FEP Medical Policy Manual

FEP 2.04.96 Genetic Testing for Statin-Induced Myopathy

Effective Policy Date: April 1, 2021

Original Policy Date: March 2018

Related Policies:

None

Genetic Testing for Statin-Induced Myopathy

Description

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 patients at risk of statin-induced myopathy is considered **not medically necessary**.

POLICY GUIDELINES

None

BENEFIT APPLICATION

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.

FDA REGULATORY STATUS

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 *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.[17] 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.

REFERENCES

1. Vladutiu GD. Genetic predisposition to statin myopathy. Curr Opin Rheumatol. Nov 2008; 20(6): 648-55. PMID 18946323
2. Maggo SD, Kennedy MA, Clark DW. Clinical implications of pharmacogenetic variation on the effects of statins. Drug Saf. Jan 01 2011; 34(1): 1-19. PMID 21142270
3. Pasternak RC, Smith SC, Bairey-Merz CN, et al. ACC/AHA/NHLBI Clinical Advisory on the Use and Safety of Statins. Circulation. Aug 20 2002; 106(8): 1024-8. PMID 12186811
4. Link E, Parish S, Armitage J, et al. SLCO1B1 variants and statin-induced myopathy--a genomewide study. N Engl J Med. Aug 21 2008; 359(8): 789-99. PMID 18650507
5. McKenney JM, Davidson MH, Jacobson TA, et al. Final conclusions and recommendations of the National Lipid Association Statin Safety Assessment Task Force. Am J Cardiol. Apr 17 2006; 97(8A): 89C-94C. PMID 16581336
6. Law M, Rudnicka AR. Statin safety: a systematic review. Am J Cardiol. Apr 17 2006; 97(8A): 52C-60C. PMID 16581329
7. Wilke RA, Ramsey LB, Johnson SG, et al. The clinical pharmacogenomics implementation consortium: CPIC guideline for SLCO1B1 and simvastatin-induced myopathy. Clin Pharmacol Ther. Jul 2012; 92(1): 112-7. PMID 22617227
8. Schech S, Graham D, Staffa J, et al. Risk factors for statin-associated rhabdomyolysis. Pharmacoepidemiol Drug Saf. Mar 2007; 16(3): 352-8. PMID 16892458
9. Luzum JA, Kitzmiller JP, Isackson PJ, et al. GATM polymorphism associated with the risk for statin-induced myopathy does not replicate in case-control analysis of 715 dyslipidemic individuals. Cell Metab. Apr 07 2015; 21(4): 622-7. PMID 25863251
10. Boston Heart Diagnostics Corp. The science behind the Boston Heart Statin Induced Myopathy (SLCO1B1) Genotype test 2016; http://www.bostonheartdiagnostics.com/science_portfolio_statin.php. Accessed September 28, 2020.
11. de Keyser CE, Peters BJ, Becker ML, et al. The SLCO1B1 c.521T C polymorphism is associated with dose decrease or switching during statin therapy in the Rotterdam Study. Pharmacogenet Genomics. Jan 2014; 24(1): 43-51. PMID 24263182
12. Danik JS, Chasman DI, MacFadyen JG, et al. Lack of association between SLCO1B1 polymorphisms and clinical myalgia following rosuvastatin therapy. Am Heart J. Jun 2013; 165(6): 1008-14. PMID 23708174
13. Xiang Q, Chen SQ, Ma LY, et al. Association between SLCO1B1 T521C polymorphism and risk of statin-induced myopathy: a meta-analysis. Pharmacogenomics J. Dec 2018; 18(6): 721-729. PMID 30250148
14. Vassy JL, Chun S, Advani S, et al. Impact of SLCO1B1 Pharmacogenetic Testing on Patient and Healthcare Outcomes: A Systematic Review. Clin Pharmacol Ther. Aug 2019; 106(2): 360-373. PMID 30137643
15. Voora D. Genetically Guided Statin Therapy (Report no. AFRL-SA-WP-TR-2017-0005). Wright-Patterson Air Force Base, OH: USAF School of Aerospace Medicine; 2017.
16. Hoffman JM, Haidar CE, Wilkinson MR, et al. PG4KDS: a model for the clinical implementation of pre-emptive pharmacogenetics. Am J Med Genet C Semin Med Genet. Mar 2014; 166C(1): 45-55. PMID 24619595

17. Ramsey LB, Johnson SG, Caudle KE, et al. The clinical pharmacogenetics implementation consortium guideline for SLCO1B1 and simvastatin-induced myopathy: 2014 update. Clin Pharmacol Ther. Oct 2014; 96(4): 423-8. PMID 24918167

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.