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>
<tbody>
<tr>
<td><strong>LDL apheresis</strong></td>
<td>Low-density lipoprotein (LDL) apheresis may be considered medically necessary in patients with homozygous familial hypercholesterolemia as an alternative to plasmapheresis.</td>
</tr>
</tbody>
</table>

*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
  
<table>
<thead>
<tr>
<th>OR</th>
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<tbody>
<tr>
<td>Functional hypercholesterolemic heterozygotes with LDL $\geq 200$ mg/dL <strong>and</strong> documented coronary artery disease</td>
</tr>
</tbody>
</table>

*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>
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</thead>
<tbody>
<tr>
<td>Low-density lipoprotein (LDL) apheresis</td>
<td>LDL apheresis is considered investigational for all other uses not listed in this policy, including but not limited to:</td>
</tr>
<tr>
<td></td>
<td>• Non–arteritic acute anterior ischemic optic neuropathy</td>
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<td></td>
<td>• Nonfamilial hypercholesterolemia</td>
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<td></td>
<td>• Peripheral artery disease</td>
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<td>• Preeclampsia</td>
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</table>
### Treatment

<table>
<thead>
<tr>
<th>Investigational</th>
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</thead>
<tbody>
<tr>
<td>• Severe diabetic foot ulcerations</td>
</tr>
<tr>
<td>• Sudden sensorineural hearing loss</td>
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</tbody>
</table>

### Therapeutic Apheresis (0342T)

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

### Coding

#### Code Description

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>CPT</td>
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<tr>
<td>0342T</td>
<td>Therapeutic apheresis with selective HDL delipidation and plasma reinfusion</td>
</tr>
<tr>
<td>36516</td>
<td>Therapeutic apheresis; with extracorporeal selective adsorption or selective filtration and plasma reinfusion</td>
</tr>
<tr>
<td>HCPCS</td>
<td></td>
</tr>
<tr>
<td>S2120</td>
<td>Low density lipoprotein (LDL) apheresis using heparin-induced extracorporeal LDL precipitation</td>
</tr>
</tbody>
</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 colesevelam (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 isolate plasma. The LDLSs 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>
<th>Planned Enrollment</th>
<th>Completion Date</th>
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<tr>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT01967355</td>
<td>Prolongation of Pregnancy in Preeclampsia by Therapeutic Lipid Apheresis</td>
<td>15</td>
<td>Jun 2017</td>
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<tr>
<td>NCT01518205</td>
<td>HELP-Apheresis in Diabetic Ischemic Foot Treatment (H.A.D.I.F): an RC Trial to Evaluate the Effect of LDL-apheresis on the Recovery of Diabetic Ulcers in Patients With Peripheral Vasculopathy Not Susceptible to Revascularization</td>
<td>132</td>
<td>Dec 2017</td>
</tr>
<tr>
<td>NCT02791802</td>
<td>Effect of Lipoprotein(a) Elimination by Lipoprotein Apheresis on Cardiovascular Outcomes</td>
<td>1000</td>
<td>Feb 2021</td>
</tr>
</tbody>
</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.\(^{25}\) 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

• Phytic 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.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.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 exemption\(^1\) 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] \(\geq 60\) mL/min/1.73 m\(^2\)

**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


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<table>
<thead>
<tr>
<th>Date</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>09/07/99</td>
<td>Add to Therapy Section - New Policy</td>
</tr>
<tr>
<td>11/12/02</td>
<td>Replace Policy - Policy reviewed without literature review; new review date only</td>
</tr>
<tr>
<td>05/13/03</td>
<td>Replace Policy - Update CPT code only.</td>
</tr>
<tr>
<td>02/10/04</td>
<td>Replace Policy - Policy reviewed without literature review; codes added.</td>
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<td>05/10/05</td>
<td>Replace Policy - Policy reviewed with a literature search; no change to policy statement.</td>
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<td>05/09/06</td>
<td>Replace Policy - Policy reviewed with a literature search; reference added; no change to policy statement.</td>
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<td>05/26/06</td>
<td>Update Scope and Disclaimer - No other changes.</td>
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<td>05/13/08</td>
<td>Replace Policy - Policy updated with literature search. Policy statement expanded to include LDL apheresis for all other uses, including use in preeclampsia as investigational. References and code added.</td>
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<td>Replace Policy. Policy reviewed, literature search through July 2012 resulted in no additions to the reference section. Policy statement is unchanged.</td>
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<td>Update Related Policies, change title to policy 8.02.02.</td>
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<td>10/14/13</td>
<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>12/23/13</td>
<td>Coding Update. Add CPT 0342T effective 01/01/14.</td>
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<td>05/28/14</td>
<td>Correct policy effective date from 10/14/14 to 10/14/13.</td>
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<tr>
<td>10/13/14</td>
<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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<tr>
<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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<tr>
<td>03/24/17</td>
<td>Policy moved into new format; no change to policy statements.</td>
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<tr>
<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 &quot;Maximum tolerated drug therapy...&quot; 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>
</tr>
</tbody>
</table>

