FEP 2.04.96 Genetic Testing for Statin-Induced Myopathy

Effective Date: April 1, 2019
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

Genetics Nomenclature Update
The Human Genome Variation Society nomenclature is used to report information on variants found in DNA and serves as an international standard in DNA diagnostics. It is being implemented for genetic testing medical evidence review updates starting in 2017 (see Table PG1). The Society’s nomenclature is recommended by the Human Variome Project, the Human Genome Organization, and by the Human Genome Variation Society itself.

The American College of Medical Genetics and Genomics and the Association for Molecular Pathology standards and guidelines for interpretation of sequence variants represent expert opinion from both organizations, in addition to the College of American Pathologists. These recommendations primarily apply to genetic tests used in clinical laboratories, including genotyping, single genes, panels, exomes, and genomes. Table PG2 shows the recommended standard terminology—“pathogenic,” “likely pathogenic,” “uncertain significance,” “likely benign,” and “benign”—to describe variants identified that cause Mendelian disorders.

Table PG1. Nomenclature to Report on Variants Found in DNA

<table>
<thead>
<tr>
<th>Previous</th>
<th>Updated</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mutation</td>
<td>Disease-associated variant</td>
<td>Disease-associated change in the DNA sequence</td>
</tr>
</tbody>
</table>
FEP 2.04.96 Genetic Testing for Statin-Induced Myopathy

<table>
<thead>
<tr>
<th>Variant</th>
<th>Change in the DNA sequence</th>
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<tbody>
<tr>
<td>Familial variant</td>
<td>Disease-associated variant identified in a proband for use in subsequent targeted genetic testing in first-degree relatives</td>
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Table PG2. ACMG-AMP Standards and Guidelines for Variant Classification

<table>
<thead>
<tr>
<th>Variant Classification</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathogenic</td>
<td>Disease-causing change in the DNA sequence</td>
</tr>
<tr>
<td>Likely pathogenic</td>
<td>Likely disease-causing change in the DNA sequence</td>
</tr>
<tr>
<td>Variant of uncertain significance</td>
<td>Change in DNA sequence with uncertain effects on disease</td>
</tr>
<tr>
<td>Likely benign</td>
<td>Likely benign change in the DNA sequence</td>
</tr>
<tr>
<td>Benign</td>
<td>Benign change in the DNA sequence</td>
</tr>
</tbody>
</table>

ACMG: American College of Medical Genetics and Genomics; AMP: Association for Molecular Pathology

GENETIC COUNSELING

Genetic counseling is primarily aimed at patients who are at risk for inherited disorders, and experts recommend formal genetic counseling in most cases when genetic testing for an inherited condition is considered. The interpretation of the results of genetic tests and the understanding of risk factors can be very difficult and complex. Therefore, genetic counseling will assist individuals in understanding the possible benefits and harms of genetic testing, including the possible impact of the information on the individual’s family. Genetic counseling may alter the utilization of genetic testing substantially and may reduce inappropriate testing. Genetic counseling should be performed by an individual with experience and expertise in genetic medicine and genetic testing methods.

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.

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

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.

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.

RATIONALE

Summary of Evidence

For individuals who are taking statin drugs who receive genetic testing for SLCO1B1 variants, the evidence includes a randomized controlled trial. Relevant outcomes are symptoms, quality of life, morbidity...
FEP 2.04.96 Genetic Testing for Statin-Induced Myopathy

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Effective Policy Date: April 1, 2019

Page: 3 of 4

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 specific drug) has positive outcomes in terms of lower rates of myopathy with adequate lipid control and tolerability of alternative treatments. 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

The Clinical Pharmacogenetics and Pharmacogenomics Implementation Consortium (2012) issued guidelines for SLCO1B genotypes and simvastatin-induced myopathy, which were updated in 2014.16. 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 (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

REFERENCES


POLICY HISTORY

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
<th>Description</th>
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<tr>
<td>March 2018</td>
<td>New Policy</td>
<td>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.</td>
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