following:
 - Individual's mean pulmonary arterial pressure is greater than 20 mm Hg
 - PAWP of 15 mm Hg or less
 - PVR is greater than 2.0 WU
- The individual meets the NYHA Functional Classification requirement of Class II-IV.

In addition, treprostinil sodium (Remodulin), IV or subcutaneous infusion, is considered medically necessary and, therefore, covered for individuals requiring transition from epoprostenol (Flolan) to diminish the rate of clinical deterioration.*

*Clinical deterioration is defined as an increase in epoprostenol (Flolan) dose, hospitalization due to PAH.

ILOPROST (VENTAVIS®)

Iloprost (Ventavis) inhalation is considered medically necessary and, therefore, covered when the dosing and frequency requirements listed in Attachment A and all of the following criteria are met:

- The individual has a confirmed diagnosis of PAH, in accordance with the WHO Group 1 classification.

- The diagnosis of PAH has been confirmed by a catheterization (right heart or Swan-Ganz) or echocardiography.
- Documentation all of the following:
 - Individual's mean pulmonary arterial pressure is greater than 20 mm Hg
 - PAWP of 15 mm Hg or less
 - PVR is greater than 2.0 WU
- The individual meets the NYHA Functional Classification requirements of Class III-IV for iloprost (Ventavis)

TREPROSTINIL (TYVASO®)

Treprostinil (Tyvaso) inhalation is considered medically necessary and, therefore, covered when the dosing and frequency requirements listed in Attachment A and either of the following criteria are met:

- The individual has a confirmed diagnosis of PAH, in accordance with the WHO Group 1 classification, and all of the following criteria are met:
 - The diagnosis of PAH has been confirmed by a catheterization (right heart or Swan-Ganz) or echocardiography.
 - The individual has a right heart catheterization (RHC) within 1 year with the following documented parameters:
 - PVR greater than 2 WU
 - PCWP of 15 mm Hg or less
 - A mean pulmonary arterial pressure (mPAP) of 20 mm Hg or greater
 - The individual meets the NYHA Functional Classification requirements Class III.
- The individual has a confirmed diagnosis of pulmonary hypertension (PH) associated with interstitial lung disease (PH-ILD) WHO Group 3 when all of the following criteria are met:
 - The individual has a confirmed diagnosis of WHO Group 3 PH based on computer tomography (CT) imaging, which demonstrates evidence of diffuse parenchymal lung disease performed within 6 months.
 - The individual may have any form of ILD or combined pulmonary fibrosis and emphysema (CPFE).

- The individual has a RHC within 1 year with the following documented parameters:
 - PVR greater than 2 WU
 - A PCWP of 15 mm Hg or less
 - A mean pulmonary arterial pressure (mPAP) of 20 mm Hg or greater
- The individual has a baseline 6MWD 100 meters or greater
- For the individual receiving chronic medication for underlying lung disease (e.g., pirfenidone, nintedanib), the dose must be stable and optimized for 30 days or longer prior to treatment.
- For the individual with connective tissue disease (CTD), the baseline forced vital capacity (FVC) must be less than 70 percent.

SILDENAFIL (REVATIO®)

Sildenafil (Revatio) IV infusion for continued treatment of individuals who are currently prescribed oral sildenafil (Revatio) and who are temporarily unable to take oral medication, is considered medically necessary and, therefore, covered, when the dosing and frequency requirements listed in Attachment A are met.

SELEXIPAG (UPTRAVI®)

Selexipag (Uptravi) IV infusion for continued treatment of individuals who are currently prescribed oral selexipag (Uptravi) and who are temporarily unable to take oral medication, is considered medically necessary and, therefore, covered, when the dosing and frequency requirements listed in Attachment A are met.

EXPERIMENTAL/INVESTIGATIONAL

All other uses for epoprostenol (Flolan; Veletri), treprostinil sodium (Remodulin), iloprost (Ventavis), treprostinil (Tyvaso), sildenafil (Revatio), and selexipag (Uptravi), are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the medical policy on off-label coverage for prescription drugs and biologics.

Although the US Food and Drug Administration (FDA) has approved a fully implantable IV infusion pump system used to deliver pharmacological agents (prostanoids) for the treatment of PAH, the Company has determined that the safety and/or effectiveness of this device cannot be established by review of the available published peer-reviewed literature. Therefore, a fully implantable IV infusion pump system used to deliver pharmacological agents (prostanoids) for the treatment of PAH is considered experimental/investigational by the Company and not covered.

NOT ELIGIBLE FOR SEPARATE REIMBURSEMENT

The Company covers the use of IV fluids for the preparation (e.g., dilution, reconstitution) of pharmaceuticals, biologics, and other substances for IV administration; however, such use is considered to be integral to the administration of the pharmaceutical, biologic, or other substance and is, therefore, not eligible for separate reimbursement. Participating providers may **not** bill members for this service.

DOSING AND FREQUENCY REQUIREMENTS

Refer to Attachment A for dosing and frequency requirements for epoprostenol (Flolan) (Veletri); treprostinil sodium (Remodulin); iloprost (Ventavis); treprostinil (Tyvaso); sildenafil (Revatio); and selexipag (Uptravi).

The Company reserves the right to modify the Dosing and Frequency Requirements listed in this Policy to ensure consistency with the most recently published recommendations for the use of epoprostenol (Flolan; Veletri); treprostinil sodium (Remodulin); iloprost (Ventavis); treprostinil (Tyvaso); sildenafil (Revatio); and selexipag (Uptravi). Changes to these guidelines are based on a consensus of information obtained from resources such as, but not limited to, the FDA; Company-recognized authoritative pharmacology compendia; or published peer-reviewed clinical research. The professional provider must supply supporting documentation (i.e., published peer-reviewed literature) in order to request coverage for an amount of epoprostenol (Flolan; Veletri); treprostinil sodium (Remodulin); iloprost (Ventavis); treprostinil (Tyvaso); sildenafil (Revatio); and selexipag (Uptravi) outside of the Dosing and Frequency Requirements listed in this Policy. For a list of Company-recognized pharmacology compendia, view our policy on off-label coverage for prescription drugs and biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of this drug. If the member's dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider must submit those changes to the Company for a new approval based on those changes as part of the precertification process. The Company reserves the right to conduct postpayment review and audit procedures for any claims submitted for epoprostenol

(Flolan; Veletri); treprostinil sodium (Remodulin); iloprost (Ventavis); treprostinil (Tyvaso); sildenafil (Revatio); and selexipag (Uptravi).