**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.
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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PO Box 91102, Seattle, WA 98111
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:
U.S. Department of Health and Human Services
200 Independence Avenue SW, Room S90F, HH Building Washington, D.C. 20201, 1-800-368-1019, 800-537-7697 (TTY) 800-842-5357
Email AppealsDepartmentInquiries@Premera.com

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).

Oromo (Cushite):

Français (French):

Kreyòl ayisyen (Creole):
Avi silica a gen enfòmasyon enpòtan lidadd. Avi silica a kapab genyen enfòmasyon enpòtan konsèn a plaksan yon lwa oso konsèn vovètli a silsil ilan travay Premera Blue Cross. Kapab genyen dat ki enpòtan nan avi silica a. Ou ka gen pou pou trés akny a le yon aven seti nan dat limit pou ka konba vovètli a silsil ilan ay ca yo ka ek ede ay akny de yon avon yon. Se dwa w pou resevwa enfòmasyon sa a ak asistans nan lang ou pale a, san ou pa gen pou pea pou sa. Rate nan 800-722-1471 (TTY: 800-842-5357).

Deutsche (German):

Hmoob (Hmong):

Ilokano (Ilocano):
Daytoy a Pakdaara ket naglaon iti Napateg nga Impormasion. Daytoy a pakdaara mabalini nga adda ket naglaon iti napateg nga impormasion maipanggepp iti aplikasyonoy weno coverage babaen iti Premera Blue Cross. Daytoy ket mabalini dagiti importante a petsa iti daytoy a pakdaara. Mabalini nga adda rumbeng nga aramidennoy weno adda sakhay dagiti partikular a naituding nga alatow yaplatinalaydo ti coverage ti salun-ayyo weno tulong kadayot gastos. Adda karbenganyo a mangala iti daytoy nga impormasion ken tulong ti bakodyo a pagasasao nga awan ti bayadanoy. Tumawag ti numero nga 800-722-1471 (TTY: 800-842-5357).

Italiano (Italian):
Japanese (Japanese):
この通知には重要な情報が含まれています。この通知には、Premera Blue Crossの申請または補償範囲に関する重要な情報が含まれている場合があります。この通知に記載されている情報がある場合をご確認ください。健康保険や無料サポートを維持するには、特定の日までに行動を取らないとなりません。ご使用の言語による情報とサポートが無料で提供されます。800-722-1471（TTY: 800-842-5357）までお電話ください。

한국어 (Korean):
본 통지서에는 중요한 정보가 들어 있습니다. 즉 이 통지서는 귀하의 신청에 관하여 그리고 Premera Blue Cross를 통한 커버리지에 관한 정보를 포함하고 있습니다. 본 통지서에는 캠프이 되는 날짜이 있을 수 있습니다. 귀하의 귀하의 건강 커버리지를 계속 유지하려면 귀하의 일정한 마감일까지 조치를 취해야 할 필요가 있을 것입니다.
귀하의 이러한 정보와 도움을 귀하의 인터페이스 비용 부담없이 얻을 수 있는 권리가 있습니다. 800-722-1471（TTY: 800-842-5357）로 전화하십시오.

Română (Romanian):

Русский (Russian):
Настоящее уведомление содержит важную информацию. Это уведомление может содержать важную информацию о вашем заявлении или страховом покрытии через Premera Blue Cross. В настоящем уведомлении могут быть указаны ключевые даты. Вам, возможно, потребуется принять меры к определенным предельным срокам для сохранения страхового покрытия или помощи с расходами. Вы имеете право на бесплатное получение этой информации и помощь на вашем языке. Звоните по телефону 800-722-1471（TTY: 800-842-5357）.

