Introduction

Familial hypercholesterolemia (FH) is an inherited disorder that causes abnormally high levels of low-density lipoprotein (LDL), often called bad cholesterol, in the blood at any early age. The excess cholesterol forms thick, sticky, hard fatty clumps called plaque. The plaque builds up in the arteries, and as a result, the arteries can become clogged or clots can form. These clogged arteries and clots can then cause high blood pressure, heart attacks and strokes. If left untreated, familial hypercholesterolemia can also cause problems that are related to poor blood flow to the arms, legs, and feet. A definite diagnosis of FH may be required to qualify for specialty medications such as PCSK9 inhibitors. Genetic testing may be done when an individual has symptoms that are suspicious for FH and other diagnostic tests for the disorder are abnormal or uncertain. Genetic testing may be indicated for children whose parents have FH to determine their risk of developing the disorder. See Policy Criteria for more specific information.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.
<table>
<thead>
<tr>
<th>Service</th>
<th>Medical Necessity</th>
</tr>
</thead>
</table>
| Confirm a diagnosis of familial hypercholesterolemia (FH) | Genetic testing to confirm a diagnosis of familial hypercholesterolemia (FH) may be considered medically necessary when a definitive diagnosis is required in order to qualify for specialty medications used to lower cholesterol levels (see Additional Information). The following criteria also must be met:  
  - Genetic testing is targeted to individuals who are in an “uncertain category” according to clinical criteria (personal and family history, physical exam, lipid levels) (see Additional Information)  
    AND  
    - Alternative treatment considerations are in place for individuals who have an uncertain diagnosis of FH and a negative genetic test.  
  Genetic testing to confirm a diagnosis of heterozygous FH is considered investigational in all other situations. |
| Testing of children of individuals with FH        | Genetic testing of children of individuals with FH to determine future risk of disease may be considered medically necessary when the following criteria are met:  
  - A pathogenic variation is present in a parent  
    AND  
    - General lipid screening is not recommended based on age or other factors  
  Note: When there is a clinical diagnosis of FH but no known pathogenic variant in the family, it is necessary to test an index case to determine variant status. Coverage of testing an index case to benefit family members depends on contract benefit language. |
| Testing of adults who are close relatives of       | Genetic testing of adults who are close relatives of individuals with FH to determine future risk of disease is considered investigational. |
| with FH                                           |                                                                                                                                                                                                                  |
### Service

<table>
<thead>
<tr>
<th>Service</th>
<th>Investigational</th>
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</thead>
<tbody>
<tr>
<td><strong>individuals with FH</strong></td>
<td><strong>investigational.</strong></td>
</tr>
</tbody>
</table>

**Note:** See additional information below.

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**Additional Information**

**To confirm a diagnosis of familial hypercholesterolemia (FH)**

- Eligibility for specialty medicines (eg, PCSK9 inhibitors) may require a definitive diagnosis of FH. The labeled indications for these agents state they are indicated for individuals with FH, although criteria for diagnosis are not given. In the key trials that led to U.S. Food and Drug Administration approval of these inhibitors, having a diagnosis of FH served as an eligibility criterion. The diagnosis in these trials was based on clinical factors with or without genetic testing.

- The definition of an “uncertain” diagnosis of familial hypercholesterolemia (FH) is not standardized. However, available diagnostic tools provide guidance on when a diagnosis is and is not definitive. When FH is suspected and evaluated against standardized diagnostic criteria, it can be interpreted that the individual is in an “uncertain” category when criteria for a definitive diagnosis are not met. Here are some examples of certain criteria not being met:

  - **Dutch Lipid Clinic Criteria.** A score of 8 or greater on the Dutch Lipid Clinic criteria is considered definitive FH. Scores between 3 and 7 are considered “possible” or “probable” FH. The latter 2 categories can be considered to represent “uncertain” FH.

  - **Simon Broome Criteria.** A definitive diagnosis of FH is made based on a total cholesterol level greater than 290 mg/dL in adults (or low-density lipoprotein >190 mg/dL), together with either positive physical exam findings or a positive genetic test. Probable FH, which can be interpreted as “uncertain” FH, is diagnosed using the same cholesterol levels, plus family history of premature coronary artery disease or total cholesterol of at least 290 mg/dL in a first- or a second-degree relative.

