FEP 2.04.94 Genetic Testing for Lactase Insufficiency

Effective Policy Date: October 1, 2019
Original Policy Date: September 2013

Genetic Testing for Lactase Insufficiency

Description
Genetic testing of adults with suspected lactase insufficiency is proposed as an alternative to current diagnostic practices, which include hydrogen breath test, lactose tolerance blood test, and intestinal biopsy.

OBJECTIVE
The objective of this evidence review is to determine whether targeted testing for the \textit{MCM6} -13910C>T variant improves the net health outcome for individuals with suspected lactase insufficiency.

POLICY STATEMENT
The use of targeted \textit{MCM6} -13910C>T variant analysis for the prediction of lactase insufficiency is considered \textit{investigational}.

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

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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>
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<tbody>
<tr>
<td>Mutation</td>
<td>Disease-associated variant</td>
<td>Disease-associated change in the DNA sequence</td>
</tr>
<tr>
<td>Variant</td>
<td>Change in the DNA sequence</td>
<td></td>
</tr>
<tr>
<td>Familial variant</td>
<td>Disease-associated variant</td>
<td>Disease-associated variant identified in a proband for use in subsequent</td>
</tr>
<tr>
<td></td>
<td></td>
<td>targeted genetic testing in first-degree relatives</td>
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</table>

Table PG2. ACMG-AMP Standards and Guidelines for Variant Classification

<table>
<thead>
<tr>
<th>Variant Classification</th>
<th>Definition</th>
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</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

Experts recommend formal genetic counseling for patients who are at risk for inherited disorders and who wish to undergo genetic testing. Interpreting the results of genetic tests and understanding risk factors can be difficult for some patients; genetic counseling helps individuals understand the impact of genetic testing, including the possible effects the test results could have on the individual or their family members. It should be noted that genetic counseling may alter the utilization of genetic testing substantially and may reduce inappropriate testing; further, 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.

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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. 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 with suspected lactase insufficiency who receive targeted testing for the MCM6 -13910C>T variant, the evidence includes genotype-phenotype studies and a meta-analysis. Relevant outcomes are symptoms, morbid events, functional outcomes, health status measures, and quality of life. Studies have demonstrated a high correlation between the -13910C>T single nucleotide variant upstream of the gene encoding the enzyme lactase, and lactase insufficiency in persons of European ancestry. Studies in white populations have reported a high degree of agreement for the diagnosis of lactase insufficiency between genotyping and both hydrogen breath test and lactose tolerance blood test. However, there is no current treatment for lactase insufficiency, and management involves dietary restriction and palliation of lactase intolerance symptoms. Therefore, an empirical diagnosis of lactose intolerance in the absence of confirmation by hydrogen breath test, lactose tolerance blood test, or genotyping, followed by treatment with dietary restriction of lactose, is suitable. Currently, the evidence does not support the conclusion that assessment of the genetic etiology of lactose intolerance would affect patient management or improve clinical outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

No guidelines or statements were identified.

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


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

<table>
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<tr>
<th>Date</th>
<th>Action</th>
<th>Description</th>
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<tbody>
<tr>
<td>September 2013</td>
<td>New policy</td>
<td>Policy updated with literature search adding references 11 and 35. No changes to the policy statement.</td>
</tr>
<tr>
<td>September 2014</td>
<td>Replace policy</td>
<td>Policy updated with literature review through March 10, 2015; references 12-13 and 17 added. Policy statements unchanged.</td>
</tr>
<tr>
<td>September 2015</td>
<td>Replace policy</td>
<td>Policy updated with literature review through July 20, 2017; no references added; note 1 updated. Policy statement unchanged.</td>
</tr>
<tr>
<td>December 2017</td>
<td>Replace policy</td>
<td>Policy updated with literature review through July 20, 2017; no references added; note 1 updated. Policy statement unchanged.</td>
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<tbody>
<tr>
<td>September 2018</td>
<td>Replace policy</td>
<td>Policy updated with literature review through March 6, 2018; no references added. Minor edit to the Policy section; statement otherwise unchanged.</td>
</tr>
<tr>
<td>September 2019</td>
<td>Replace policy</td>
<td>Policy updated with literature review through March 4, 2019; no references added. Policy statement unchanged.</td>
</tr>
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