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Duration of authorization: 12 months

Version Effective Date: 04/21/2025

Attachment A: [Treatment of Pulmonary Artery Hypertension with Intravenous, Subcutaneous, and Inhaled Pharmacologic Agents](#)

Description: Dosing and Frequency Requirements

Policy Attachment

Attachment to Policy # 08.00.25o

Attachment: A

Policy #: 08.00.25o

Description: Dosing and Frequency Requirements

Title: Treatment of Pulmonary Artery Hypertension with Intravenous, Subcutaneous, and Inhaled Pharmacologic Agents

DOSING AND FREQUENCY REQUIREMENTS

The Company reserves the right to modify the Dosing and Frequency Requirements listed in this Policy to ensure consistency with the most recently published recommendations for the use of epoprostenol (Flolan®) (Veletri®); treprostinil sodium (Remodulin®); iloprost (Ventavis®); and treprostinil (Tyvaso®); sildenafil (Revatio®); and selexipag (Uptravi®). Changes to these guidelines are based on a consensus of information obtained from resources such as, but not

limited to: the US Food and Drug Administration (FDA); Company-recognized authoritative pharmacology compendia; or published peer-reviewed clinical research. The professional provider must supply supporting documentation (i.e., published peer-reviewed literature) in order to request coverage for an amount of epoprostenol (Flolan®) (Veletri®); treprostinil sodium (Remodulin®); iloprost (Ventavis®); treprostinil (Tyvaso®); sildenafil (Revatio®); and selexipag (Uptravi®) outside of the Dosing and Frequency Requirements listed in this Policy. For a list of Company-recognized pharmacology compendia, view our policy on off-label coverage for prescription drugs and biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of this drug. If the member's dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider must submit those changes to the Company for a new approval based on those changes as part of the precertification process. The Company reserves the right to conduct post-payment review and audit procedures for any claims submitted for epoprostenol (Flolan®) (Veletri®); treprostinil sodium (Remodulin®); iloprost (Ventavis®); treprostinil (Tyvaso®); sildenafil (Revatio®); and selexipag (Uptravi®) .

DOSING AND FREQUENCY REQUIREMENTS FOR EPOPROSTENOL (FLOLAN®) (VELETRI®)	
Indication	Dosing and Frequency
pulmonary arterial hypertension (PAH), in accordance with the World Health Organization (WHO) Group 1 classification. New York Heart Association (NYHA) Functional	epoprostenol (Flolan®) - Initiate intravenous infusion through a central venous catheter at 2 ng/kg/min - Change dose in 1-to 2-ng/kg/min increments at intervals of at least 15 minutes based on clinical response. - Administration VELETRI® is administered by continuous intravenous infusion via a central venous catheter using an ambulatory infusion pump. - Infusion Rate (mL/hr) = $\frac{[\text{Dose (ng/kg/min)} \times \text{Weight (kg)} \times 60 \text{ min/hr}]}{\text{Final Concentration (ng/mL)}}$
	epoprostenol (VELETRI®)
	Infusion of VELETRI® should be initiated at 2 ng/kg/min and increased in increments of 2 ng/kg/min every 15 minutes or

Classification requirement of Class III-IV	longer until dose-limiting pharmacologic effects are elicited or until a tolerance limit to the drug is established. - If symptoms of pulmonary hypertension persist or recur after improving -the infusion should be increased by 1-to 2-ng/kg/min increments at intervals sufficient to allow assessment of clinical response; these intervals should be at least 15 minutes. - Administration VELETRI® is administered by continuous intravenous infusion via a central venous catheter using an ambulatory infusion pump. - Infusion Rate (mL/hr) = $\frac{[\text{Dose (ng/kg/min)} \times \text{Weight (kg)} \times 60 \text{ min/hr}]}{\text{Final Concentration (ng/mL)}}$
DOSING AND FREQUENCY REQUIREMENTS FOR TREPROSTINIL SODIUM (REMODULIN®)	
Indication	Dosing and Frequency
pulmonary arterial hypertension (PAH), in accordance with the World Health Organization (WHO) Group 1 classification. New York Heart Association (NYHA) Functional Classification requirement of Class II-IV	treprostinil sodium (Remodulin®) - Initial dose for patients new to prostacyclin infusion therapy: 1.25 ng/kg/min; increase based on clinical response (increments of 1.25 ng/kg/min per week for the first 4 weeks of treatment, later 2.5 ng/kg/min per week). Avoid abrupt cessation. Infusion, subcutaneous, continuous/Intravenous route - subcutaneous infusion rate (mL/hr) = $\frac{[\text{dose (ng/kg per minute)} \times \text{weight (in kg)} \times 0.00006]}{\text{treprostinil vial strength (mg/mL)}}$ - diluted IV treprostinil concentration (mg/mL) = $\frac{[\text{dose (ng/kg per minute)} \times \text{weight (in kg)} \times 0.00006]}{\text{IV infusion rate (mL/hr)}}$; amount of treprostinil injection (mL) = $\frac{[\text{diluted IV treprostinil concentration (mg/mL)} \div \text{treprostinil vial strength (mg/mL)}] \times \text{total reservoir volume (mL)}}{1}$ - Mild to moderate hepatic insufficiency: Decrease initial dose to 0.625 ng/kg/min. - Pulmonary arterial hypertension, in individuals requiring transition from epoprostenol (Flolan®) Titration:

Step	Epoprostenol	Treprostinil
1	Unchanged	10% Starting epoprostenol dose
2	80% Starting epoprostenol dose	30% Starting epoprostenol dose
3	60% Starting epoprostenol dose	50% Starting epoprostenol dose
4	40% Starting epoprostenol dose	70% Starting epoprostenol dose
5	20% Starting epoprostenol dose	90% Starting epoprostenol dose
6	5% Starting epoprostenol dose	110% Starting epoprostenol dose
7	0	110% Starting epoprostenol dose plus additional 5% to 10% increments as needed

DOSING AND FREQUENCY REQUIREMENTS FOR ILOPROST (VENTAVIS®)

Indication	Dosing and Frequency
pulmonary arterial hypertension (PAH), in accordance with the World Health Organization (WHO) Group 1 classification. New York Heart Association	iloprost (Ventavis®) - Individuals should receive 6 to 9 doses (inhalations) per day (minimum of 2 hours between doses during waking hours) as follows: - Starting dose: 2.5 mcg - Uptitrate to 5 mcg if 2.5 mcg is well tolerated - Maintenance dose: 5 mcg - The 20 mcg/mL concentration is for individuals who repeatedly experience extended treatment times Delivered dose from ampule of :

(NYHA) Functional Classification requirement of Class III-IV	Nebulizer	10 mcg/mL	20 mcg/mL
	I-neb Adaptive Aerosol Delivery (AAD) System	2.5 or 5 mcg from one ampule	5 mcg from one ampule
The maximum daily dose evaluated in clinical studies was 45 mcg (5 mcg 9 times per day).			
DOSING AND FREQUENCY) REQUIREMENTS FOR TREPROSTINIL (TYVASO®)			
Indication	Dosing and Frequency		
- pulmonary arterial hypertension (PAH), in accordance with the World Health Organization (WHO) Group 1 classification. New York Heart Association (NYHA) Functional Classification requirement of Class III - pulmonary hypertension associated	treprostinil (Tyvaso®) - Administer undiluted, as supplied. A single breath of Tyvaso delivers approximately 6 mcg of treprostinil. - Administer in 4 separate treatment sessions each day approximately four hours apart, during waking hours. - Initial dosage: 3 breaths (18 mcg) per treatment session. If 3 breaths are not tolerated, reduce to 1 or 2 breaths. - Dosage should be increased by an additional 3 breaths per session at approximately 1-2 week intervals if tolerated. - Titrate to target maintenance dosage of 9 breaths or 54 mcg per treatment session as tolerated. Initial Dosage: - Therapy should begin with 3 breaths of Tyvaso (18 mcg of treprostinil), per treatment session, 4 times daily. If 3 breaths are not tolerated, reduce to 1 or 2 breaths and subsequently increase to 3 breaths, as tolerated.		

with interstitial lung disease (PH- ILD; WHO Group 3)	Maintenance Dosage: - Dosage should be increased by an additional 3 breaths per treatment session at approximately 1- to 2week intervals, if tolerated, until the target dose of 9 breaths (54 mcg of treprostinil) is reached, 4 times daily. If adverse effects preclude titration to target dose, Tyvaso should be continued at the highest tolerated dose. - If a scheduled treatment session is missed or interrupted, therapy should be resumed as soon as possible at the usual dose. - The maximum recommended dosage is 9 breaths per treatment session, 4 times daily.

