Genetic Testing for Statin-Induced Myopathy

Policy # 00377
Original Effective Date: 08/21/2013
Current Effective Date: 09/13/2021

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.

Note: Cochlear Implant is addressed separately in medical policy 00017.

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 *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.

Rationale/Source

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.

For individuals who are taking statin drugs who receive genetic testing for *SLCO1B1* variants, the evidence includes a systematic review and a randomized controlled trial. 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. One randomized controlled trial was identified that evaluated adherence to medication and 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 with knowledge of the *SLCO1B1* haplotype status. There was a decrease in low-density lipoprotein cholesterol at 3 months but not at 8 months in the active intervention group. Interpretation of this trial is limited due to the lack of blinding of participants and short-term outcomes, which might have affected adherence to medications and patient responses on questionnaires. The evidence is insufficient to determine the effects of the technology on health outcomes.

Supplemental Information

Practice Guidelines and Position Statements

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
Some currently ongoing and unpublished trials that might influence this review are listed in Table 1.

Table 1. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT02871934	Clinical Safety and Efficacy of Pharmacogenetics in Veteran Care	408	Dec 2020

NCT: national clinical trial.

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Policy History

Original Effective Date: 08/21/2013
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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
08/23/2017	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
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.
08/01/2019	Medical Policy Committee review
08/14/2019	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

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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
08/11/2021	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 08/2022

Coding

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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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Code Type	Code
CPT	81328, 81400, 81479
HCPCS	No codes
ICD-10 Diagnosis	G71.14, T46.6X5 Added codes eff 10/1/2020: G71.20, G71.21, G71.220, G71.228, G71.29

**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.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.