Introduction

Cholesterol is a waxy material that is found in all of the body’s cells. The body needs some cholesterol to perform normal functions like making hormones and vitamin D. Cholesterol travels through the blood in bundles called lipoproteins. There are two kinds of lipoproteins: low-density (LDL) and high-density (HDL). A healthy balance of both is needed to help the body work at its best. LDL cholesterol is sometimes called the “bad” cholesterol because too much of it can clog arteries and lead to serious health problems. The usual way to reduce high levels of bad cholesterol is through diet, exercise, and drugs. In unusual cases where the standard treatment doesn’t work and bad cholesterol is very high, there is a treatment that can filter it out of the blood. This filtering is called lipid apheresis. It uses a machine that works a little bit like kidney dialysis. Blood is removed from a vein and the machine separates out the plasma. (Plasma is a yellow colored liquid and is what’s left after red and white cells and platelets are removed from the blood.) The plasma is filtered to remove the bad cholesterol and is then returned to the patient. This policy describes when lipid apheresis may be medically necessary.

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.
## Policy Coverage Criteria

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Medical Necessity</th>
</tr>
</thead>
</table>
| LDL apheresis              | **Low-density lipoprotein (LDL) apheresis** may be considered medically necessary in patients with homozygous familial hypercholesterolemia as an alternative to plasmapheresis. **

**LDL apheresis** may be considered medically necessary in patients with heterozygous familial hypercholesterolemia (FH). The patient must meet following criteria:

- Have had a positive genetic test for familial hypercholesterolemia

**AND**

- Have tried and failed at least six months of diet therapy, and maximal combination drug therapy that includes the use of a PSK9 inhibitor

**AND**

- Meet one of the following FDA approved indications (All LDL levels represent best achievable LDL level after diet and drug therapy)
  - Functional hypercholesterolemic heterozygotes with LDL $\geq 300$ mg/dL
  - OR
    - Functional hypercholesterolemic heterozygotes with LDL $\geq 200$ mg/dL and documented coronary artery disease

*For definitions of maximum tolerated drug therapy and documented coronary artery disease, please see Definition of Terms.*

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Investigational</th>
</tr>
</thead>
</table>
| Low-density lipoprotein (LDL) apheresis | **LDL apheresis** is considered investigational for all other uses not listed in this policy, including but not limited to:

- Non–arteritic acute anterior ischemic optic neuropathy
- Nonfamilial hypercholesterolemia
- Peripheral artery disease
- Preeclampsia
<table>
<thead>
<tr>
<th>Treatment</th>
<th>Investigational</th>
</tr>
</thead>
</table>
|           | • Severe diabetic foot ulcerations  
|           | • Sudden sensorineural hearing loss |

**Therapeutic apheresis (0342T)**

Therapeutic apheresis with selective high-density lipoprotein (HDL) delipidation and plasma reinfusion is considered investigational.

### Coding

<table>
<thead>
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<th>Code</th>
<th>Description</th>
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<td><strong>CPT</strong></td>
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<tr>
<td>0342T</td>
<td>Therapeutic apheresis with selective HDL delipidation and plasma reinfusion</td>
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<td>36516</td>
<td>Therapeutic apheresis; with extracorporeal selective adsorption or selective filtration and plasma reinfusion</td>
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<tr>
<td><strong>HCPCS</strong></td>
<td></td>
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<tr>
<td>S2120</td>
<td>Low density lipoprotein (LDL) apheresis using heparin-induced extracorporeal LDL precipitation</td>
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</table>

**Note:** CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

### Related Information

**Definition of Terms**

**Delipidation:** This term refers to the removal of lipids from the blood.

**Documented coronary artery disease:** This includes a history of myocardial infarction, coronary artery bypass surgery, percutaneous transluminal coronary angioplasty or alternative revascularization procedure, or progressive angina documented by exercise or non-exercise stress test.

**Low density lipoproteins (LDL):** Plasma proteins that are the major carriers of cholesterol in the blood; high levels are associated with atherosclerosis.
Maximum tolerated drug therapy: This is defined as a trial of drugs from at least 2 separate classes of hypolipidemic agents such as bile acid sequestrants, HMG-CoA reductase inhibitors, fibric acid derivatives, or niacin/nicotinic acids. In addition the patient needs to have used a PSK9 inhibitor with a statin.

Plasma: This is the fluid portion of the blood in which the blood cells are suspended; clear to yellowish colored.