DOSING AND FREQUENCY REQUIREMENTS FOR SILDENAFIL (REVATIO®)

Indication	Dosing and Frequency
pulmonary arterial hypertension (PAH), in accordance with the World Health Organization (WHO) Group 1 classification. New York Heart Association (NYHA) Functional Classification requirement of Class II-III	sildenafil (Revatio®) - Individuals are currently prescribed oral REVATIO® and who are temporarily unable to take oral medication 10 mg three times a day administered as an intravenous bolus injection

DOSING AND FREQUENCY REQUIREMENTS FOR SELEXIPAG (UPTRAVI®)

Indication	Dosing and Frequency
UPTRAVI is a prostacyclin receptor	selexipag (Uptravi®) Individuals are currently prescribed oral UPTRAVI® and who are temporarily unable to take oral medication

agonist indicated for the treatment of pulmonary arterial hypertension (PAH, WHO Group I) to delay disease progression and reduce the risk of hospitalization for PAH.	- Administer UPTRAVI for injection twice daily by intravenous infusion at a dose that corresponds to the patient’s current dose of UPTRAVI tablets (See Table Below). Administer UPTRAVI for injection as an 80-minute intravenous infusion. - Dosing Table for UPTRAVI intravenous based on current UPTRAVI tablets dose																											
	<table><tr><th>UPTRAVI tablets dose (mcg) for twice daily dosing</th><th>Corresponding IV UPTRAVI Dose (mcg) for twice daily dosing</th><th>Reconstituted tra volume (mL) for dilution</th></tr><tr><td>200</td><td>225</td><td>1.0</td></tr><tr><td>400</td><td>450</td><td>2.0</td></tr><tr><td>600</td><td>675</td><td>3.0</td></tr><tr><td>800</td><td>900</td><td>4.0</td></tr><tr><td>1000</td><td>1125</td><td>5.0</td></tr><tr><td>1200</td><td>1350</td><td>6.0</td></tr><tr><td>1400</td><td>1575</td><td>7.0</td></tr><tr><td>1600</td><td>1800</td><td>8.0</td></tr></table>	UPTRAVI tablets dose (mcg) for twice daily dosing	Corresponding IV UPTRAVI Dose (mcg) for twice daily dosing	Reconstituted tra volume (mL) for dilution	200	225	1.0	400	450	2.0	600	675	3.0	800	900	4.0	1000	1125	5.0	1200	1350	6.0	1400	1575	7.0	1600	1800	8.0
	UPTRAVI tablets dose (mcg) for twice daily dosing	Corresponding IV UPTRAVI Dose (mcg) for twice daily dosing	Reconstituted tra volume (mL) for dilution																									
	200	225	1.0																									
	400	450	2.0																									
	600	675	3.0																									
	800	900	4.0																									
	1000	1125	5.0																									
	1200	1350	6.0																									
	1400	1575	7.0																									
1600	1800	8.0																										

Title: Treatments for Complex Regional Pain Syndrome (CRPS)

MEDICALLY NECESSARY

The following interventions are considered medically necessary, and, therefore, covered, for treatment of complex regional pain syndrome (CRPS) when their respective criteria are met:

- Local anesthetic sympathetic nerve blocks (i.e., stellate ganglion block for upper extremity pain or lumbar sympathetic block for lower extremity pain) related to CRPS when first-line pain management strategies (e.g., oral medications [e.g, nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, opioids, antiepileptics, antidepressants, clonidine, muscle relaxants], physical therapy, or occupational therapy) tried for at least a 2-week period have failed to diminish or eliminate the individual's pain.
 - Following a positive response to the initial diagnostic stellate ganglion block, and sustained benefit in pain and function after three sympathetic blocks from baseline (preblock) pain and function; additional regional sympathetic blocks of up to a maximum of six total blocks in a 12-month period, performed at a frequency of no more than two two per week, are considered medically necessary, and, therefore, covered when all the following criteria have been met:
 - Benefit has been demonstrated by prior blocks as evidenced by all of the following:
 - Decreased use of pain medication
 - Improved level of function (e.g., increased range of motion, strength, and use of extremity in activities of daily living)
 - Improved tolerance to touch (e.g., decreased allodynia) or other objective measures
 - The intervention is being provided as part of a comprehensive pain management program (physical therapy, patient education, psychosocial support, and oral medication).
- Epidural or intrathecal opioids: A preliminary trial of opioid drug administration for the treatment of severe, chronic, intractable pain via a temporary intrathecal/epidural catheter is indicated for individuals who are unresponsive to less-invasive medical therapy such as orally administered systemic opioids and/or nerve blocks with local anesthetics and steroids.
 - If this preliminary trial demonstrates pain relief and a degree of side effects that are adequately acceptable (including effects on activities of daily living) and has

the individual's acceptance, a permanent implantable infusion pump may be considered for continuous intrathecal or epidural administration of opioids.

- The drug being administered and the purpose of its administration must be consistent with the indicated uses in the pump's US Food and Drug Administration (FDA)–approved labeling.
- The individual has a life expectancy of at least 3 months.
- Intrathecal ziconotide (Prialt®): The administration of intrathecal ziconotide (Prialt®) is indicated for the management of severe chronic pain in individuals for whom intrathecal therapy is warranted and who are intolerant of, or refractory to, other treatments such as systemic analgesics (e.g., NSAIDs, opioids, antiepileptics, antidepressants) adjunctive therapies (e.g., physical therapy, nerve blocks, spinal cord stimulation), or intrathecal morphine.
- Intrathecal baclofen: A preliminary trial of intrathecal baclofen is indicated when pain is caused by spasticity for individuals who are unresponsive to, or intolerant of, at least a 6-week trial of noninvasive medical therapy, such as orally administered antispasmodic drugs.
 - If this preliminary trial demonstrates pain relief and a degree of side effects that are adequately acceptable (including effects on activities of daily living) and has the individual's acceptance, a permanent implantable infusion pump may be considered for continuous intrathecal or epidural administration of opioids.
 - The drug being administered and the purpose of its administration must be consistent with the indicated uses in the pump's FDA-approved labeling.