  - **MEDPED (Make Early Diagnosis Prevent Early Death) Criteria.** These criteria provide a yes/no answer for whether an individual has FH, based on family history, age, and cholesterol levels. An individual who meets criteria for FH can be considered to have definitive FH; however, there is no “possible” or “probable” category that allows assignment of an “uncertain” category.

  **Note:** See Evidence Review for more information about these tests.
Additional Information

Testing of adults who are close relatives of individuals with FH

- It is unlikely that screening of adults who are close relatives of an index case of FH will improve outcomes because management decisions will be made according to lipid levels and will not differ based on a diagnosis of FH. However, there are conditions under which testing of relatives will lead to improved outcomes, particularly when testing is performed as part of a formal cascade screening program. Cascade testing refers to a coordinated program of population screening intended to identify additional patients with FH. Cascade screening may involve a combination of lipid levels and genetic testing; conversely, cascade screening may be performed with genetic testing alone. Beginning with an index case, close relatives are screened. For patients who screen positive, all close relatives are then identified and screened. This process is repeated until no further close relative eligible for screening can be identified. While such programs exist in Western Europe, there are barriers to implementation in the United States, such as lack of an infrastructure to identify all individuals in the cascade; additionally, there exists a lack of coordination for patients with different types of medical insurance.

Coding

<table>
<thead>
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<th>Code</th>
<th>Description</th>
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<td>CPT</td>
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<tr>
<td>81401</td>
<td>Molecular pathology procedure, Level 2 (eg, 2-10 SNPs, 1 methylated variant, or 1 somatic variant [typically using nonsequencing target variant analysis], or detection of a dynamic mutation disorder/triplet repeat)</td>
</tr>
<tr>
<td></td>
<td>Includes: APOB (apolipoprotein B) (eg, familial hypercholesterolemia type B), common variants (eg, R3500Q, R3500W)</td>
</tr>
<tr>
<td>81405</td>
<td>Molecular pathology procedure, Level 6 (eg, analysis of 6-10 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 11-25 exons, regionally targeted cytogenomic array analysis)</td>
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<tr>
<td></td>
<td>Includes: LDLR (low density lipoprotein receptor) (eg, familial hypercholesterolemia), duplication/deletion analysis</td>
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<tr>
<td>81406</td>
<td>Molecular pathology procedure, Level 7 (eg, analysis of 11-25 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 26-50 exons, cytogenomic array analysis for neoplasia)</td>
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<tr>
<td>Code</td>
<td>Description</td>
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<tr>
<td></td>
<td>Includes: LDLR (low density lipoprotein receptor) (eg, familial hypercholesterolemia), full gene sequence</td>
</tr>
<tr>
<td></td>
<td>PCSK9 (proprotein convertase subtilisin/kexin type 9) (eg, familial hypercholesterolemia), full gene sequence</td>
</tr>
</tbody>
</table>

The Ambry Genetics **FHNext** panel, for example, includes all 4 of the analyses above so it would be reported with codes 81401, 81405, and 2 units of 81406.

**Related Information**

**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 the understanding of risk factors can be very 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**

Recommendations indicate that, when possible, genetic testing for familial hypercholesterolemia be performed in an affected family member so that testing in unaffected, at-risk family members can focus on the mutation found in the affected family member. However, coverage for testing of the affected index case (proband) depends on the member’s contract.

Specific contract language must be reviewed and considered when determining coverage for testing. In some cases, coverage for testing the index case may be available through the unaffected, at-risk individual who will benefit from knowing the results of the genetic test.
Summary

Familial hypercholesterolemia (FH) is an inherited disorder characterized by markedly elevated low-density lipoprotein levels, physical exam signs of cholesterol deposition, and premature cardiovascular disease. FH can be either homozygous or heterozygous. Heterozygous FH, which is more common and more difficult to diagnose, is the focus of this medical policy. Genetic testing for heterozygous FH can potentially improve the ability to make a diagnosis of FH, and can identify asymptomatic relatives of affected individuals at risk for developing FH.