Additional Information

A scientific statement from American Heart Association for the treatment of heterozygous familial hypercholesterolemia (FH) has indicated that adults should be treated with available pharmacotherapy, usually with a statin, with an initial goal of reducing low-density lipoprotein cholesterol (LDL-C) by at least 50%. This treatment can be followed by achieving an LDL-C of less than 100 mg/dL (absent coronary artery disease [CAD] or other major risk factors)) or 70 mg/dL (presence of CAD or other major risk factors). The following approach for pharmacotherapy is suggested:

- High-intensity statin therapy using medications such as rosuvastatin or atorvastatin to target >50% LDL-C reduction.
- If the patient is adherent and LDL-C is above the target goal after 3 months, consider adding ezetimibe.
- If the patient is adherent and LDL-C is above the target goal after 3 months, consider adding a PCSK9 inhibitor or colesvelam (or other bile acid sequestrant or niacin).
- If the patient is adherent and LDL-C is above the target goal after 3 months, proceed to complex therapy combination such as a 4-drug combination plus LDL apheresis.

The frequency of LDL apheresis varies, but typically averages once every 2 weeks to obtain an interapheresis level of LDL-C less than 120 mg/dL. Patients with homozygous FH may be treated more frequently. Patients are simultaneously treated with diet and drug therapy.
Description

This use of low-density lipoprotein (LDL) apheresis has been proposed to treat various types of familial hypercholesterolemia (FH) and other significant hyperlipidemia and to reduce atherosclerosis in cardiovascular disease. Lipid apheresis specifically removes LDL particles from plasma while leaving other factors intact, allowing the filtrated plasma to be returned to the patient.

Background

**Low-Density Lipoprotein-Apheresis**

Low-density lipoprotein (LDL) apheresis (also referred to as lipid apheresis) involves the extracorporeal removal of apolipoprotein B (apo B)–containing lipoproteins, including LDL, lipoprotein(a), and very LDL.

The apheresis procedure is designed to isolate plasma. The LDLs are then selectively removed from the plasma by immunoadsorption, heparin-induced extracorporeal LDL precipitation (HELP), dextran sulfate adsorption, or double-filtration plasma pheresis of lipoprotein. In immunoadsorption, polyclonal antihuman apo B antibodies from sheep selectively bind and remove LDL, because apo B is the protein moiety of LDL. In HELP, LDL and other particles containing apo B are precipitated by heparin at an acidic pH. Dextran sulfate adsorption removes LDL by binding the positively charged apo B to dextran sulfate particles bound to cellulose.

Therapeutic apheresis with selective high-density lipoprotein (HDL) delipidation and plasma reinfusion is removes plasma from the body by apheresis, processed through a delipidation device, and then returned to the patient. The delipidation procedure selectively removes cholesterol from HDL, converting the major α-HDL to pre-β-like HDL, a form of HDL that enhances cholesterol transport to the liver and is thought to reduce atherosclerosis development and burden. The plasma with pre-β-like HDL is then reinfused into the patient.

**Diseases Treated With LDL Apheresis**

Lipid apheresis is used for disorders with marked hyperlipidemia, primarily familial hypercholesterolemia (FH). A dominantly inherited disorder, FH results from a mutation in the gene that encodes for the specific cell surface receptor responsible for LDL uptake by the cells.
The heterozygous form affects about 1 in 500 people. The number of LDL receptors is halved in this condition, resulting in serum low-density lipoprotein cholesterol (LDL-C) levels that are approximately 2 to 3 times levels considered acceptable (ie, >300 mg/dL). Affected male patients typically develop coronary heart disease in their thirties and forties, while women develop the disease in their fifties. Depending on the patient, heterozygous FH may or may not respond adequately to lipid-lowering drugs.

Homozygous hypercholesterolemia is rare, occurring in only in 1 in 1 million subjects. Due to the total lack of functioning LDL receptors, serum levels of LDL-C may be elevated 6-fold (>500 mg/dL). Homozygotes may develop severe aortic stenosis and coronary heart disease by 20 years of age. These patients typically do not adequately respond to drug or diet modification therapies. In the past, patients with homozygous FH may have been treated with plasma exchange, but the advent of LDL apheresis provides a more targeted approach by permitting selective removal of LDL from plasma.