EXPERIMENTAL/INVESTIGATIONAL

All other interventions are considered experimental/investigational and, therefore, not covered for the treatment of CRPS because their safety and/or effectiveness cannot be established by review of the available published peer-reviewed literature (not an all-inclusive list):

- Chemical sympathectomy
- Continuous peripheral nerve block with any drug
- Epidural clonidine
- Intramuscular botulinum toxin
- Intramuscular ketamine
- Intramuscular magnesium sulfate

- Intrathecal clonidine
- Intrathecal glycine
- Intrathecal methylprednisolone
- Intrathecal opioids in combination with bupivacaine or lidocaine
- Intrathoracic administration of analgesics
- Intravenous regional sympathetic nerve block (IVRB) with any drug (e.g., bretylium, guanethidine, ketamine, ketanserin, lidocaine, phenoxybenzamine, reserpine)
- Intravenous (systemic) administration with any of the following agents:
 - Intravenous bisphosphonates
 - Intravenous bupivacaine
 - Intravenous dexmedetomidine
 - Intravenous dimethylsulfoxide (DMSO)
 - Intravenous immunoglobulin G (IVIG)
 - Intravenous ketamine
 - Intravenous lidocaine
 - Intravenous magnesium
 - Intravenous mannitol
 - Intravenous opioids
- Plasma exchange
- Plasmapheresis
- Cervical plexus catheter nerve block with any drug
- Brachial plexus catheter nerve block with any drug
- Lumbar plexus catheter nerve block with any drug
- Sacral plexus catheter nerve block with any drug

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity of the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the service.

BILLING REQUIREMENTS

Inclusion of a code in this policy does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

If there is no specific Healthcare Common Procedure Coding System (HCPCS) code available for the drug administered, then the drug must be reported with the most appropriate unlisted code along with the corresponding National Drug Code (NDC).

Duration of authorization: 12 months

Version Effective Date: 10/01/2024

Title: Triamcinolone Acetonide Extended-Release Injectable (Zilretta®)

MEDICALLY NECESSARY

Triamcinolone Acetonide Extended-Release (ER) Injectable (Zilretta) is considered medically necessary and, therefore, covered when all of the following criteria are met:

- The individual is 18 years of age or older
- The individual has a documented diagnosis of osteoarthritis of the knee
- The individual has not previously been treated with triamcinolone acetonide ER injectable (Zilretta)
- The individual has a documented inadequate response to conservative non-pharmacologic therapy (e.g., weight loss, strengthening and range of motion exercises, etc)
- The individual has a documented failure of, contraindication to, or inadequate response to at least a two-week trial of oral or topical non-steroidal anti-inflammatory drugs (NSAIDs) or tramadol
- The individual has a documented inadequate response to previous treatment with intra-articular steroid injection (triamcinolone, methylprednisolone, betamethasone, dexamethasone)
- The dose does not exceed 32 mg as a single intra-articular injection to the knee

EXPERIMENTAL/INVESTIGATIONAL

All other uses for triamcinolone acetonide ER injectable (Zilretta), **including repeat administration into same knee**, are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Duration of authorization: 12 months

Version Effective Date: 04/30/2025

Title: Trilaciclib (Cosela™)

MEDICALLY NECESSARY

TRILACICLIB (COSELA™)

Initial Therapy

Trilaciclib (Cosela) is considered medically necessary and, therefore, covered when used to decrease the incidence of chemotherapy-induced myelosuppression in adult individuals and one of the following criteria are met:

- Administered prior to a platinum/etoposide-containing regimen
- Administered prior to topotecan-containing regimen for extensive-stage (when cancer has spread beyond the lungs) small cell lung cancer (ES-SCLC).
- As a prophylactic option for management of neutropenia to decrease the incidence of chemotherapy-induced myelosuppression when administered for any of the following indications
 - Administered prior to (prophylactic granulocyte-colony stimulating factor may be administered after cycle 1) platinum/etoposide ± immune checkpoint inhibitor-containing regimens
 - Administered prior to topotecan-containing regimen for extensive-stage small cell lung cancer (ES-SCLC)

Continuation Therapy

Trilaciclib (Cosela) is considered medically necessary and, therefore, covered for continuation therapy when the initial criteria are met, until disease progression or death.

EXPERIMENTAL/INVESTIGATIONAL

All other uses for trilaciclib (Cosela) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include but are not limited to: records from the professional provider's

office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Duration of authorization: 12 months

Version Effective Date: 06/11/2025

Title: Ublituximab-xiiy (Briumvi®) for intravenous use

MEDICALLY NECESSARY

Ublituximab-xiiy (Briumvi®) is considered medically necessary and, therefore, covered for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome (CIS), relapsing-remitting multiple sclerosis (RRMS), and active secondary progressive multiple sclerosis (SPMS), in adults when **all** of the following are met:

- The individual has a confirmed diagnosis of relapsing MS (RMS)
- The individual has active disease
- The individual does not have a diagnosis of primary progressive MS (PPMS)

EXPERIMENTAL/INVESTIGATIONAL

All other uses for ublituximab-xiiy (Briumvi) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on Off-label Coverage for Prescription Drugs and Biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the service.

Duration of authorization: 12 months

Version Effective Date: 03/06/2024

Title: Ustekinumab (Stelara®)

Policy

Coverage is subject to the terms, conditions, and limitations of the member's contract.

The Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition.

INITIAL THERAPY WITH USTEKINUMAB (STELARA)

CROHN'S DISEASE AND ULCERATIVE COLITIS

Ustekinumab (Stelara) is considered medically necessary and, therefore, covered for the treatment of individuals with moderate-to-severe active Crohn's disease or moderate-to-severe active ulcerative colitis when both of the following criteria and the Dosing and Frequency Requirements listed below are met:

- The individual is at least 18 years of age.
- There is documentation of failure, contraindication, or intolerance to a trial of one of the following:
 - Immunomodulators (e.g., azathioprine, 6-mercaptopurine, methotrexate)
 - Corticosteroids (e.g., budesonide [Entocort EC], prednisone, hydrocortisone, methylprednisolone)
 - Biologic therapy (e.g., certolizumab [Cimzia], adalimumab [Humira], infliximab [Remicade]), vedolizumab [Entyvio])

IMMUNE-CHECKPOINT INHIBITOR-RELATED TOXICITY MANAGEMENT

Ustekinumab (Stelara) is considered medically necessary and, therefore, covered for the management of the following autoimmune-like toxicities (also known as immune-related adverse events), when other etiologies have been ruled out and any of the following criteria and the Dosing and Frequency Requirements listed below are met:

- Mild (Grade 1) diarrhea or colitis if persistent or progressive symptoms after standard symptomatic treatments and positive lactoferrin/calprotectin
- Infliximab- and/or vedolizumab-refractory moderate (Grade 2) or severe (Grade 3-4) diarrhea or colitis

PLAQUE PSORIASIS

Ustekinumab (Stelara) for subcutaneous injection is considered medically necessary and, therefore, covered for the treatment of individuals with moderate-to-severe chronic plaque

psoriasis who are candidates for systemic therapy or phototherapy, when both of the following criteria and the Dosing and Frequency Requirements listed below are met:

- The individual is at least 6 years of age.
- There is documentation of failure, contraindication, or intolerance to a trial of at least one of the following:
 - Topical steroids
 - Topical nonsteroids (e.g., topical calcipotriene [Dovonex], topical anthralin, topical retinoids [Tazorac])
 - Topical immune modulators (e.g., Elidel, Protopic)
 - Methotrexate (MTX) (e.g., Trexall, Rheumatrex)
 - Retinoids (e.g., acitretin [Soriatane])
 - Cyclosporine (e.g., Neoral, Gengraf)

PSORIATIC ARTHRITIS

Ustekinumab (Stelara) for subcutaneous injection is considered medically necessary and, therefore, covered when used alone or in combination with MTX for the treatment of individuals with active psoriatic arthritis when both of the following criteria and the Dosing and Frequency Requirements listed below are met:

- The individual is at least 6 years of age.
- Documented failure, contraindication, or intolerance to a trial of at least one disease-modifying antirheumatic drug (DMARD) that include but are not limited to the following:
 - Sulfasalazine (e.g., Azulfidine)
 - Azathioprine (e.g., Imuran)
 - Hydroxychloroquine
 - Cyclosporine (e.g., Neoral, Gengraf)
 - Methotrexate (e.g., Trexall, Rheumatrex)
 - Anti-tumor necrosis factor agents

CONTINUATION THERAPY WITH USTEKINUMAB (STELARA)

Continuation therapy is considered medically necessary and, therefore, covered when the

individual has met the coverage criteria for Initial Therapy, and the treatment with ustekinumab (Stelara) resulted in documented improvement of symptoms or functions of affected areas.

DOSING AND FREQUENCY OF ADMINISTRATION

The following dosage and frequency information was taken from the Prescribing Information for this product at the time the policy was being developed:

CROHN'S DISEASE, ULCERATIVE COLITIS, AND IMMUNE-CHECKPOINT INHIBITOR–RELATED TOXICITY MANAGEMENT (DIARRHEA, COLITIS)

- For initial intravenous infusion:
 - For persons whose weight is up to 55 kg, the recommended dose is 260 mg (two vials).
 - For persons whose weight is more than 55 kg to 85 kg, the recommended dose is 390 mg (three vials).
 - For persons whose weight is more than 85 kg, the recommended dose is 520 mg (four vials).
- For subcutaneous injection as maintenance treatment:
 - The recommended dose is 90 mg 8 weeks after the initial intravenous dose, then every 8 weeks thereafter (for immune-checkpoint inhibitor–related toxicities, for a maximum of three maintenance doses).

PSORIASIS: subcutaneous injection

Adults:

- For persons whose weight is 100 kg (220 lbs) or less, the recommended dose is 45 mg initially and 4 weeks later, followed by 45 mg every 12 weeks.
- For persons whose weight is more than 100 kg (220 lbs), the recommended dose is 90 mg initially and 4 weeks later, followed by 90 mg every 12 weeks.

Pediatrics 6–17 years of age:

- For persons whose weight is less than 60 kg (132 lbs), the recommended dose is 0.75 mg/kg initially, 4 weeks later, followed by 0.75 mg/kg every 12 weeks.
- For persons whose weight is 60 kg to 100 kg (132–220 lbs), the recommended dose is 45 mg initially, 4 weeks later, followed by 45 mg every 12 weeks.

- For persons whose weight is more than 100 kg (220 lbs), the recommended dose is 90 mg initially, 4 weeks later, followed by 90 mg every 12 weeks.

PSORIATIC ARTHRITIS: SUBCUTANEOUS INJECTION

Adults:

- The recommended dose is 45 mg initially and 4 weeks later, followed by 45 mg every 12 weeks.
- For persons with coexistent moderate-to-severe plaque psoriasis who weigh greater than 100 kg (220 lbs), the recommended dose is 90 mg initially and 4 weeks later, followed by 90 mg every 12 weeks.

Pediatrics 6–17 years of age:

- For persons whose weight is less than 60 kg (132 lbs), the recommended dose is 0.75 mg/kg initially, 4 weeks later, followed by 0.75 mg/kg every 12 weeks.
- For persons whose weight is 60 kg (132 lbs) or more, the recommended dose is 45 mg initially, 4 weeks later, followed by 45 mg every 12 weeks.
- For persons whose weight is more than 100 kg (220 lbs) with coexistent moderate-to-severe plaque psoriasis, the recommended dose is 90 mg initially and 4 weeks later, followed by 90 mg every 12 weeks.

EXPERIMENTAL/INVESTIGATIONAL

All other uses of ustekinumab (Stelara) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the medical policy on off-label coverage for prescription drugs and biologics.

DOSING AND FREQUENCY REQUIREMENTS

The Company reserves the right to modify the Dosing and Frequency Requirements listed in this policy to ensure consistency with the most recently published recommendations for the use of ustekinumab (Stelara). Changes to these guidelines are based on a consensus of information obtained from resources such as, but not limited to, the US Food and Drug Administration (FDA); Company-recognized authoritative pharmacology compendia; or published peer-reviewed clinical research. The professional provider must supply supporting documentation (i.e., published peer-reviewed literature) in order to request coverage for an amount

of ustekinumab (Stelara) outside of the Dosing and Frequency Requirements listed in this policy. For a list of Company-recognized pharmacology compendia, view our policy on off-label coverage for prescription drugs and biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of this drug. If the member's dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider must submit those changes to the Company for a new approval based on those changes as part of the precertification process. The Company reserves the right to conduct postpayment review and audit procedures for any claims submitted for ustekinumab (Stelara).

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

When coverage of ustekinumab (Stelara) is requested outside of the Dosing and Frequency Requirements listed in this policy, the prescribing professional provider must supply documentation (i.e., published peer-reviewed literature) to the Company that supports this request.

Duration of authorization: 12 months

Version Effective Date: 10/04/2023

Title: Valoctocogene roxaparvovec-rvox (ROCTAVIAN™)

MEDICALLY NECESSARY

Valoctocogene roxaparvovec-rvox (Roctavian™) is considered medically necessary and, therefore, covered for the treatment of severe hemophilia A in individuals who meet ALL of the following criteria:

- Diagnosis of hemophilia A; **and**
- Age 18 years or older; **and**
- Baseline factor VIII level is less than 1 international unit (IU) per deciliter (dL) (or 1% endogenous factor VIII); **and**
- Poor disease control meeting one or more of the following:
 - One or more episodes of spontaneous bleeding into a joint or the central nervous system while receiving routine prophylaxis factor replacement therapy; **or**
 - Four or more episodes of soft tissue bleeding in an 8-week period while receiving routine prophylaxis factor replacement therapy; **or**
 - At least 12 bleeding episodes during the previous year while receiving on-demand therapy.