Epidemiology of Familial Hypercholesterolemia (FH)

Familial Hypercholesterolemia encompasses a group of inherited disorders characterized by markedly elevated low-density lipoprotein (LDL) levels, physical exam signs of cholesterol deposition, and premature cardiovascular disease. FH can be categorized as homozygous or heterozygous. Homozygous FH is an extremely rare disorder that arises from biallelic variants in a single gene, and has a prevalence of between 1:160,000 and 1:1,000,000. Individuals with homozygous FH have extreme elevations of LDL, develop coronary artery disease (CAD) in the second or third decade, and are generally diagnosed easily.

Heterozygous FH is more common, with an estimated prevalence between 1 in 200 to 1 in 500 patients and is present in childhood. Some populations, such as Ashkenazi Jews and South Africans, have a higher prevalence of FH, up to 1 in 100. For affected individuals, the burden of illness is high. Patients with FH and increased LDL cholesterol (>190 mg/dL) have a three times higher risk of CAD than those with increased LDL cholesterol alone. The average age for presentation with CAD is in the fourth decade for men and the fifth decade for women, and there is a 30% to 50% increase in risk for men and women in the fifth and sixth decades, respectively. Increased risk of CAD is associated with a higher rate of death due to cardiovascular causes in patients with homozygous and heterozygous FH.

Diagnosis

The diagnosis of FH relies on elevated LDL levels in conjunction with a family history of premature CAD and physical exam signs of cholesterol deposition. There is wide variability in
cholesterol levels for patients with FH, and considerable overlap in levels between patients with FH and patients with non-FH. Physical exam findings can include tendinous xanthomas, xanthelasma, and corneal arcus, but these are not often helpful in making a diagnosis. Xanthelasma and corneal arcus are common in the elderly population and therefore not specific. Tendinous xanthomas are relatively specific for FH but are not sensitive findings. They occur mostly in patients with higher LDL levels and treatment with statins likely delays or prevents the development of xanthomas.

Because of the variable cholesterol levels, and the low sensitivity of physical exam findings, there are a considerable number of patients in whom the diagnosis is uncertain. For these individuals, there are a number of formal diagnostic tools for determining the likelihood of FH.\footnote{6}

- **Make Early Diagnosis Prevent Early Deaths Program Diagnostic Criteria (MEDPED)**
  - This tool relies on a combination of total cholesterol levels, age, and family history. For example, a 20-year-old individual who has no family history is diagnosed with FH if total cholesterol is 270 mg/dL or higher. A 25-year-old individual with a first-degree relative who has FH is diagnosed with FH if his/her total cholesterol is 240 mg/dL or higher.
  - Genetic testing is not considered as part of the diagnostic workup with this tool.

- **Dutch Lipid Clinic Criteria**
  - This tool assigns points for family history, CAD in the individual, physical exam signs of cholesterol deposition, LDL levels, and results of genetic testing. The diagnosis of definite FH is made when the score is 8 or higher and probable FH when the score is 6 to 8.
  - The diagnosis can be made with or without genetic testing. A positive genetic test is given 8 points, which is the highest for any criterion and indicates that a positive genetic test alone is sufficient to make a definitive diagnosis.

- **Simon Broome Registry Criteria**
  - Using these criteria, a definite diagnosis of FH is made based on a total cholesterol greater than 290 mg/dL in adults (or LDL >190 mg/dL) together with tendinous xanthoma in the individual or in a first-degree relative.
  - A definite diagnosis can also be made using cholesterol levels and a positive genetic test.
  - Probable FH is diagnosed by cholesterol levels and either a family history of premature CAD or a family history of total cholesterol 290 mg/dL or higher in a first- or a second-degree relative.
Treatment

Treatment of FH is generally similar to that for non-FH, and is based on LDL levels. Treatment may differ in that the approach to treating FH is more aggressive (ie, treatment may be initiated sooner and a higher intensity medication regimen may be used). In adults, there are no specific treatment guidelines that indicate treatment for FH differs from the standard treatment of hypercholesterolemia. There may be more differences in children, for whom the presence of a pathogenic variant may impact the timing of starting medications.

As with other forms of hypercholesterolemia, statins are the mainstay of treatment for FH. However, because of the degree of elevated LDL in many patients with FH, statins will not be sufficient to achieve target lipid levels. Additional medications can be used in these patients. Ezetimibe inhibits absorption of cholesterol from the gastrointestinal tract, and is effective for reducing LDL levels by up to 25% in patients already on statins. The IMPROVE-IT trial randomized patients with acute coronary syndrome to a combination of ezetimibe plus statins versus statins alone, and reported that cardiovascular events were reduced for patients treated with combination therapy.