**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>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
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<th>Completion Date</th>
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<td>NCT01518205</td>
<td>HELP-Apheresis in Diabetic Ischemic Foot Treatment (H.A.D.I.F): an RC Trial</td>
<td>132</td>
<td>Dec 2017</td>
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<tr>
<td></td>
<td>to Evaluate the Effect of LDL-apheresis on the Recovery of Diabetic Ulcers</td>
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<td></td>
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<tr>
<td></td>
<td>in Patients With Peripheral Vasculopathy Not Susceptible to Revascularization</td>
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<td></td>
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<tr>
<td>NCT02791802</td>
<td>Effect of Lipoprotein(a) Elimination by Lipoprotein Apheresis on Cardiovascular Outcomes</td>
<td>1000</td>
<td>Feb 2021</td>
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</table>

NCT: national clinical trial.
Summary of Evidence

Familial Hypercholesterolemia

For individuals with homozygous familial hypercholesterolemia (FH) who are unable to achieve their target low-density lipoprotein cholesterol (LDL-C) level with maximally tolerated pharmacotherapy and who receive low-density lipoprotein (LDL) apheresis, the evidence includes multiple nonrandomized prospective and retrospective small cohort studies and 1 systematic review. Relevant outcomes are overall survival, disease-specific survival, change in disease status, morbid events, and treatment-related morbidity. These studies have shown that drastically lowering LDL by lipoprotein apheresis increases longevity in homozygous FH. Studies have reported reductions ranging from 57% to 75% in LDL-C levels after apheresis. Currently, the direct evidence does not demonstrate that reductions in LDL-C levels after LDL apheresis will reduce adverse cardiovascular events. Randomized controlled trials (RCTs) comparing drug therapy alone, apheresis alone, no intervention, usual care, or apheresis plus drug therapy are not feasible, and unlikely to resolve any clinical uncertainty because lipid apheresis is generally used as a treatment of last resort when maximally tolerated pharmacotherapy has failed to achieve target LDL-C levels. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals with heterozygous FH who are unable to achieve their target LDL-C with maximally tolerated pharmacotherapy and who receive LDL apheresis, the evidence includes multiple nonrandomized prospective and retrospective small cohort studies as well as a systematic review. Relevant outcomes are overall survival, disease-specific survival, change in disease status, morbid events, and treatment-related morbidity. These studies have shown that drastically lowering LDL-C using LDL apheresis decreases cardiovascular morbidity in FH heterozygotes refractory to or intolerant of statins. Studies have reported reductions ranging from 58% to 63% in LDL-C levels after apheresis. Currently, the direct evidence does not demonstrate that reductions in LDL-C levels seen with LDL apheresis will reduce adverse cardiovascular events. Randomized controlled trials (RCTs) comparing drug therapy alone, apheresis alone, no intervention, usual care, or apheresis plus drug therapy are not feasible, and unlikely to resolve any clinical uncertainty because lipid apheresis is generally used as a treatment of last resort when maximally tolerated pharmacotherapy has failed to achieve target LDL-C levels. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.
**Nonfamilial Hypercholesterolemia**

For individuals with non-FH who receive LDL apheresis, the evidence includes multiple nonrandomized cohort studies, both retrospective and prospective. Relevant outcomes are overall survival, disease-specific survival, change in disease status, morbid events, and treatment-related morbidity. These studies have reported improvements in lipid levels pre- and posttreatment. Randomized trials in patient populations that are well-characterized regarding previous treatments, lipid levels, and comorbidities are necessary to demonstrate improvements in health outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Nephrotic Syndrome**

For individuals with treatment-resistant nephrotic syndrome who receive LDL apheresis, the evidence includes multiple nonrandomized prospective and retrospective cohort studies. Relevant outcomes are symptoms, change in disease status, and treatment-related morbidity. Using variable schedules of LDL apheresis with short-term follow-up, these studies have reported that LDL apheresis may improve proteinuria and lipid abnormalities in patients with steroid-resistant nephrotic syndrome. Additional studies with concurrent controls and longer term follow-up are necessary to determine whether outcomes are improved with the use of LDL apheresis in nephrotic syndrome. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Other Indications**