and

- No contraindications to infusion (if any of the following are present, treatment is contraindicated):
 - Detectable pre-existing immunity to the AAV5 capsid as measured by AAV5 transduction inhibition or AAV5 total antibodies; **or**
 - History of factor VIII inhibitor; **or**
 - Active infection; **or**
 - Immunosuppressive disorder; **or**
 - Liver cirrhosis; **or**
 - Active hepatitis B or C; **or**
 - Alanine transaminase (ALT) greater than 3 times the upper limit of normal; **or**
 - Bilirubin greater than 3 times the upper limit of normal; **or**

- Alkaline phosphatase greater than 3 times the upper limit of normal; **or**
- International normalized ratio (INR) greater than 1.4.; **or**
- Prior infusion of valoctocogene roxaparvovec-rvox (Roctavian)

NOTE:

Evio has been selected by the Company to administer clinical outcomes monitoring for individuals receiving certain high-cost drug therapies. Valoctocogene roxaparvovec-rvox (ROCTAVIAN™) is included in the portfolio of high-cost drug/biologic therapies for which Evio will be tracking clinical outcomes. If an individual meets all medical policy criteria, the requesting physician and/or individual being treated must agree to providing clinical outcomes data and information via Evio's secure web portal as requested.

EXPERIMENTAL/INVESTIGATIONAL

All other uses for valoctocogene roxaparvovec-rvox (Roctavian) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to, records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Duration of authorization: 12 months

Version Effective Date: 05/28/2025

Title: Vedolizumab (Entyvio®) for Injection for Intravenous Use

MEDICALLY NECESSARY

Vedolizumab (Entyvio) is considered medically necessary and, therefore, covered when all of the following criteria, including Dosing and Frequency Requirements listed below, are met for any of the following indications:

ULCERATIVE COLITIS (UC)

- In adult individuals with moderately to severely active UC who meet all of the following criteria:
 - Inadequate response, lost response, or intolerance to a 3-month trial of a tumor necrosis factor (TNF) blocker (e.g., adalimumab Humira®) or immunomodulator (e.g., azathioprine, 6-mercaptopurine), or inadequate response to, intolerance of, or demonstrated dependence on, corticosteroids
 - Vedolizumab (Entyvio) is dosed at 300 mg intravenous (IV) infusion at 0, 2, and 6 weeks, and then every 8 weeks thereafter. The US Food and Drug Administration (FDA) labeling indicates that therapy be discontinued in individuals who show no evidence of therapeutic benefit by Week 14.

CROHN'S DISEASE (CD)

- In adult individuals with moderately to severely active CD who meet all of the following criteria:
 - Inadequate response with, lost response to, or were intolerant of, a 3-month trial of a tumor necrosis factor (TNF) blocker (e.g., adalimumab Humira) or immunomodulator (e.g., azathioprine, 6-mercaptopurine, methotrexate), or had an inadequate response with, were intolerant to, or demonstrated dependence on, corticosteroids
 - Vedolizumab (Entyvio) is dosed at 300 mg IV infusion at 0, 2, and 6 weeks, and then every 8 weeks thereafter. The FDA labeling indicates that therapy should be discontinued in individuals who show no evidence of therapeutic benefit by Week 14.

MANAGEMENT OF IMMUNOTHERAPY-RELATED TOXICITIES

Immune Checkpoint Inhibitor–Related Toxicities

- In adult individuals with an immune checkpoint inhibitor (e.g., ipilimumab, nivolumab)–related diarrhea and or colitis who meet all of the following criteria:
 - The individual has any of the following immunotherapy-related toxicities:
 - mild grade one (G1) diarrhea or colitis with persistent or progressive symptoms and positive lactoferrin/calprotectin
 - moderate grade two (G2) diarrhea or colitis (defined as four to six bowel movements above baseline per day, colitis symptoms, not interfering with activities of daily living [ADLs])
 - severe (G3-4) diarrhea or colitis (Severe diarrhea [grade 3] is defined as ≥ 7 stools per day above baseline, and grade 3 colitis is defined by the presence of peritoneal signs with ileus and fever consistent with bowel perforation. A grade 4 designation is distinct from grade 3, reflecting increased severity and the life-threatening nature of symptoms).
 - Vedolizumab (Entyvio) is dosed at 300 mg IV infusion at 0, 2, and 6 weeks (induction only)

Hematopoietic Cell Transplantation

- In adult individuals with hematopoietic cell transplantation who meet all of the following criteria:
 - adult individuals with acute* graft-versus-host disease (GVHD) as additional therapy in conjunction with systemic corticosteroids following no response (steroid-refractory disease) to first-line therapy options
- Vedolizumab (Entyvio) is dosed at 300 mg IV infusion at week 0, 2, and 6 and then every 8 weeks thereafter

*National Comprehensive Cancer Network (NCCN) note: therapy for steroid-refractory acute GVHD is often used in conjunction with the original immunosuppressive agent.

EXPERIMENTAL/INVESTIGATIONAL

All other uses for vedolizumab (Entyvio), including uses for pediatric population (younger than 18 years of age), are considered experimental/investigational and, therefore, not covered

unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

DOSING AND FREQUENCY REQUIREMENTS

The Company reserves the right to modify the Dosing and Frequency Requirements listed in this policy to ensure consistency with the most recently published recommendations for the use of vedolizumab (Entyvio). Changes to these guidelines are based on a consensus of information obtained from resources such as, but not limited to: the FDA; Company-recognized authoritative pharmacology compendia; or published peer-reviewed clinical research. The professional provider must supply supporting documentation (i.e., published peer-reviewed literature) in order to request coverage for an amount of vedolizumab (Entyvio) outside of the Dosing and Frequency Requirements listed in this policy. For a list of Company-recognized pharmacology compendia, view our policy on off-label coverage for prescription drugs and biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of these drugs. If the member's dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider must submit those changes to the Company for a new approval based on those changes as part of the precertification process. The Company reserves the right to conduct post-payment review and audit procedures for any claims submitted for vedolizumab (Entyvio).

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

When coverage of vedolizumab (Entyvio) is requested outside of the Dosing and Frequency Requirements listed in this policy, the prescribing professional provider must supply documentation (i.e., published peer-reviewed literature) to the Company that supports this request.

BILLING REQUIREMENTS

For drugs that have more than one method of administration, application of the JA modifier is required to indicate the route of administration.

- To report the intravenous route of administration, append the following modifier: JA Administered Intravenously

Inclusion of a code in this policy does not imply reimbursement. Eligibility, benefits, limitations, exclusions, utilization management/referral requirements, provider contracts, and Company policies apply.