The PCSK9 inhibitors are the most recently approved drugs for hyperlipidemia. These medications have potent LDL-lowering properties and have been tested in patients with FH. When added to statins, these drugs can result in additional LDL reduction of 30% to 70% and have been reported to reduce the incidence of nonfatal myocardial infarction. Other antilipid medications (eg, bile acid sequestrants, niacin) are effective at reducing LDL levels but have not demonstrated efficacy in reducing cardiovascular events when added to statins. For patients who continue to have elevated LDL levels despite maximum medical treatment, lipid apheresis is an option.

Genetic Markers for FH

FH is generally inherited as an autosomal dominant condition. The primary physiologic defect in FH is impaired ability to clear LDL from the circulation, resulting in elevated serum levels. Three genes have been identified as harboring variants associated with FH.

- The LDL receptor gene (LDLR) is the most common variant identified, accounting for between 60% and 80% of FH.
The LDL receptor binds LDL thus allowing removal of LDL from the circulation. A defect in the LDL receptor leads to reduced clearance of LDL.

- Over 1500 different pathogenic variants have been identified in this gene.\textsuperscript{1,6} Characterization of the frequency and spectrum of variants is ongoing.\textsuperscript{8}

- The APOB gene accounts for approximately 1% to 5% of FH cases.\textsuperscript{1}
  - Apolipoprotein B is a cofactor in the binding of LDL to the LDL receptor, and variants in APOB lead to reduced clearance of LDL.
  - There are a limited number of variants of this gene, allowing targeted testing.

- The PCSK9 gene accounts for approximately 0% to 3% of FH.\textsuperscript{1}
  - This variant results in increased PCSK9 levels, which impair the function of the LDL receptors leading to reduced clearance of LDL.
  - There are a limited number of known pathogenic variants, allowing targeted testing.

Penetrance for all FH genes is 90% or higher.\textsuperscript{1} Therefore, nearly all patients found to have a pathogenic variant will eventually develop clinical disease. There is some degree of variable clinical expressivity that might be mediated by both environmental factors such as diet and exercise, and unknown genetic factors that modify gene expression.

**Summary of Evidence**

For individuals who have signs and/or symptoms of FH and need a definitive diagnosis in order to establish their eligibility for specialty medications or else are undergoing lipid lowering therapy, the evidence includes case series and cross-sectional studies. Relevant outcomes are test accuracy and validity, other test performance measures, symptoms, change in disease status, and morbid events. No published empirical evidence on analytic validity was identified; however, there are claims in the literature that the analytic validity approaches 100%. For clinical validity, there are large samples of individuals with FH who have been systematically tested for FH variants. In these cohorts of patients, the clinical sensitivity ranges from 50% to 70% for those with definite FH. For suspected FH, the sensitivity is lower, ranging from 10% to 30%. Clinical specificity ranges from 99% to 100%. False positives are expected to be low for known pathogenic variants, but the false-positive rate is unknown for novel variants or for variants of unknown significance. Direct evidence for clinical utility is lacking. The clinical utility of genetic testing was evaluated through an indirect chain of evidence in the following situations:
• **When a definitive diagnosis of FH is required to establish eligibility for specialty medications.** A chain of evidence demonstrates that clinical utility is present. For patients who are in an uncertain diagnostic category, a positive genetic test can confirm the diagnosis of FH and establish eligibility for specialty medications. Specialty medications (eg, PCSK9 inhibitors) have known efficacy in patients with FH and uncontrolled lipid levels despite treatment with statins and/or other medications. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

• **All other situations.** Clinical utility of testing for diagnosis cannot be demonstrated through a chain of evidence in other situations. No changes in management occur as a result of establishing a definitive diagnosis with genetic testing compared to standard clinical evaluation. For adolescents and adults, measurement of lipid levels is indicated, and management decisions will be made primarily on lipid levels and will not differ in the presence of FH. Therefore, an improvement in health outcomes cannot be demonstrated. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have a close relative with a diagnosis of FH who receive genetic testing to determine future risk of FH, the evidence includes case series and cross-sectional studies. Relevant outcomes include test accuracy and validity, other test performance measures, symptoms, change in disease status, and morbid events. No published empirical evidence on analytic validity was identified; however, there are claims in the literature that the analytic validity approaches 100%. For clinical validity, there are large samples of individuals with FH who have been systematically tested for FH variants. In these cohorts of patients, the clinical sensitivity ranges from 30% to 70% for individuals with definite FH. For suspected FH, the sensitivity is lower, ranging from 1% to 30%. Clinical specificity ranges from 99% to 100%. False positives are expected to be low for known pathogenic variants, but the false-positive rate is unknown for novel variants or for variants of unknown significance. Direct evidence for clinical utility is lacking. Clinical utility was evaluated through a chain of evidence in the following situations.

