Prior Authorization Review Panel
MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: Keystone First	**Submission Date**: 10/1/2024
Policy Number: ccp.1321	**Effective Date:** 8/2017 **Revision Date:** October 1, 2024
Policy Name: Hand and arm transplants	

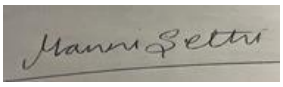
Type of Submission – Check all that apply:

- ☐ **New Policy**
- ☒ **Revised Policy***
- ☐ **Annual Review – No Revisions**
- ☐ **Statewide PDL**

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any clarifying information for the policy below:

See tracked changes below.

Name of Authorized Individual (Please type or print): Manni Sethi, MD, MBA, CHCQM	**Signature of Authorized Individual:** 

Hand and arm transplants

Clinical Policy ID: CCP.1321

Recent review date: 9/2024

Next review date: 1/2026

Policy contains: Composite tissue allotransplantation; forearm transplant; hand transplant.

Keystone First- CHIP has developed clinical policies to assist with making coverage determinations. Keystone First- CHIP's clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation are considered by Keystone First- CHIP, on a case by case basis, when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. Keystone First- CHIP's clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. Keystone First- CHIP's clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Keystone First- CHIP will update its clinical policies as necessary. Keystone First- CHIP's clinical policies are not guarantees of payment.

Coverage policy

Hand and arm transplants are investigational/not clinically proven and, therefore, not medically necessary.

Limitations

All other uses of hand and arm transplants are not medically necessary.

Alternative covered services

- Limb replantation.
- Upper limb prosthesis.
- Physical and occupational therapy.

Background

In the United States, approximately 2.1 million people live with limb loss, a number expected to double by 2050 (Access Prosthetics, 2017). Upper-limb amputations make up a minority – between one fifth and one sixth – of total amputations. Seventy percent of upper-limb amputations are below the elbow, with 10% of these at the hand or wrist (Fahrenkopf, 2018).

Composite tissue allotransplantation is the transfer of vascularized or non-vascularized heterogeneous tissues with different antigenicities from one person to another. Unlike a solid organ transplant, vascularized composite tissue allotransplantation involves multiple tissues (e.g., skin, muscle, tendon, bone, cartilage, fat, nerves, and blood vessels). Composite tissue allotransplantation is a complex procedure requiring multidisciplinary technical skills and understanding of its immunologic aspects. It is a treatment for complex injuries that leave patients with

structural, functional, and aesthetic deficits that cannot be addressed by other means (American Society of Transplantation, 2015).

Hand and arm transplantations are forms of vascularized composite tissue allotransplantation. Hand transplantation is an extremely complex procedure that can last from eight to ten hours; following the procedure, transplant recipients require life-long immunosuppressive therapy and intensive physical therapy to regain hand and arm function (The Johns Hopkins University, 2024).

The first hand transplant was attempted in 1964 in South America without success. In the United States, advances in surgical technique and immunosuppression allowed for the first successful hand transplant in 1999. Vascularized composite tissue allotransplantation is regulated, as are all solid organ transplants, within the Organ Procurement and Transplantation Network (80 FR 26464). Since 1998, 18 unilateral and 19 bilateral upper limb transplants have been performed in the United States (Organ Procurement and Transplantation Network, 2024).

Findings

Upper extremity transplants are quality-of-life procedures, not lifesaving procedures. They have been performed in individuals who lost one or both hands due to trauma or to life-saving interventions that caused permanent injury to the hand. They have not been performed for congenital anomalies or loss of a limb due to cancer.

Guidelines

Current guidelines do not recommend upper extremity transplants, as it is unclear if the long-term functional benefits outweigh the risks associated with long-term immunosuppression (Health Quality Ontario, 2016; National Institute for Health and Care Excellence, 2011).

Evidence reviews

As with any elective procedure, proper patient selection and preoperative education are essential to transplant success. Patient selection criteria continue to evolve. Inclusion criteria used by many transplant centers in the United States are (MacKay, 2014):

- Ages 18 to 69 years.
- No medical condition with negative immunologic, surgical, or functional implications.
- No psychosocial issues.
- No cancer in the past 10 years.
- No human immunodeficiency virus.
- Willingness to consent to cell collection and storage and bone marrow infusion.
- More than six months since extremity injury with attempt at rehabilitation.

Similarly, Mendenhall (2020) outlined important clinical criteria to be considered for patient selection based on 20 years of experience at a transplant center. Ideally, the recipient is an adult aged 18 to 65 years, or if pediatric, aged eight years and above with bilateral upper limb loss. The recipient should have no significant coexisting medical or psychosocial issues, must be human immunodeficiency virus-negative, and have a negative cross-match with the donor. The recipient should exhibit significant quality of life burden and a previous unsuccessful trial with prostheses (Mendenhall, 2020). A qualitative study examining the preferences of 50 candidates for, or recipients of, an upper extremity vascularized composite allotransplantation found patient preferences for candidacy were similar (Vanterpool, 2023).