Duration of authorization: 12 months

Version Effective Date: 09/09/2024

Attachment A: [Vedolizumab \(Entyvio®\) for Injection for Intravenous Use](#)

Description: ICD-10 CODES AND NARRATIVES

Policy Attachment

Attachment to Policy # 08.01.18i

Attachment: A

Policy #: 08.01.18i

Description: ICD-10 CODES AND NARRATIVES

Title: Vedolizumab (Entyvio®) for Injection for Intravenous Use

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

ICD-10 CODES AND NARRATIVES

D89.810 Acute graft-versus-host disease

D89.812 Acute on chronic graft-versus-host disease

D89.813 Graft-versus-host disease, unspecified

K50.00 Crohn's disease of small intestine without complications

K50.011 Crohn's disease of small intestine with rectal bleeding

K50.012 Crohn's disease of small intestine with intestinal obstruction

K50.013 Crohn's disease of small intestine with fistula

K50.014 Crohn's disease of small intestine with abscess

K50.018 Crohn's disease of small intestine with other complication

K50.019 Crohn's disease of small intestine with unspecified complications

K50.10 Crohn's disease of large intestine without complications

K50.111 Crohn's disease of large intestine with rectal bleeding

K50.112 Crohn's disease of large intestine with intestinal obstruction

K50.113 Crohn's disease of large intestine with fistula

K50.114 Crohn's disease of large intestine with abscess

K50.118 Crohn's disease of large intestine with other complication

K50.119 Crohn's disease of large intestine with unspecified complications

K50.80 Crohn's disease of both small and large intestine without complications

K50.811 Crohn's disease of both small and large intestine with rectal bleeding

K50.812 Crohn's disease of both small and large intestine with intestinal obstruction

K50.813 Crohn's disease of both small and large intestine with fistula

K50.814 Crohn's disease of both small and large intestine with abscess

K50.818 Crohn's disease of both small and large intestine with other complication

K50.819 Crohn's disease of both small and large intestine with unspecified complications

K50.90 Crohn's disease, unspecified, without complications

K50.911 Crohn's disease, unspecified, with rectal bleeding

K50.912 Crohn's disease, unspecified, with intestinal obstruction

K50.913 Crohn's disease, unspecified, with fistula

K50.914 Crohn's disease, unspecified, with abscess

K50.918 Crohn's disease, unspecified, with other complication

K50.919 Crohn's disease, unspecified, with unspecified complications

K51.00 Ulcerative (chronic) pancolitis without complications

K51.011 Ulcerative (chronic) pancolitis with rectal bleeding

K51.012 Ulcerative (chronic) pancolitis with intestinal obstruction

K51.013 Ulcerative (chronic) pancolitis with fistula

K51.014 Ulcerative (chronic) pancolitis with abscess

K51.018 Ulcerative (chronic) pancolitis with other complication

K51.019 Ulcerative (chronic) pancolitis with unspecified complications

K51.20 Ulcerative (chronic) proctitis without complications

K51.211 Ulcerative (chronic) proctitis with rectal bleeding

K51.212 Ulcerative (chronic) proctitis with intestinal obstruction

K51.213 Ulcerative (chronic) proctitis with fistula

K51.214 Ulcerative (chronic) proctitis with abscess

K51.218 Ulcerative (chronic) proctitis with other complication

K51.219 Ulcerative (chronic) proctitis with unspecified complications

K51.30 Ulcerative (chronic) rectosigmoiditis without complications

K51.311 Ulcerative (chronic) rectosigmoiditis with rectal bleeding

K51.312 Ulcerative (chronic) rectosigmoiditis with intestinal obstruction

K51.313 Ulcerative (chronic) rectosigmoiditis with fistula

K51.314 Ulcerative (chronic) rectosigmoiditis with abscess

K51.318 Ulcerative (chronic) rectosigmoiditis with other complication

K51.319 Ulcerative (chronic) rectosigmoiditis with unspecified complications

K51.50 Left sided colitis without complications

K51.511 Left sided colitis with rectal bleeding

K51.512 Left sided colitis with intestinal obstruction

K51.513 Left sided colitis with fistula
K51.514 Left sided colitis with abscess
K51.518 Left sided colitis with other complication
K51.519 Left sided colitis with unspecified complications
K51.80 Other ulcerative colitis without complications
K51.811 Other ulcerative colitis with rectal bleeding
K51.812 Other ulcerative colitis with intestinal obstruction
K51.813 Other ulcerative colitis with fistula
K51.814 Other ulcerative colitis with abscess
K51.818 Other ulcerative colitis with other complication
K51.819 Other ulcerative colitis with unspecified complications
K51.90 Ulcerative colitis, unspecified, without complications
K51.911 Ulcerative colitis, unspecified with rectal bleeding
K51.912 Ulcerative colitis, unspecified with intestinal obstruction
K51.913 Ulcerative colitis, unspecified with fistula
K51.914 Ulcerative colitis, unspecified with abscess
K51.918 Ulcerative colitis, unspecified with other complication
K51.919 Ulcerative colitis, unspecified with unspecified complications
K52.1 Toxic gastroenteritis and colitis
R19.7 Diarrhea, unspecified
T86.09 Other complications of bone marrow transplant

Version Effective Date: 09/09/2024

Title: Velmanase alfa (Lamzede)

MEDICALLY NECESSARY

Initial criteria

Velmanase alfa-tycv (Lamzede) is considered medically necessary and, therefore, covered for the treatment of non-central nervous system manifestations (i.e., skeletal abnormalities, myopathy, motor function disturbances, immunodeficiency, etc.) of alpha-mannosidosis (AM) in pediatric and adult individuals when all of the following criteria are met, including dosing and frequency:

- The individual at least three years old
- Prescribed by or in consultation with a geneticist or metabolic specialist
- Diagnosis is confirmed by either of the following:
 - Confirmation of diagnosis by biochemical assay showing decreased alpha-mannosidase activity in white blood cells or skin fibroblasts less than 10 percent of normal values
 - Genotyping revealing two pathogenic mutations of the MAN2B1 gene
- Documented baseline age-appropriate values for one or more of the following:
 - 6-minute walk test (6-MWT),
 - 3-minute stair climb test (3-MSCT),
 - pulmonary function tests (e.g., forced vital capacity[FVC]),
 - motor function (i.e., Bruininks-Oseretsky Test of Motor Proficiency [BOT-2])
- The individual does **not** have any of the following :
 - A history of a hematopoietic stem-cell transplantation (HSCT) or bone marrow transplant
 - The individual cannot walk without support
- Dosing and frequency: children, adolescents and adults dosing intravenous infusion : 1 mg/kg once every week

NOTE: For very young individuals in which FVC or 6-MWT are not suitable for measuring, requests will be reviewed on a case-by case basis.

Continuation criteria:

- The individual continues to meet the initial criteria
- The individual has demonstrated a beneficial response to therapy or stabilization of disease compared to pretreatment age-appropriate baseline values in one or more of the following:
 - Stability or improvement in serum oligosaccharide concentration
 - Stability or improvement in 6-minute walking test (6-MWT)
 - Stability or improvement in 3-minute stair climbing test (3-MSCT)
 - Stability or improvement in forced vital capacity (FVC) (% predicted)
 - Stabilization or slowing in the rate of disease progression or clinical decline

EXPERIMENTAL/INVESTIGATIONAL

All other uses of velmanase alfa-tycv (Lamzede) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

DOSING AND FREQUENCY REQUIREMENTS

The Company reserves the right to modify the Dosing and Frequency Requirements listed in this policy to ensure consistency with the most recently published recommendations for the use of velmanase alfa-tycv (Lamzede). Changes to these guidelines are based on a consensus of information obtained from resources such as, but not limited to: the US Food and Drug Administration (FDA); Company-recognized authoritative pharmacology compendia; or published peer-reviewed clinical research. The professional provider must supply supporting documentation (i.e., published peer-reviewed literature) in order to request coverage for an amount of velmanase alfa-tycv (Lamzede) outside of the Dosing and Frequency Requirements listed in this policy. For a list of Company-recognized pharmacology compendia, view our policy on off-label coverage for prescription drugs and biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of this drug. If the member's dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider must submit those changes to the Company for a new approval based on those changes as part of the utilization management activities. The Company reserves the right to conduct post-payment review and audit procedures for any claims submitted for velmanase alfa-tycv (Lamzedo).