For individuals with sudden sensorineural hearing loss who receive LDL and fibrinogen apheresis, the evidence includes 2 RCTs. Relevant outcomes are symptoms, change in disease status, and treatment-related morbidity. One RCT compared LDL apheresis with the standard treatment of prednisolone, hydroxyethyl starch, and pentoxifylline; it reported no statistically significant differences in hearing recovery between groups. The second RCT compared the combination of a single lipid apheresis procedure plus standard treatment with standard treatment alone; it reported statistically significant differences in hearing recovery with the addition of apheresis to standard treatment. An a priori primary end point, power calculations, and the statistical plan to control for type I error for multiple comparisons were not reported in the second trial. Further evaluation and replication of these findings are required given the
inconsistent reporting. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with severe diabetic foot ulcerations who receive LDL apheresis, the evidence includes a single prospective case series. Relevant outcomes are symptoms, change in disease status, morbid events, and treatment-related morbidity. In the case series, patients underwent from 1 to 7 treatment procedures and were followed for 2 to 73 months. Authors reported improved wound healing and reductions in the risk of lower leg amputations, but, ultimately, results were insufficient to ascertain the effects on outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with peripheral artery disease who receive LDL apheresis, the evidence includes a single prospective case series. Relevant outcomes are change in disease status and treatment-related morbidity. Improvements in symptomatic parameters such as coldness, numbness, and resting pain were reported, but were insufficient to ascertain the effects on outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with preeclampsia who receive LDL apheresis, the evidence includes a prospective case series. Relevant outcomes are overall survival, disease-specific survival, change in disease status, morbid events, and treatment-related morbidity. Improvements in gestation were reported, but insufficient to ascertain the effects on outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with non–arteritic acute anterior ischemic optic neuropathy who receive LDL apheresis, the evidence includes a prospective case series. Relevant outcomes are symptoms, change in disease status, and treatment-related morbidity. Improvement in visual outcomes was reported, but insufficient to ascertain the effects on outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Acute Coronary Syndrome**

For individuals with acute coronary syndrome who receive selective high-density lipoprotein (HDL) delipidation and plasma reinfusion, the evidence includes an RCT. Relevant outcomes are overall mortality, disease-specific survival, change in disease status, morbid events, and treatment-related morbidity. Results have shown improvements in certain biochemical measures (eg, pre-β-like HDL and α-HDL levels). There were no significant changes in atheroma volume. Larger randomized trials, with longer follow-up and clinically relevant outcomes, are needed to determine the impact of delipidated HDL plasma on acute coronary syndrome. The evidence is insufficient to determine the effects of the technology on health outcomes.
Practice Guidelines and Position Statements

**National Institute for Health and Care Excellence**

The National Institute for Health and Care Excellence’s 2016 guidance on familial hypercholesterolemia (FH) states the following:

1.3.3.1 Healthcare professionals should consider offering LDL [low-density lipoprotein] apheresis for the treatment of adults and children/young people with homozygous FH. The timing of initiation of LDL apheresis should depend on factors such as the person’s response to lipid-modifying drug therapy and presence of coronary heart disease.

1.3.3.2 In exceptional instances (such as when there is progressive, symptomatic coronary heart disease, despite maximal tolerated lipid-modifying drug therapy and optimal medical and surgical therapy), healthcare professionals should consider offering LDL apheresis for the treatment of people with heterozygous FH. This should take place in a specialist center on a case-by-case basis and data recorded in an appropriate registry.²

**European Atherosclerosis Society**

In 2014, the European Atherosclerosis Society (EAS) issued guidelines on the management of homozygous FH, which made the following recommendations on use of low-density lipoprotein (LDL) apheresis: “This Consensus Panel recommends that lipoprotein apheresis be considered in patients with HoFH [homozygous familial hypercholesterolemia]. Treatment should be started as soon as possible, ideally by age 5 and not later than 8 years.”²²

In 2013, EAS issued a consensus statement on the management of heterozygous FH: “This Consensus Panel recommends that lipoprotein apheresis be considered in patients with treatment resistant HeFH [heterozygous familial hypercholesterolemia].”²³

**International FH Foundation**

In 2015, the International FH Foundation published integrated guidelines on treatment of familial hypercholesterolemia, which made the following recommendations about the use of lipid apheresis²⁴:
• Lipoprotein apheresis (LA) should be considered in all patients with homozygous or compound heterozygous FH (ie, homozygous FH phenotype) and carried out in a dedicated centre with the relevant expertise. (Level 1A recommendation)

• LA should be considered in patients with heterozygous FH with CHD who cannot achieve LDL-cholesterol targets despite maximal drug therapy or because they cannot tolerate statins. (Level 2A recommendation)

• LA should be considered in children with homozygous FH by the age of five and no later than eight years. (Level 2A recommendation)

• Diet and drug therapy to lower LDL cholesterol should be continued during treatment with LA. (Level 2A recommendation.)

