Policy Title:	Policy – Hemochromatosis HFE Genetic Testing	Number & Version:	UM-Gene HFE.v.1
Functional Unit:	Utilization Management	Effective Date:	09/01/2022
Policy Owner (Title):	Director, Utilization Management	Page Number:	1 of 6

I. POLICY STATEMENT and PURPOSE

The purpose of this policy is to describe the circumstances under which HFE-related Hemochromatosis gene testing would or would not be considered medically necessary for members under the guidelines used for clinical review of organizational determinations.

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 (MFMER, 2022).

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 is level is higher than 1,000 ng/mL, the risk of cirrhosis of the liver is increased. Other conditions noted 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).

HH 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 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 (MFMER, 2022).

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 (MFMER, 2022).

HH or Hemochromatosis – HH or Hemochromatosis may also be referred to as Hemochromatosis Type 1, HFE-Associated Hemochromatosis, or HFE-HH and is a hereditary disease that causes the accumulation of too much iron in the liver, pancreas, skin, heart, pituitary gland, and joints (Barton, 2000) (CDC, 2022).

Genetic Testing - A medical test that looks for changes in DNA. Genetic tests analyze cells or tissue to look for any changes in genes, chromosomes, and proteins (NIH, 2021).

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.

V. OWNERSHIP & TRAINING

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

VI. PROTOCOLS / COVERAGE POLICY

Hemochromatosis Genetic Testing for HFE is considered **not medically necessary** because of a lack of peer-reviewed studies that support the clinical usefulness of genetic testing for HFE

gene variants in symptomatic or asymptomatic patients who are suspected of HH and who have biochemical iron overload (AAFP, 2022) (Bacon, 2011) (Hayes, 2021).

VII. REGULATORY REFERENCES / CITATIONS

CMS National Coverage Determinations (NCDs) None
CMS Local Coverage Determinations (LCDs) L34519, L35000

See Table Next

ID	Title	Type	Contractor
Title Results (3)			
L34519	Molecular Pathology Procedures	LCD	First Coast Service Options, Inc.
L35000	Molecular Pathology Procedures	LCD	National Government Services, Inc.

NOTE: A table on the last page of the policy lists the states covered by the contractor.

VIII. PROFESSIONAL REFERENCES / CITATIONS

1. American Academy of Family Physicians (AAFP). Publications. American Family Physician Collections. Choosing Wisely. 284. 2022. Choosing Wisely Recommendations. Don't order HFE genetic testing for a patient without iron overload or a family history of HFE-associated hereditary hemochromatosis. Accessed at: https://www.aafp.org/pubs/afp/collections/choosing-wisely/284.html on June 29, 2022.

2. Bacon, Bruce R., et. al. Hepatology. Vol. 54, No. 1, 2011. AASLD Practice Guideline. Diagnosis and Management of Hemochromatosis: 2011 Practice Guideline by the American Association for the Study of Liver Diseases. Accessed at: https://www.aasld.org/sites/default/files/2019-06/Hemochromatosis2011.pdf on June 29, 2022.

3. Barton JC, Edwards CQ. HFE Hemochromatosis. 2000 Apr 3 [Updated 2018 Dec 6]. In: Adam MP, Mirzaa GM, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1440/ Accessed at: https://www.ncbi.nlm.nih.gov/books/NBK1440/#:~:text=Individuals%20with%20clinical%20HFE%20hemochromatosis,Age%20of%20onset on June 29, 2022.

4. Centers for Disease Control and Prevention (CDC). Office of Science (OS), Office of Genomics and Precision Public Health. Hereditary Hemochromatosis. May 20, 2022. Accessed at: https://www.cdc.gov/genomics/disease/hemochromatosis.htm#:~:text=Hereditary%20hemochromatosis%20is%20a%20genetic,about%20testing%20for%20hereditary%20hemochromatosis on June 29, 2022.

5. Hayes. Knowledge Center. Search Results. Genetic Testing for Hereditary Hemochromatosis in Patients with Iron Overload. September 29, 2021. Accessed at: https://evidence.hayesinc.com/report/gtu.hemochromatosis.1405 on June 29, 2022.