• **Adults.** Clinical utility cannot be demonstrated through a chain of evidence. While targeted genetic testing is superior to standard risk stratification for determining future risk of disease, it is unlikely that management changes will occur as a result of genetic testing. Adults who are close relatives of individuals with FH will have their lipid levels tested, and management decisions for adults are made primarily by low-density lipoprotein levels and will not differ for patients with a diagnosis of FH. The evidence is insufficient to determine the effects of the technology on health outcomes.
- **Children.** Clinical utility can be demonstrated through a chain of evidence. Targeted genetic testing is superior to standard risk stratification for determining future risk of disease. It is recommended that children of individuals who have a pathogenic variant begin screening at an earlier age; further, the affected children should begin treatment with statins as early as possible. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

**Ongoing and Unpublished Clinical Trials**

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

**Table 1. Summary of Key Trials**

<table>
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<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
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<td>NCT01524289</td>
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<td>Oct 2018</td>
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<td>NCT03253432</td>
<td>IN-TANDEM Familial Hypercholesterolemia Pilot Study</td>
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<td>Dec 2018</td>
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<tr>
<td>NCT01960244</td>
<td>Study of Awareness and Detection of Familial Hypercholesterolemia (CASCADE-FH)</td>
<td>5000</td>
<td>Oct 2020</td>
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NCT: national clinical trial

**Practice Guidelines and Position Statements**

*National Lipid Association Expert Panel*

Recommendations on the diagnosis and screening for familial hypercholesterolemia (FH) were developed by the National Lipid Association Expert Panel on Familial Hypercholesterolemia and published in 2011. The following recommendations relevant to genetic testing were included:

- “Formal clinical diagnosis of FH can be made by applying any one of several validated sets of criteria [U.S. Make Early Diagnosis Prevent Early Death (MEDPED), Dutch Lipid Clinic [22]...
Network, Simon-Broome Registry]. It should be noted that LDL [low-density lipoprotein] cholesterol cut points usually vary with age...

- Genetic screening for FH is generally not needed for diagnosis or clinical management but may be useful when diagnosis is uncertain.

- Identification of a causal mutation may provide additional motivation for some patients to implement appropriate treatment.

- Importantly, a negative genetic test does not exclude FH, since approximately 20% of clinically definite FH patients will not be found to have a mutation despite an exhaustive search using current methods...

- Cascade screening involves testing lipid levels in all first-degree relatives of diagnosed FH patients.

- As cascade screening proceeds, newly identified FH cases provide additional relatives who should be considered for screening.

- Cascade screening is the most cost-effective means of finding previously undiagnosed FH patients and is also cost-effective in terms of cost per year of life saved. General population screening of a young population (before age 16) is similarly cost-effective in terms of cost per year of life saved, given that effective cholesterol treatment is begun in all those identified.”

**American College of Cardiology and American Heart Association**

The American College of Cardiology and American Heart Association task force recommendations on the treatment of blood cholesterol to reduce atherosclerotic disease in adults (follow-up report to Adult Treatment Recommendations from the National Cholesterol Education Panel) were published in 2013. These recommendations did not mention genetic testing. Treatment recommendations are based on LDL levels and clinical factors, and there were no separate treatment recommendations for individuals with FH.
National Heart, Lung, and Blood Institute

Recommendations from an expert panel on cardiovascular health and risk reduction in children and adolescents were published in 2011. The report contained the following recommendations (see Table 2).

