Genetic Testing for Statin-Induced Myopathy

Policy # 00377
Original Effective Date: 08/21/2013
Current Effective Date: 09/12/2022

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the “Company”), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Services Are Considered Not Medically Necessary
Based on review of the available data, the use of genetic testing for the presence of variants in the \textit{SLCO1B1} gene to identify patients at risk of statin-induced myopathy is considered to be not medically necessary.**

Background/Overview

Statins
HMG-CoA reductase inhibitors, or statin drugs, are the primary pharmacologic treatment for hypercholesterolemia worldwide. In the U.S., an estimated 38 million people took statins in 2008. The use of statins is associated with an approximately 30\% reduction in cardiovascular events across a wide variety of populations.

Commercially Available SLCO1B Molecular Diagnostic Tests
Several commercial and academic labs offer genetic testing for statin-induced myopathy (SLCO1B1) variants, including Boston Heart Diagnostics and ARUP Laboratories. Other labs offer panel tests for drug metabolism that include the SLCO1B1 gene; for example, ApolloGen.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments. The Boston Heart Statin Induced Myopathy (SLCO1B1) Genotype test and ARUP Laboratories Statin Sensitivity SLCO1B1 are available under the auspices of the Clinical Laboratory Improvement Amendments. Laboratories that offer laboratory-developed tests must be licensed by the Clinical Laboratory Improvement Amendments for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of this test.
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Rationale/Source
This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

HMG-CoA reductase inhibitors, or statins, which are widely used to treat hypercholesterolemia, can cause muscle-related adverse events. Serious myopathy (ie, myositis, rhabdomyolysis) can also occur and may be associated with variants in the SLCO1B1 gene. Commercially available tests for the presence of SLCO1B1 variants are marketed for use in predicting the risk of myopathy for patients taking statins.

Summary of Evidence
For individuals who are taking statin drugs who receive genetic testing for SLCO1B1 variants, the evidence includes a systematic review and two randomized controlled trials. Relevant outcomes are symptoms, quality of life, morbid events, and treatment-related morbidity. Direct evidence for clinical utility in this setting would come from studies demonstrating that using the SLCO1B1 genotype to inform statin therapy (statin dose or choice of a specific drug) has positive outcomes in terms of lower rates of myopathy with adequate lipid control and tolerability of alternative treatments. The systematic review findings suggested that certain alleles carry less risk of statin-induced myopathy compared with others. Two randomized controlled trials were identified that evaluated adherence to medication and/or lipid control in patients whose physicians were informed of the SLCO1B1 haplotype at the beginning or at the end of the study. No significant benefits were identified in adherence to medications or in pain related to myopathy with knowledge of the SLCO1B1 haplotype status. There was a short-term (3-month) decrease in low-density lipoprotein (LDL) in the active treatment group in one trial, but knowledge of SLCO1B1 status did not provide benefit in LDL lowering in the other trial after 12 months. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.
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Supplemental Information
Practice Guidelines and Position Statements
Guidelines or position statements will be considered for inclusion in ‘Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

Clinical Pharmacogenetics and Pharmacogenomics Implementation Consortium
In 2012, the Clinical Pharmacogenetics and Pharmacogenomics Implementation Consortium issued guidelines for SLCO1B genotypes and simvastatin-induced myopathy, which were updated in 2014. These guidelines on patient management for various SLCO1B genotypes recommended prescribing a lower dose or considering an alternative statin and considering routine creatinine kinase surveillance in patients with SLCO1B genotypes consistent with intermediate or low statin metabolism.

U.S. Preventive Services Task Force Recommendations
Not applicable.

Medicare National Coverage
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials
A search of ClinicalTrials.gov in October 2021 did not identify any ongoing or unpublished trials that would likely influence this review.

References
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Policy History
Original Effective Date: 08/21/2013
Current Effective Date: 09/12/2022
08/01/2013 Medical Policy Committee review
08/21/2013 Medical Policy Implementation Committee approval. New policy.
08/07/2014 Medical Policy Committee review
08/20/2014 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/06/2015 Medical Policy Committee review
08/19/2015 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/04/2016 Medical Policy Committee review
08/17/2016 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/01/2017 Coding update: Removing ICD-9 Diagnosis Codes
08/03/2017 Medical Policy Committee review
01/01/2018 Coding update
02/06/2018 Coding update
08/09/2018 Medical Policy Committee review
08/15/2018 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

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08/01/2019 Medical Policy Committee review
08/14/2019 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/06/2020 Medical Policy Committee review
08/12/2020 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
09/14/2020 Coding update
08/05/2021 Medical Policy Committee review
08/04/2022 Medical Policy Committee review
08/10/2022 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 08/2023

Coding
The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®), copyright 2021 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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Current Effective Date:  09/12/2022

contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

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Codes used to identify services associated with this policy may include (but may not be limited to) the following:

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<tr>
<td>CPT</td>
<td>81328, 81400, 81479</td>
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<tr>
<td>HCPCS</td>
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<td>ICD-10 Diagnosis</td>
<td>G71.14, G71.20, G71.21, G71.220, G71.228, G71.29, T46.6X5</td>
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**Medically Necessary (or “Medical Necessity”)** - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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NOTICE: If the Patient’s health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

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