6. Mayo Foundation for Medical Education and Research (MFMER). Patient Care & Health Information. Diseases & Conditions. Hemochromatosis. Accessed at: https://www.mayoclinic.org/diseases-conditions/hemochromatosis/symptoms-causes/syc-20351443 and https://www.mayoclinic.org/diseases-conditions/hemochromatosis/diagnosis-treatment/drc-20351448 on June 29, 2022.

7. National Institutes of Health (NIH). MedlinePlus. Bethesda (MD): National Library of Medicine (US). Updated June 11, 2021. Medical Test. Genetic Testing. Accessed at: https://medlineplus.gov/genetictesting.html on June 15, 2022.

IX. RELATED POLICIES / PROCEDURES

None

X. ATTACHMENTS

See Section VII.

APPROVALS:

	Printed Name	Signature
Senior Medical Director, UM:	Michael Fusco, MD	
Corporate Chief Medical Officer (QMMC Chair):	Debbie Zimmerman, MD	

VERSION HISTORY:

Version #	Date	Author	Purpose/Summary of Major Changes
01	08/12/2022	Gina Vehige	Original – Approved by Lumeris QMMC 08/12/2022

Medicare Administrative Contractors (MACs)
As of June 2021

MAC Jurisdiction	Processes Part A & Part B Claims for the following states/territories:	MAC
DME A	Connecticut, Delaware, District of Columbia, Maine, Maryland, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, Vermont	Noridian Healthcare Solutions, LLC
DME B	Illinois, Indiana, Kentucky, Michigan, Minnesota, Ohio, Wisconsin	CGS Administrators, LLC
DME C	Alabama, Arkansas, Colorado, Florida, Georgia, Louisiana, Mississippi, New Mexico, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, West Virginia, Puerto Rico, U.S. Virgin Islands	CGS Administrators, LLC
DME D	Alaska, Arizona, California, Hawaii, Idaho, Iowa, Kansas, Missouri, Montana, Nebraska, Nevada, North Dakota, Oregon, South Dakota, Utah, Washington, Wyoming, American Samoa, Guam, Northern Mariana Islands	Noridian Healthcare Solutions, LLC
5	Iowa, Kansas, Missouri, Nebraska	Wisconsin Physicians Service Government Health Administrators
6	Illinois, Minnesota, Wisconsin **HH + H for the following states: Alaska, American Samoa, Arizona, California, Guam, Hawaii, Idaho, Michigan, Minnesota, Nevada, New Jersey, New York, Northern Mariana Islands, Oregon, Puerto Rico, US Virgin Islands, Wisconsin and Washington	National Government Services, Inc.
8	Indiana, Michigan	Wisconsin Physicians Service Government Health Administrators
15	Kentucky, Ohio **HH + H for the following states: Delaware, District of Columbia, Colorado, Iowa, Kansas, Maryland, Missouri, Montana, Nebraska, North Dakota, Pennsylvania, South Dakota, Utah, Virginia, West Virginia, and Wyoming	CGS Administrators, LLC
E	California, Hawaii, Nevada, American Samoa, Guam, Northern Mariana Islands	Noridian Healthcare Solutions, LLC
F	Alaska, Arizona, Idaho, Montana, North Dakota, Oregon, South Dakota, Utah, Washington, Wyoming	Noridian Healthcare Solutions, LLC
H	Arkansas, Colorado, New Mexico, Oklahoma, Texas, Louisiana, Mississippi	Novitas Solutions, Inc.
J	Alabama, Georgia, Tennessee	Palmetto GBA, LLC
K	Connecticut, New York, Maine, Massachusetts, New Hampshire, Rhode Island, Vermont **HH + H for the following states: Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, and Vermont	National Government Services, Inc.
L	Delaware, District of Columbia, Maryland, New Jersey, Pennsylvania (includes Part B for counties of Arlington and Fairfax in Virginia and the city of Alexandria in Virginia)	Novitas Solutions, Inc.
M	North Carolina, South Carolina, Virginia, West Virginia (excludes Part B for the counties of Arlington and Fairfax in Virginia and the city of Alexandria in Virginia) **HH + H for the following states: Alabama, Arkansas, Florida, Georgia, Illinois, Indiana, Kentucky, Louisiana, Mississippi, New Mexico, North Carolina, Ohio, Oklahoma, South Carolina, Tennessee, and Texas	Palmetto GBA, LLC
N	Florida, Puerto Rico, U.S. Virgin Islands	First Coast Service Options, Inc.

**Also Processes Home Health and Hospice claims