Español (Spanish):
Este Aviso contiene información importante. Es posible que este aviso contenga información importante acerca de su solicitud o cobertura a través de Premera Blue Cross. Es posible que haya fechas claves en este aviso. Es posible que deba tomar alguna medida antes de determinadas fechas para mantener su cobertura médica o ayuda con los costos. Usted tiene derecho a recibir esta información y ayuda en su idioma sin costo alguno. Llame al 800-722-1471（TTY: 800-842-5357）.

Tagalog (Tagalog):
Ang Panawala na ito ay naglalaman ng mahalagang impormasyon. Ang panawala na ito ay naglalaman ng mahalagang impormasyon tungkol sa iyong aplikasyon o pagsakop sa pamamagitan ng Premera Blue Cross. Maaaring may mga mahalagang peta pata sa panawala. Maaring mangailangan ka na magsagawa ng hakbang sa ilang mga itanong panahon unang mapanatili ang iyong pagsakop sa kalusugan o tulong na tulong sa walang gastoso. May karapatan ka na makatutulungan sa galingan impormasyon at tulong sa iyong wika ng walang gastoso. Tumawag sa 800-722-1471（TTY: 800-842-5357）.

ไทย (Thai):
ความรู้สึกนี้ในเรื่องสิ่งที่เกิดขึ้นเกี่ยวกับการซื้อประกันสุขภาพของคุณ Premera Blue Cross และการเรียนรู้ในสถานการณ์ที่คุณควรจะดูแลการเงินของคุณในสถานการณ์ที่เกิดขึ้นเพื่อที่จะรักษาสุขภาพของคุณการช่วยเหลือซึ่งมีที่นี่มีสิทธิที่จะได้รับข้อมูลและความช่วยเหลือในภาษาของคุณโดยไม่มีค่าใช้จ่าย โทร 800-722-1471（TTY: 800-842-5357）.

Farsi (Farsi):
این اطلاعیه خطور نشان می‌دهد که شما می‌توانید اطلاعات مهمی از طریق Premera Blue Cross پرداخت داشته باشید. شما امکان استفاده از روش و روشی که شما نیاز ندارید را به راحتی هزینه‌های ردیابی ندارید. برای تخرج شما و نیاز شما ممکن است باید در راه‌نوردی‌هایی که شما نیاز دارید همراه باشید. شما حق این را دارد که اطلاعات و کمک را به زبان خود به طور رایگان دریافت نماید. (TTY: 800-842-5357)

Polski (Polish):
To ogłoszenie może zawierać ważne informacje. To ogłoszenie może zawierać ważne informacje odnośnie Polskiego wniosku lub zakresu świadczeń poprzez Premera Blue Cross. Prosimy zwróć uwagę na kluczowe daty, które mogą być zawarte w tym ogłoszeniu aby nie przekroczyć terminów w przypadku utraty polisy ubezpieczeniowej lub pomocy związanej z kosztami. Macie prawo do bezpłatnej informacji we własnym języku. Zadzwonite pod 800-722-1471（TTY: 800-842-5357）.

Português (Portuguese):
Este aviso contém informações importantes. Este aviso poderá conter informações importantes a respeito de sua aplicação ou cobertura por meio do Premera Blue Cross. Poderão existir datas importantes neste aviso. Talvez seja necessário que você tome providências dentro de determinados prazos para manter sua cobertura de saúde e ajuda de custos. Você tem o direito de obter esta informação e ajuda em seu idioma e em custos. Ligue para 800-722-1471（TTY: 800-842-5357）.

Tiếng Việt (Vietnamese):
Thông báo này cung cấp thông tin quan trọng. Thông báo này có thông tin quan trọng về đơn xin tham gia hoặc hỗ trợ bảo hiểm của quý vị qua quan hệ của Premera Blue Cross. Xin xem ngay quan trọng thông báo này. Quý vị có thể phải thực hiện các thông báo trong thời hạn để duy trì bảo hiểm sức khỏe hoặc được trợ giúp thêm về chi phí. Quý vị có quyền được biết thông tin này và được trợ giúp bằng ngôn ngữ của mình miễn phí. Xin gọi số 800-722-1471（TTY: 800-842-5357）.