BlueCross BlueShield Federal Employee Program.

FEP Medical Policy Manual

FEP 2.04.96 Genetic Testing for Statin-Induced Myopathy

Annual Effective Policy Date: April 1, 2026

Original Policy Date: March 2018

Related Policies:

None

Genetic Testing for Statin-Induced Myopathy

Description

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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.

OBJECTIVE

The objective of this evidence review is to determine whether genetic testing for *SLCO1B1* variants improves the net health outcome when used to predict myopathy among individuals taking statins.

POLICY STATEMENT

Genetic testing for the presence of variants in the *SLCO1B1* gene to identify individuals at risk of statin-induced myopathy is considered **investigational**.

POLICY GUIDELINES

None

BENEFIT APPLICATION

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

Screening (other than the preventive services listed in the brochure) is not covered. Please see Section 6 General exclusions.

Benefits are available for specialized diagnostic genetic testing when it is medically necessary to diagnose and/or manage a patient's existing medical condition. Benefits are not provided for genetic panels when some or all of the tests included in the panel are not covered, are experimental or investigational, or are not medically necessary.

FDA REGULATORY STATUS

Some Plans may have contract or benefit exclusions for genetic testing, or have state mandates for biomarker testing coverage.

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

Summary of Evidence

For individuals who are taking statin drugs who receive genetic testing for statin-induced myopathy (*SLCO1B1)* variants, the evidence includes a systematic review, a network meta-analysis, and 2 randomized controlled trials (RCTs). 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 RCTs 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 1 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.

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.

American Heart Association

In 2019, the American Heart Association (AHA) published a scientific statement focused on statin safety and associated adverse events.[9] Regarding genetic testing for SLCO1B1 variants, the AHA noted that: *"..polymorphisms in the SLCO1B1 gene account for a small proportion of cases of statin-induced myopathy."* No specific recommendations for or against testing were provided.

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 and again in 2022.[17] The 2022 guideline update reorganized genotype-phenotype categories and expanded upon recommendations for statin selection and dosing recommendations according to phenotype, statin intensity according to 2018 American College of Cardiology/American Heart Association guidelines, and strength of supportive data.

Dutch Pharmacogenetics Working Group

In 2024, the Dutch Pharmacogenetics Working Group (DPWG) issued guidelines for *SLCO1B* genotypes and simvastatin-induced myopathy as well as *CYP2C9* genotypes for sulfonylureas. [34] The DPWG believes that genetic testing for *SLCO1B* variants is 'essential' for simvastatin 80 mg/day, 'beneficial" for simvastatin up to 40 mg/day, and 'potentially beneficial" for atorvastatin and rosuvastatin thus, issuing the following recommendations:

- "For simvastatin, the DPWG recommends choosing an alternative in homozygotes for these gene variant and to preferably choose an alternative in heterozygotes.
- For atorvastatin, the DPWG recommends to preferably choose an alternative in carriers of this gene variant having additional risk factors for myopathy.
- For rosuvastatin, the DPWG recommends keeping the dose as low as possible in carriers of this gene variant with additional risk factors.
- For fluvastatin and pravastatin, no therapy adjustment is required in carriers of this gene variant"

National Lipid Association

In 2023, the National Lipid Association (NLA) published a clinical perspective focused on the assessment and management of statin-associated muscle symptoms (SAMS).[10] Regarding genetic testing for SLCO1B1 variants, the NLA noted: *"The SLCO1B1 rs4149056 variant...has the most evidence supporting its association with the SAMS phenotype, but it has not been routinely measured in clinical care."* Furthermore, the publication notes that: *"Genetic testing has not become the standard of care because some patients with pharmacologic SAMS may have no identifiable causative variants, while others with known causative variants never develop SAMS."*

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.

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POLICY HISTORY - THIS POLICY WAS APPROVED BY THE FEP® PHARMACY AND MEDICAL POLICY COMMITTEE ACCORDING TO THE HISTORY BELOW:

Date	Action	Description
March 2018	New policy	Genetic testing for the presence of variants in the SLCO1B1 gene for the purpose of identifying patients at risk of statin-induced myopathy is considered not medically necessary.
March 2019	Replace policy	Policy updated with literature review through September 4, 2018; references 13-14 added. Policy statement unchanged.
March 2020	Replace policy	Policy updated with literature review through September 9, 2019; references added. Policy statement unchanged.
March 2021	Replace policy	Policy updated with literature review through September 14, 2020; no references added. Policy statement unchanged.
March 2022	Replace policy	Policy updated with literature review through October 4, 2021; reference added. Policy statement unchanged.
March 2023	Replace policy	Policy updated with literature review through September 23, 2022; references added. Not Medically Necessary policy statement changed to Investigational and other minor editorial refinements to policy statements; intent unchanged.
March 2024	Replace policy	Policy updated with literature review through September 19, 2023; references added. Policy statement unchanged.
March 2025	Replace policy	Policy updated with literature review through September 25, 2024; references added. Policy statement unchanged.
March 2026	Replace policy	Policy updated with literature review through September 25, 2025; references added. Policy statement unchanged.