Policy Title:	Hemochromatosis HFE Genetic Testing	Number & Version:	UM-HFE Gene v4
Functional Unit:	Utilization Management	Effective Date:	04/18/2025
Policy Owner (Title):	Senior Director, Utilization Management	Page Number:	1 of 4

I. POLICY STATEMENT and PURPOSE

In its administration of Medicare Advantage plans (Health Plans), the Company shall determine benefits in accordance with the requirements of the Centers for Medicare & Medicaid Services (CMS). Where CMS has established a national coverage policy on an item or service or a local Medicare contractor has done so as authorized by CMS, the Company follows the Medicare coverage policy. In the absence of fully established Medicare coverage criteria, the Company may develop and implement internal criteria based on current evidence in widely used treatment guidelines or clinical literature. Internal criteria are reviewed and approved by the Medical Management Committee and are made publicly accessible.

CMS has not established national coverage criteria for Hemochromatosis HFE Genetic Testing, therefore the Company has developed and implemented this coverage policy to ensure that patients receive clinically appropriate, medically necessary care at the appropriate level, which allows for the best clinical outcome and prevents harm such as inpatient acquired illness. The purpose of this policy is to describe the circumstances under which Hemochromatosis HFE Genetic Testing would be considered medically necessary.

II. BACKGROUND

A gene called "HFE" is most often the cause of hereditary hemochromatosis (HH). Each parent contributes one HFE gene to their offspring. The HFE gene has two common mutations, C282Y and H63D, which can be identified via genetic testing. Individuals who inherit two abnormal genes may develop hemochromatosis and pass the mutation on to their children. Not all people who inherit these two abnormal genes develop problems linked to the iron overload of hemochromatosis. If an individual inherits one abnormal gene, they are unlikely to develop hemochromatosis but are considered a gene mutation carrier and can pass the mutation on to their children. This individual's children would not develop the disease unless they also inherited another abnormal gene from the other parent (Mayo, 1998-2025).

Clinical HFE hemochromatosis is distinguished by storage of excessive iron in the liver, skin, pancreas, heart, joints, and anterior pituitary gland. Initial symptoms may manifest as pain in the abdomen, fatigue, weakness, loss of weight, joint pain, and diabetes. If the serum ferritin level is higher than 1,000µg/L, the risk of cirrhosis of the liver is increased. Other conditions can include progressive increase in skin pigmentation, congestive heart failure, arrhythmias, arthritis, and hypogonadism. The condition is more common in men than women (Barton, 2000).

Hereditary hemochromatosis can be safely and effectively treated by removing blood from the body (phlebotomy) on a regular basis. The goal of phlebotomy is to reduce the iron levels to normal. The amount of blood removed and how often it is removed depends on the patient's age, overall health, and degree of iron overload. Initially, this treatment may be done once or

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twice a week. When iron levels return to normal, the treatment will typically be performed every two or three months. Maintenance treatment depends on how rapidly the iron re-accumulates. Treating hereditary hemochromatosis can help ease the symptoms of tiredness, abdominal pain and skin darkening and can help prevent complications such as liver disease, heart disease and diabetes. Some of these conditions can be slowed or reversed. Phlebotomy will not reverse cirrhosis or joint pain, but it can slow the progression. If phlebotomy is not feasible, because of anemia or heart complications, chelation medication to remove excess iron may be used. The medication can be injected, or it can be taken as a pill. Chelation is not a common treatment for hereditary hemochromatosis (Mayo, 2023).

III. SCOPE

This Policy applies to Hemochromatosis Genetic Testing for HFE.

IV. DEFINITIONS

Chelation – The use of medication to bind excess (in this case, iron) allowing the body to expel the substance through urine or stool (Mayo, 1998-2025).

Hereditary Hemochromatosis (HH) – a hereditary disease that causes the accumulation of too much iron in the liver, pancreas, skin, heart, pituitary gland, and joints (Barton, 2024).

Genetic Testing – medical testing that examines DNA (the chemical database that drives the body's functions) for changes (mutations) in genes that may cause illness or disease. (Mayo, 1998-2025).

Medically Necessary - Covered Services rendered by a Health Care Provider that the Plan determines are:

1) Safe and effective
2) Not experimental or investigational
3) Appropriate for patients,
   a) including the duration and frequency that is considered appropriate for the item or service, in terms of whether it is—
      i) furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member,
      ii) furnished in a setting appropriate to the patient's medical needs and condition,
      iii) ordered and furnished by qualified personnel,
      iv) one that meets, but does not exceed, the patient's medical need; and
      v) is at least as beneficial as existing and available medically appropriate alternatives.

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V. OWNERSHIP & TRAINING

The Senior Director of Utilization Management is responsible for administration, oversight, and training regarding performance under this Policy.

VI. PROTOCOLS / COVERAGE POLICY

The Protocols/Coverage policies that follow pertain ONLY to the following states: AR, KY, IN, MO, OH, MI.

Hemochromatosis Genetic Testing for HFE is considered medically necessary in patients with evidence of iron overload (measured transferrin saturation greater than 45% and ferritin greater than 300µg/L; Lanktree, 2015). Liver biopsy for iron overload should be reserved when analysis of the patient's condition is not feasible through non-invasive means or when second overlapping liver disease is being considered (Palmer, 2018). The genotyping of patients with iron overload of uncertain etiology is allowed only once per lifetime.

VII. SUMMARY OF EVIDENCE

Hemochromatosis Genetic Testing for HFE is considered medically necessary when the patient has iron overload of unknown etiology, and the practitioner is trying to avoid performing a liver biopsy. This test is allowed once per lifetime.

VIII. REGULATORY REFERENCES / CITATIONS

CMS National Coverage Determinations (NCDs)	none
CMS Local Coverage Determinations (LCDs)	L35000
CMS Local Coverage Article (LCAs)	none

ID	Title	Type	Service Area	Contractor
L35000	Molecular Pathology Procedures	LCD	CT, IL, MA, ME, MN, NH, NY, RI, VT, WI	National Government Services, Inc. (MAC - Part A, MAC - Part B)

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IX. PROFESSIONAL REFERENCES / CITATIONS

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2. Lanktree, Matthew B.; et. al. Examining the clinical use of hemochromatosis genetic testing. National Center for Biotechnology Information. Volume 29; Issue 1; Pg. 41-45. Issued 2015. Accessed March 2025. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4334066/

3. Mayo Clinic; Diseases & Conditions: Hemochromatosis, and Related Associated Procedures: Genetic Testing. Published 1998-2025. Accessed March 2025. https://www.mayoclinic.org/diseases-conditions/hemochromatosis/symptoms-causes/syc-20351443, and https://www.mayoclinic.org/tests-procedures/genetic-testing/about/pac-20384827

4. Palmer, William C.; et. al. Diagnosis and Management of Genetic Iron Overload Disorders. National Center for Biotechnology Information. Volume 33; Issue 12. Issued 2018. Accessed March 2025. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6258594/

APPROVALS:

Chief Medical Officer
(MMC Chair): Saria Saccocio, MD

VERSION HISTORY:

Version	Date	Author	Purpose/Summary of Major Changes
01	08/12/2022	Gina Vehige	Annual review. Approved by Lumeris QMMC 08/12/2022
02	08/02/2023	Gina Vehige	Annual review. Updated MAC table, updated links, no changes to criteria.
03	04/24/2024	Gina Vehige	Annual review. Addition to policy statement, reference checks; summary of evidence. Approval by MMC 6/7/2024.
04	03/17/2025	Sheila Gray / Kerrie Stehl	Annual review; reference checks; no substantive changes. Approved by MMC 04/16/2025.

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