American Society for Apheresis

In 2013, the Writing Committee of the American Society for Apheresis issued guidelines for use of apheresis in 78 conditions. LDL apheresis for homozygous FH is considered first-line treatment (Category I) with a Grade IA recommendation (strong recommendation, high-quality evidence). Heterozygous FH is considered appropriate as a second-line (Category II), Grade 1A recommendation.

Other indications listed for LDL apheresis in the American Society for Apheresis guidelines include:

• Lipoprotein (a) hyperlipoproteinemia- Category II; Grade IB strong recommendation, moderate quality evidence;

• Peripheral vascular diseases- Category III- optimum role not established, Grade 2C- weak recommendation, low quality evidence

• Phytanic acid storage disease (Refsum’s disease) - Category II, Grade 2C;

• Sudden sensorineural hearing loss- Category III; Grade 2A- weak recommendation, high-quality evidence

American Heart Association

A 2006 scientific statement from American Heart Association (AHA) on the treatment of heterozygous FH has indicated that adults should be treated with available pharmacotherapy
with an initial goal of reducing low-density lipoprotein cholesterol (LDL-C) by at least 50%, usually with a statin, and treatment should be intensified based on response. It also stated that there are no data to inform pediatric treatment goals, whether to target an LDL-C level of less than 100 or 130 mg/dL or to aim to achieve a 50% reduction in LDL-C from baseline.\(^\text{26}\)

For homozygous patients, lipid-lowering therapy, usually statins, should be instituted at diagnosis and as early as possible. Among the 2 currently available proprotein convertase subtilisin/kexin type 9 inhibitors in the United States, only alirocumab has been approved for homozygous FH patients, in whom it has been shown that the addition of alirocumab to standard treatment (statins and ezetimibe but not lipid apheresis) reduces LDL-C by an additional 31%. AHA recommended that lipid apheresis should be considered by 5 years of age or earlier in exceptional circumstances and should be used after maximally tolerated pharmacotherapy fails to achieve target LDL-C levels. The LDL-C selection criteria for lipid apheresis include a reduction in LDL-C of less than 50% by other treatments and residual severe LDL-C elevation of more than 300 mg/dL or more than 200 mg/dL with prevalent cardiovascular disease.

**Ministry of Health of Ontario**

In 2007, the Ministry of Health of Ontario published an evidence-based analysis of the available literature for the period of January 1998 to May 2007. For homozygous FH patients, there was a strong recommendation based on low- to very low quality evidence that the benefits of LDL apheresis outweigh risks and burdens. In contrast, there was a weak recommendation based on low- to very low quality evidence favoring apheresis for heterozygous people. For the small number of heterozygous people intolerant to lipid-lowering medications or unable to reach lipid level targets on maximal diet and medication, LDL apheresis was indicated to be likely as beneficial and less likely to have fewer adverse effects as plasmapheresis. No guidelines on therapeutic apheresis with selective HDL delipidation and plasma reinfusion were identified.

**Medicare National Coverage**

National Coverage Decision 110.14 APHERESIS (therapeutic pheresis) lists the indications for which apheresis is a covered benefit in cellular and immune-complex mediated disorders. There is no determination for hypercholesterolemia or LDL apheresis.\(^\text{27}\)
Regulatory Status

Two low-density lipoprotein (LDL) apheresis systems have received approval from the U.S. Food and Drug Administration (FDA) for marketing. In February 1996, dextran sulfate device “Liposorber® LA-15 System” (Kaneka Pharma, New York, NY) was approved by FDA through the premarket approval process for use to “acutely remove LDL-C from the plasma of high-risk patient populations for whom diet has been ineffective or not tolerated.”

In October 2013, the Liposorber® LA-15 System received approval for additional indications through the humanitarian device exemption¹ process for the treatment of pediatric patients with primary focal segmental glomerulosclerosis, when the following conditions apply:

- Standard treatment options, including corticosteroid and/or calcineurin inhibitor treatments, are unsuccessful or not well-tolerated, and the patient has a GFR [glomerular filtration rate] ≥60 mL/min/1.73 m²

OR

- The patient is post–renal transplantation

In September 2007, the HELP® System (B. Braun, Melsungen, Germany), a heparin-induced extracorporeal LDL precipitation, was approved by FDA through the premarket approval process for use in the above indication.