In addition, among hand transplantation centers around the world, Laspro (2023) identified the capacity to manage the allograft post-transplantation (e.g., access to follow-up, insurance coverage, psychological stability,

and history of medical compliance), as a common criterion. Factors related to the impact of immunosuppression were less underscored, and few factors were considered absolute contraindications.

A systematic review (Honeyman, 2021) of 15 articles (n = 37 patients with 39 vascularized composite allograft transplantation) suggests recipients of a solid organ transplant may be amenable to vascularized composite tissue allotransplantation without presenting additional short-term risk, but higher quality data reporting is needed.

Low-quality evidence from registry data and anecdotal reports suggests hand or forearm transplants are technically feasible, but data on functional outcomes are sparse, which affects the certainty of cost-effectiveness analyses. Ethical considerations for elective procedures require assessment of procedural risks against the quality-of-life benefit. The risks are associated with surgery, lifelong immunosuppression, and graft loss. Limited outcome data suggest restoration of functional status and normal body image and elimination of phantom limb phenomenon can be achieved. Functional outcomes may approximate those of hand replantation and be superior to those of prostheses in some patients, but a lack of agreement on appropriate outcome measures and varied levels of transplant make comparison of functional improvement difficult.

Considerably more surgical experience supports the hand replant procedure as the primary option after acute amputation. When a replant fails or is not possible, low-quality evidence suggests hand transplant may offer similar outcomes with respect to motor function, sensation, cosmesis, patient satisfaction/quality of life, adverse events, and side effects. The most common cause of transplant failure is acute rejection and immunosuppression-related side effects, while vascular insufficiency remains the main cause of replant failure. Hand transplant recipients typically receive more complex post-operative management than replant recipients, particularly immunosuppression, intense rehabilitation, and psychological support. Both procedures require significant patient commitment and realistic expectations to achieve the best possible outcomes (Heineman, 2020).

A systematic review reported complications in 66 recipients of upper extremity transplantation. The most common acute surgical complication was vascular anastomosis thrombosis (17%). Other postoperative complications included hematoma (2%) and seroma (2%). Immunological complications were acute rejection (92%) and chronic rejection (8%); 22% required allograft removal. The most frequent complications related to immunosuppression therapy were opportunistic infection (52%), impaired glucose metabolism (62%), renal insufficiency (26%), hypertension (15%), and hyperlipidemia (10%) (Milek, 2023).

A systematic review of 108 studies (n = 96 with 148 hand transplants), in which 57 patients experienced acute rejection, but disability scores of the arm, shoulder, and hand declined significantly, especially for distal transplants, and significant restoration of function and form was observed (Wells, 2022). A comparison of 26 hand transplants and 45 myoelectric prostheses in persons with upper extremity amputation showed similar quality-adjusted life-years between groups (P = .36), but significantly higher quality-adjusted life-years among myoelectric prostheses for unilateral amputees (P = .0015) (Efanov, 2022).

In 2018, we did not identify any relevant newly published guidelines or peer-reviewed reports. The policy ID was changed from 14.03.11 to CCP.1321.

In 2019, we did not identify any relevant newly published guidelines or peer-reviewed reports.

In 2020, we added a systematic review (Heineman, 2020) to the policy. The results warrant no policy change.

In 2021, We added results of a systematic review (Honeyman, 2021). No policy changes are warranted.

In 2022, we added a systematic review (Wells, 2022) and an analysis comparing hand transplant and myoelectric prosthesis outcomes (Efanov, 2022). No policy changes are warranted.

In 2023, we added an article with clinical criteria governing hand and upper extremity transplantation selection, contraindications, and outcomes measurement (Mendenhall, 2020).

In 2024, we added two systematic reviews (Laspro, 2023; Milek, 2023) and one qualitative study (Vanterpool, 2023) and deleted several older references from the policy. No policy changes are warranted.

References

On July 30, 2024, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were “Vascularized Composite Allotransplantation” (MeSH), “Transplantation, Homologous" (MeSH), “Upper Extremity” (MeSH), “Composite Tissue Allografts” (MeSH), “arm transplant,” and “hand transplant.” We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

80 FR 26464. Organ Procurement and Transplantation: Implementation of the HIV Organ Policy Equity Act.

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Efanov JI, Izadpanah A, Bou-Merhi J, Lin SJ, Danino MA. Applying health utility outcome measures and quality-adjusted life-years to compare hand allotransplantation and myoelectric prostheses for upper extremity amputations. *Plast Reconstr Surg*. 2022;149(3):465e-474e. Doi: 10.1097/PRS.0000000000008846.

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The Johns Hopkins University. Comprehensive Transplant Center. Comprehensive hand transplant program. https://www.hopkinsmedicine.org/transplant/programs/reconstructive-transplant/hand-arm-transplant.html. Published 2024.

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Policy updates

7/2017: initial review date and clinical policy effective date: 8/2017

9/2018: Policy references updated. Policy ID changed.

9/2019: Policy references updated.

9/2020: Policy references updated.

9/2021: Policy references updated.

9/2022: Policy references updated.

9/2023: Policy references updated.

9/2024: Policy references updated.