**LETTER OF MEDICAL NECESSITY FOR**

**SITOSTEROLEMIA GENETIC TESTING**

Date: Date of Service/claim

To: Utilization Review Department

Insurance Company Name, Address, City, State

Re: Patient Name, DOB, ID #

ICD-10 Codes:

The ICD-10 codes listed below are commonly received by Ambry from ordering providers for the testing described in this letter. Ambry provides this information as a customer service but makes no recommendations regarding the use of any diagnosis codes. As a reminder, it is the ordering provider’s responsibility to always determine, for the specific date of service, the appropriate diagnostic codes based on the patient’s signs and symptoms.

Code Description

E78.00 PURE HYPERCHOLESTEROLEMIA, UNSPECIFIED

E78.01 FAMILIAL HYPERCHOLESTEROLEMIA

Z84.81 FAMILY HISTORY OF CARRIER OF GENETIC DISEASE

This letter is regarding my patient and your subscriber, refenced above, to request full coverage of medically indicated genetic testing for sitosterolemia to be performed by Ambry Genetics Corporation.

Sitosterolemia is an autosomal recessive disorder characterized by mild hypercholesterolemia, tendon or tuberous xanthomas, premature atherosclerosis, macrothrombocytopenia and hemolytic anemia.  Some individuals present with the hematological manifestations and age of presentation may depend on diet.  As the usual clinical test for plasma concentration of cholesterol does not directly measure plant sterols, sitosterolemia is likely to be underdiagnosed.  Some patients may be misdiagnosed as having familial hypercholesterolemia, which has a different etiology and different management strategies.  Left undiagnosed and untreated or mismanaged, **patients are at risk for myocardial infarction and sudden death**.1,2,3

The genetic etiology of sitosterolemia is established and is associated with genes involved in the absorption and excretion of phytosterols (such as *ABCG5* and *ABCG8*). **Significant aspects of my patient’s personal and/or family medical history that suggest sitosterolemia**2 **include:** [check all that apply]

* Hypercholesterolemia that shows unexpected significant response to low-fat diet modification or to bile acid sequestrant (e.g., cholestyramine) therapy
* Hypercholesterolemia that does not respond to statin therapy
* Tendon xanthomas or tuberous xanthomas
* Premature atherosclerosis (which may lead to angina, myocardial infarction, and sudden death)
* Hemolytic anemia (usually associated with abnormally shaped erythrocytes called stomatocytes) and/or thrombocytopenia (usually associated with large platelets/macrothrombocytopenia)
* Other: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**The clinical utility of genetic testing for sitosterolemia has been recognized and is supported as standard of care**.1,2,3,5

Identification of a mutation through genetic testing confirms a diagnosis of sitosterolemia or a predisposition to sitosterolemia.  Genetic testing also informs prognosis, screening and treatment options, prevention efforts and genetic counseling, which can vary depending on the specific gene implicated in the disease.1,2 Published management guidelines are available for sitosterolemia.5 For example, compared to individuals with Familial Hypercholesterolemia:

* Individuals with sitosterolemia need to follow a diet *low* in plant sterols and also low in shellfish.3 While plant sterols are recommended in patients with typical hypercholesterolemia, they are contraindicated in sitosterolemia.5
* Ezetimibe is useful as it specifically targets plant sterols.3,4 Sitosterolemia does not respond to standard statin treatment.5
* Bile acid sequestrants such as cholestryramine may be considered in those with incomplete response to ezetimibe.2,3,5

Specifically for this patient, the results of the genetic test are necessary to consider in the following areas: [check all that apply]

* Genetic testing could allow immediate management and treatment to anticipate and control common clinical findings based on the results of the testing
* Genetic testing could inform lifestyle modifications for the patient
* Genetic testing could assist in long-term management and monitoring of suspected disease progression based on the results of the testing
* Genetic testing will lead to changes in diagnostic procedures such that more potentially invasive alternative procedures could be avoided, reducing unnecessary tests and cost
* Genetic testing will lead to informed decisions for other family members with similar conditions, or that may be at risk for similar conditions
* Genetic testing could alleviate the need for long-term clinical surveillance in individuals who test negative for any disease-causing variants found in my patient
* Other: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Due to the risks associated with these mutations and the interventions available to reduce these risks, **I am requesting coverage for this testing as medically necessary care and affirm that my patient has provided informed consent for genetic testing.** I recommend that you support this request for coverage of diagnostic genetic testing for sitosterolemia in my patient.

Thank you for your time and please don’t hesitate to contact me with any questions.

Sincerely,

Ordering Clinician Name (Signature Provided on Test Requisition Form)

(MD/DO, Clinical Nurse Specialist, Nurse-Midwives, Nurse Practitioner, Physician Assistant, Genetic Counselor\*)

\*Authorized clinician requirements vary by state

**Test Details**

Test Name: Sitosterolemia

CPT codes: 81479

Laboratory: Ambry Genetics Corporation (TIN 33-0892453 / NPI 1861568784), a CAP-accredited and CLIA-certified laboratory located at 7 Argonaut, Aliso Viejo, CA 92656

**References**

1. Tada H, et al. Sitosterolemia, Hypercholesterolemia, and Coronary Artery Disease.  [J Atheroscler Thromb.](https://www.ncbi.nlm.nih.gov/pubmed/30033951) 2018 Sep 1;25(9):783-789.
2. Myrie SB, et al. Sitosterolemia. 2013 Apr 4 [Updated 2020 July 16]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022.
3. Tzavella E, et al. Sitosterolemia: A multifaceted metabolic disorder with important clinical consequences.  [J Clin Lipidol.](https://www.ncbi.nlm.nih.gov/pubmed/28545928) 2017 Jul - Aug;11(4):1095-1100.
4. Tsubakio-Yamamoto K, et al. Current therapy for patients with sitosterolemia--effect of ezetimibe on plant sterol metabolism.  [J Atheroscler Thromb.](https://www.ncbi.nlm.nih.gov/pubmed/?term=Tsubakio-Yamamoto+sitosterolemia) 2010 Sep 30;17(9):891-900.
5. Tada H, et al. Diagnosis and Management of Sitosterolemia 2021. [J Atheroscler Thromb.](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8326170/) 2021 Aug 1; 28(8): 791–801.