FDA product code: MMY

No devices have been approved by FDA specifically for HDL delipidation. The Lipid Sciences Plasma Delipidation System-2 (Lipid Sciences, Pleasanton, CA) was tested in clinical studies, but the company ceased business operations in 2012.

References


<table>
<thead>
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<th>Date</th>
<th>Comments</th>
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</thead>
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<td>Replace Policy - Update CPT code only.</td>
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<td>05/13/08</td>
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<td>Replace policy. Policy guideline deleted as not applicable stated “Since LDL apheresis represents a chronic, lifelong therapy, Plans may consider requiring precertification or prior approval to ensure that the patient meets the patient selection criteria”. Policy guidelines codes and descriptions reformatted for ease of use. Rationale updated with literature search through June 2013. Reference 8 added, previous reference 8 deleted; others renumbered/removed. Policy statements unchanged.</td>
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<td>Correct policy effective date from 10/14/14 to 10/14/13.</td>
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<td>Annual Review. Policy updated with literature review through July 24, 2014; references 7-8 and 10-11 added; added policy statement indicating therapeutic apheresis with selective high-density lipoprotein (HDL) delipidation and plasma reinfusion is investigational; title changed to Lipid Apheresis.</td>
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<td>11/01/16</td>
<td>Interim Update, approved October 11, 2016: Policy now requires genetic testing for FH, and requires the use of PSK9 inhibitor trial and failure prior to considering lipid apheresis.</td>
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<td>03/24/17</td>
<td>Policy moved into new format; no change to policy statements.</td>
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<td>08/01/17</td>
<td>Annual Review, approved July 11, 2017. Policy updated with literature review through March 23, 2017; references added. The investigational statement on LDL apheresis for all other uses expanded with, “…including but not limited to: non-FH, sudden sensorineural hearing loss, severe diabetic foot ulcerations, peripheral artery disease, and non–arteritic acute anterior ischemic optic neuropathy.” Revised Definition of Terms updated for “Maximum tolerated drug therapy…” now defined as “…a trial of drugs from at least 2 separate classes of hypolipidemic agents such as bile acid sequestrants, HMG-CoA reductase inhibitors, fibric acid derivatives, or niacin/nicotinic acids.”</td>
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**Disclaimer:** This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply.
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**Scope:** Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.
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  - Qualified interpreters
  - Information written in other languages

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Toll free 855-332-4535, Fax 425-918-5992, TTY 800-842-5357
Email AppealsDepartmentInquiries@Premera.com

You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, the Civil Rights Coordinator is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:
1. U.S. Department of Health and Human Services
200 Independence Avenue SW, Room S09F, HHH Building
Washington, D.C. 20201, 1-800-368-1019, 800-537-7697 (TDD)
Complaint forms are available at
https://ocrportal.hhs.gov/ocr/portal/lobby.jsf

There may be key dates in this notice. You may need to take action by certain deadlines to keep your health coverage or help with costs. You have the right to get this information and help in your language at no cost.

Getting Help in Other Languages

This Notice has Important Information. This notice may have important information about your application or coverage through Premera Blue Cross. There may be key dates in this notice. You may need to take action by certain deadlines to keep your health coverage or help with costs. You have the right to get this information and help in your language at no cost.

Call 800-722-1471 (TTY: 800-842-5357).

中文 (Chinese): 通知包含重要的訊息。本通知可能有關於您透過Premera Blue Cross提出的申請或保單的重要訊息。本通知可能包含重要日期。您可能需要在截止日期之前採取行動，以保留您的健康保險或費用補貼。您有權利免費以您的母語得到本訊息和幫助。請撥電話800-722-1471 (TTY: 800-842-5357)。


Ilokano (Illocano): Daytoy a Pakdaar ket naglaon iti Napateg nga Impomrason. Daytoy a pakdaar mabalini nga adda ket naglaon iti napateg nga impomrasion maipanggep iti appliesyon wu coverage babaen iti Premera Blue Cross. Daytoy ket mabalini dagiti importante a pelsa tit daytoy a pakdaar. Mabalini nga adda rumbeg nga aramideny nga adda sakybay dagiti particular a naituding nga alaw tapno mapagtalaidneyo ti coverage ti salun-atyo wenno tulong kadagiti gastos. Adda karbenganyo a mangala iti daytoy nga impomrasion ken tulgong ti bukdoyo a pagasao nga awan ti bayadanyo. Tumawag ti numero nga 800-722-1471 (TTY: 800-842-5357).