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

When coverage of velmanase alfa-tycv (Lamzedo) is requested outside of the Dosing and Frequency Requirements listed in this policy, the prescribing professional provider must supply documentation (i.e., published peer-reviewed literature) to the company that supports this request.

Duration of authorization: 12 months

Version Effective Date: 05/28/2025

Title: Voretigene Neparvovec-rzyl (Luxturna®)

MEDICALLY NECESSARY

Voretigene neparvovec-rzyl (Luxturna) is considered medically necessary and, therefore, covered for the treatment of individuals with confirmed biallelic *RPE65* variation(s) causing retinal dystrophy who are experiencing vision loss when all of the following criteria are met:

- Documentation of laboratory results confirming biallelic *RPE65* variation(s) causing retinal dystrophy
- The individual has viable retinal cells, as determined by the treating retinal specialist, and characterized by at least one of the following features:
 - An area of retina within the posterior pole of >100 µm thickness shown on optical coherence tomography
 - ≥3 Disc areas of retina without atrophy or pigmentary degeneration within the posterior pole
 - Remaining visual field within 30° of fixation as measured by III4e isopter or equivalent
- Age of individual is 3 years to <65 years of age
- Administration will occur at a certified treatment center staffed with professional providers, including retinal specialists, who have experience treating individuals with inherited retinal diseases
- Verification that a baseline full-field light sensitivity threshold (FST) test has been performed
- Individual does not have any of the following exclusion criteria:
 - Use of high-dose (>7500 retinol equivalent units [or >3300 IU] per day of vitamin A) retinoid compounds in the past 18 months
 - Intraocular surgery in the past 6 months
 - Ocular or systemic conditions that would interfere with this gene therapy
 - Pregnant individuals or individuals of child-bearing potential who are unwilling to use effective contraception for 4 months after vector administration

EXPERIMENTAL/INVESTIGATIONAL

All other uses for voretigene neparvovec-rzyl (Luxturna), including the retreatment of the same eye(s), are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Duration of authorization: 12 months

Version Effective Date: 05/15/2024

Title: Zanidatamab-hrii (Ziihera®)

MEDICALLY NECESSARY

Zanidatamab-hrii (Ziihera®), as a single agent, is considered medically necessary and, therefore, covered for the treatment of adults with previously treated (progression on or after systemic treatment), unresectable (or resected gross residual [R2] disease) or metastatic human epidermal growth factor receptor 2 (HER2)-positive immunohistochemistry (IHC) 3+ biliary tract cancer (BTC), when **ALL** of the following are met:

- Histologically or cytologically confirmed BTC, including intrahepatic cholangiocarcinoma (ICC), extrahepatic cholangiocarcinoma (ECC), and gallbladder cancer (GBC)
- Test positive for HER2 amplification by in situ hybridization (ISH) assay as detected by a US Food and Drug Administration (FDA)-approved test
- Locally advanced or metastatic BTC and not eligible for curative resection, transplantation, or ablative therapies
- Received at least one prior systemic chemotherapy regimen for advanced disease, and experienced disease progression after or developed intolerance to the most recent prior therapy
- Have not received prior treatment with HER2-targeted agents
- Left ventricular ejection fraction 50 percent or greater

EXPERIMENTAL/INVESTIGATIONAL

All other uses zanidatamab-hrii (Ziihera) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

MANDATES

PENNSYLVANIA MEMBERS

In accordance with the Commonwealth of Pennsylvania's Act 6 of 2020 or Fair Access to Cancer Treatment Act, for members who are enrolled in Pennsylvania commercial products who have Stage 4, advanced metastatic cancer, refer to the Medical Policy titled "Coverage of Anticancer Prescription Oral and Injectable Drugs and Biologics and Supportive Agents" (08.01.08) for additional information regarding the applicable coverage of drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Duration of authorization: 12 months

Version Effective Date: 04/21/2025

Title: Zolbetuximab-clzb (Vyloy®)

MEDICALLY NECESSARY

INITIAL THERAPY

Zolbetuximab-clzb (Vyloy) is considered medically necessary and, therefore, covered in adult individuals with HER2 overexpression negative AND Claudin 18 isoform 2 (CLDN18.2) positive disease when the following criteria are met:

Gastric Cancer

Zolbetuximab-clzb (Vyloy) is considered medically necessary and, therefore, covered for any of the following:

- Primary first-line treatment for medically fit individuals with surgically unresectable locoregional disease, in combination with fluorouracil or capecitabine and oxaliplatin [mFOLFOX or CAPOX regimen] (NCCN-preferred)
- Palliative therapy for individuals who are not surgical candidates or have unresectable, locally advanced, recurrent, or metastatic disease (including peritoneal-only metastatic disease, including positive cytology) and Karnofsky performance score 60% or greater or Eastern Cooperative Oncology Group (ECOG) performance score 2 or less as first-line therapy in combination with fluorouracil or capecitabine and oxaliplatin (NCCN-preferred)

Esophageal and Esophagogastric Junction Cancers

Zolbetuximab-clzb (Vyloy) is considered medically necessary and, therefore, covered for any of the following:

- First-line treatment in combination with fluoropyrimidine- and platinum-containing chemotherapy [mFOLFOX or CAPOX regimen]
- Palliative therapy for individuals who are not surgical candidates or have unresectable, locally advanced, recurrent, or metastatic disease and Karnofsky performance score 60% or greater or ECOG performance score 2 or less as first-line therapy in combination with oxaliplatin and fluorouracil or capecitabine (NCCN-preferred)

CONTINUATION THERAPY

Zolbetuximab-clzb (Vyloy) is considered medically necessary and, therefore, covered for continuation therapy when there is documentation of no evidence of unacceptable toxicity and no disease progression while on the current regimen.

MANDATES

PENNSYLVANIA MEMBERS

In accordance with the Commonwealth of Pennsylvania's Act 6 of 2020 or Fair Access to Cancer Treatment Act, for members who are enrolled in Pennsylvania commercial products who have stage 4, advanced metastatic cancer, refer to the Medical Policy titled "Coverage of Anticancer Prescription Oral and Injectable Drugs and Biologics and Supportive agents (08.01.08)" for additional information regarding the applicable coverage of drugs and biologics.

EXPERIMENTAL/INVESTIGATIONAL

All other uses for zolbetuximab-clzb (Vyloy) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the service.

Duration of authorization: 12 months

Version Effective Date: 04/21/2025