Table 2. Recommendations on Cardiovascular Health and Risk Reduction in Children and Adolescents

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>GOE</th>
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<tbody>
<tr>
<td>“The evidence review supports the concept that early identification and control of dyslipidemia throughout youth and into adulthood will substantially reduce clinical CVD risk beginning in young adult life. Preliminary evidence in children with heterozygous FH with markedly elevated LDL-C indicates that earlier treatment is associated with reduced subclinical evidence of atherosclerosis.”</td>
<td>B</td>
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<tr>
<td>“TC and LDL-C levels fall as much as 10–20% or more during puberty.”</td>
<td>B</td>
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<tr>
<td>“Based on this normal pattern of change in lipid and lipoprotein levels with growth and maturation, age 10 years (range age 9-11 years) is a stable time for lipid assessment in children. For most children, this age range will precede onset of puberty.”</td>
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</tbody>
</table>

CVD: cardiovascular disease; FH: familial hypercholesterolemia; GOE: grade of evidence; LDL-C: low-density lipoprotein cholesterol; TC: triglycerides.

U.S. Preventive Services Task Force Recommendations

The U.S. Preventive Services Task Force published recommendations for lipid disorders in adults in 2008, which was archived in 2014. This publication did not make specific recommendations for genetic testing for FH.

An evidence review on lipid screening in children and adolescents to detect familial hypercholesterolemia was published in 2016. This report stated that genetic screening for FH is beyond the scope of the report. Further, it stated that “because implementing this approach [cascade screening] in the United States would require new infrastructure, cascade screening is outside of the purview of U.S. primary care and beyond the scope of this review.”
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.

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.

References


History

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<th>Comments</th>
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<td>09/01/16</td>
<td>New policy, add to Genetic Testing section. Approved August 9, 2016. Policy created</td>
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with a literature review through March 19, 2016. Genetic testing to confirm a diagnosis of Familial Hypercholesterolemia (FH) may be considered medically necessary when a definitive diagnosis of FH may be required for eligibility for specialty medications and criteria are met. FH testing is investigational when criteria are not met. Genetic testing to determine future risk of disease may be considered medically necessary in children when criteria are met. Genetic testing to determine future risk of disease in adults is investigational when criteria are not met.

12/01/17


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  - Information written in other languages

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Deutsche (German):

Hmoob (Hmong):
Tsbab ntawv tshaj hox no muaj cov ntsiab lus tseem ceeb. Tey zuam tsab ntawv tshaj hox no muaj cov ntsiab lus tseem ceeb bkg koy dain ntawv thov kveb pab los yog koy shov kveb pab cuam los ntsawm Premera Blue Cross. Tey zuam muaj cov nhub tseem ceeb uas rau hauv daim ntawv no. Tey zuam koy koy juv uaa tau uee yam uas peb kom koy uas tis pub dhuav cov caj nyoy uas teev rau hauv daim ntawv no. Tey zuam koy koy juv uaa tau uee yam uas peb kom koy uas tis pub dhuav cov caj nyoy uas teev rau hauv daim ntawv no. Tey zuam koy koy juv uaa dau tuum koj yuav tau txais kev pab cuam los yog kov kveb pab them tej zaum koy hoo koj moh ntawv. Koy muaj cai kom lawv muab cov ntsiab lus no uas tau muab sau uaa koj hom lus pub dawv rau koy. Ju rauu 800-722-1471 (TTY: 800-842-5357).

Iloko (Ilocano):
Daytoy a Pakdaar ket naglao iti Napateg nga Impormasion. Daytoy a pakdaar mabalini nga adda ket naglao iti napateg nga impormasion maipanggep iti aplikasyon wenno coverage babaen ti Premera Blue Cross. Daytoy ket mabalini dagiti importante a pelta iti daytoy a pakdaar. Mabalini nga adda rumbeng nga aramidenyo nga addang sakbay dagiti partikular a naituding dagiti amsiyon nga adda tapo napmagatipan nga tula coverage ti salun-atyo wenno tulong kadagiti gastos. Adda karbenganyo a mangala iti daytoy nga impormasion ken tungul ti bukodyo a pagasasao nga awan ti bayadanyo. Tumawag ti numero nga oswa 800-722-1471 (TTY: 800-842-5357).

Italiano (Italian):
Premera Blue Cross.

There may be important dates in this notice. You may need to provide information about your application or coverage to Premera Blue Cross.

You may receive notice of these changes by phone or mail. You will receive information about these changes in your native language.

Premera Blue Cross covers Premera Blue Cross. You may need to provide information to Premera Blue Cross.

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