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**: 2/1/2025
Policy Number: ccp.1371	**Effective Date:** 5/2018 **Revision Date:** January 1, 2025
Policy Name: Chronic inflammatory response syndrome	

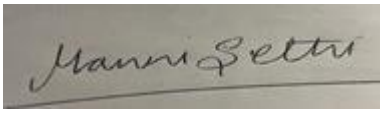
Type of Submission – Check all that apply:

- ☐ **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:

Please see tracked changes below.

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

Chronic inflammatory response syndrome

Clinical Policy ID: CCP.1371

Recent review date: 1/2025

Next review date: 5/2026

Policy contains: Chronic inflammatory response syndrome; dampness and mold hypersensitivity syndrome.

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

Chronic inflammatory response syndrome is an investigational/not clinically proven diagnosis and, therefore, not medically necessary.

Limitations

No limitations were identified during the writing of this policy.

Alternative covered services

Routine patient evaluation and management by a network health care provider.

Background

The named condition "chronic inflammatory response syndrome" seems to be related loosely to mold allergy and/or to chronic prostatitis and/or to ciguatera (fish poisoning) and other various toxicities and inflammations (e.g., Lyme disease) (Daschner, 2017). Shoemaker and colleagues (2010) first invented the phrase for multiorgan symptoms following exposure to the interior environment of a water-damaged building with toxigenic organisms along with a testing and treatment algorithm.

Findings

The condition is not recognized in Science Direct or PubMed as a pathologic entity. There is no International Statistical Classification of Diseases code assigned for chronic inflammatory response syndrome, nor are the systematic health effects of mold exposure well-understood (Daschner, 2017; World Health Organization, 2023).

There are only two single-author narrative reviews available to cite as evidence of a chronic inflammatory response syndrome (Berndtson, 2013), but neither appears to have been published in a scientific journal or peer-reviewed. These narratives state that:

> "Chronic inflammatory response syndrome (CIRS) diagnosis relies on the combination of a focused history and examination along with a systematic conduction of lab tests including genetic markers, markers of compliment, matrix metalloproteinase, anti-diuretic hormone, vascular endothelial growth factor (and others).
>
> The Shoemaker (2010) treatment protocol follows this algorithm: 1) remove from ongoing sources of exposure, 2) reduce toxin carriage in the home, office, or school as feasible, as well as in the body of the patient 3) eradicate multiple antibiotic resistant coagulase-negative staph if present, 4) normalize melanocyte stimulating hormone, 5) normalize matrix metalloproteinase, 6) normalize anti-diuretic hormone/osmolality, 7) normalize vascular endothelial growth factor, 8) normalize C4a, 9) normalize transforming growth factor beta-1, 10) normalize CD4+CD25+, 11) if symptoms persist despite scaling this pyramid, replace vasoactive intestinal polypeptide."

The cited references in these papers are in the main laboratory reports of isolated enzymatic and environmental findings proposed as pathophysiologic factors in various disease states. There are no unifying clinical studies that establish a relationship between these disparate laboratory and environmental observations and a disease entity (Australian Standing Committee on Health, Aged Care and Sport, 2018).

In 2021, we found no additional information to add to the policy.

In 2022, we updated the references with no policy changes.

In 2023, we updated the references with no policy changes.

In 2024, we updated the references with no policy changes.

In 2025, we found a 2018 consensus statement developed by a group of physicians specializing in biotoxin-related illnesses. Titled "Diagnostic Process for Chronic Inflammatory Response Syndrome (CIRS): A Consensus Statement," the document defines chronic inflammatory response syndrome as a clinical condition characterized by specific diagnostic criteria. These criteria include documented exposure to biotoxins, multi-system illness, distinct laboratory abnormalities, and a positive response to treatment. The statement identifies key diagnostic biomarkers, such as inflammatory markers (C4a, MMP9, TGF-beta-1) and regulatory neuropeptides (MSH and VIP). It also outlines symptom-based criteria, requiring the presence of at least eight out of 13 defined symptom clusters in adults. While the consensus incorporates advanced diagnostic tools like transcriptomics research and brain volumetric studies, its recommendations are primarily grounded in observational studies and clinical experience rather than large-scale randomized controlled trials (Shoemaker, 2018).

References

On December 6, 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 “chronic inflammatory response syndrome” and “dampness and mold hypersensitivity syndrome.” 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.

Australian Standing Committee on Health, Aged Care and Sport. Report on the inquiry into biotoxin-related illnesses in Australia. 3. Chronic inflammatory response syndrome (CIRS). Commonwealth of Australia. https://www.aph.gov.au/Parliamentary_Business/Committees/House/Health_Aged_Care_and_Sport/BiotoxinIllnesses/Report. Published October, 2018.

Berndtson K. Chronic inflammatory response syndrome: Overview, diagnosis, and treatment. Surviving Mold website. https://www.survivingmold.com/docs/Berndtson_essay_2_CIRS.pdf. Published 2013.

Daschner A. An Evolutionary-based framework for analyzing mold and dampness-associated symptoms in DMHS. *Front Immunol*. 2017;7:672. Doi:10.3389/fimmu.2016.00672.

Shoemaker R, Mark L, McMahon S. Research Committee report on diagnosis and treatment of chronic inflammatory response syndrome caused by exposure to the interior environment of water-damaged buildings. Pocomoke: Expert Treating Physicians Consensus. https://www.researchgate.net/profile/Jack-Thrasher-2/publication/242702167_Research_Committee_Report_on_Diagnosis_and_Treatment_of_Chronic_Inflammatory_Response_Syndrome_Caused_by_Exposure_to_the_Interior_Environment_of_Water-Damaged_Buildings/links/0deec537b7d87307b0000000/Research-Committee-Report-on-Diagnosis-and-Treatment-of-Chronic-Inflammatory-Response-Syndrome-Caused-by-Exposure-to-the-Interior-Environment-of-Water-Damaged-Buildings.pdf. Published July 27, 2010.
Shoemaker R, Johnson K, Jim L, Berry Y, Dooley M, Ryan J, McMahon S. Diagnostic process for chronic inflammatory response syndrome (CIRS): A consensus statement report of the consensus committee of Surviving Mold. *Internal Medicine Review*. 2018; 4: 1-47.

World Health Organization. International Statistical Classification of Diseases (ICD) and Related Health Problems, 11th Revision. https://icd.who.int/browse11/l-m/en. Published January 2023.

Policy updates

3/2018: initial review date and clinical policy effective date: 5/2018

4/2019: Policy references updated.

1/2020: Policy references updated.

1/2021: Policy references updated.

1/2022: Policy references updated.

1/2023: Policy references updated.

1/2024: Policy references updated.

1/2025: Policy references updated.