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<b>Medical Benefit</b>		<b>Effective Date:</b> 10/01/09	<b>Next Review Date:</b> 05/15
<b>Preauthorization</b>	No	<b>Review Dates:</b> 05/09, 05/10, 05/11, 05/12, 05/13, 05/14	

*The following Protocol contains medical necessity criteria that apply for this service. It is applicable to Medicare Advantage products unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. **Preauthorization is not required.** Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.*

### Description

Low-density lipoprotein (LDL) apheresis describes a variety of technologies used to remove LDL from the plasma. It is a specific form of plasmapheresis that discriminately removes the LDL particles from the plasma while leaving other factors intact, allowing the filtrated plasma to be returned to the patient. LDL apheresis has been investigated as a technique to treat patients with familial hypercholesterolemia (FH).

### Background

Familial hypercholesterolemia (FH) is a dominantly inherited disorder involving a mutation of the gene that encodes for the specific cell surface receptor responsible for low-density lipoprotein (LDL) uptake by the cells. The heterozygous form affects about one 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 two to three times levels that are considered acceptable (i.e., greater than 300 mg/dL). Affected male patients typically develop coronary heart disease in their thirties and forties, while women develop coronary heart disease in their fifties. Depending on the patient, heterozygous FH may or may not respond adequately to lipid-lowering drugs.

Homozygous hypercholesterolemia is rare, only occurring in one in 1 million subjects. Serum levels of LDL-C may be elevated six-fold (greater than 500 mg/dL), due to the total lack of functioning LDL receptors. Homozygotes may develop severe aortic stenosis and coronary heart disease by age 20 years. These patients typically do not adequately respond to drug or diet modification therapy. 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 the plasma.

The patient initially undergoes an apheresis procedure to isolate the plasma. The LDLs are then selectively removed from the plasma by either immunoabsorption, heparin-induced extracorporeal LDL precipitation (referred to as HELP), or dextran sulfate adsorption. In immunoabsorption, polyclonal antihuman apo B antibodies from sheep selectively bind and remove LDL. (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. LDL apheresis must be distinguished from plasma exchange (also referred to as plasmapheresis). In plasma exchange, the plasma is collected during a pheresis procedure, then discarded and replaced with crystalloids. In contrast, LDL apheresis is a selective procedure in which only pathogenic LDLs are removed. The plasma is then returned to the patient.

### Regulatory Status

Two lipid 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

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

#### *Related Protocol*

Plasma Exchange

#### **Policy (Formerly Corporate Medical Guideline)**

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 who have failed a six-month trial of diet therapy and maximum tolerated combination drug\* therapy AND who meet the following FDA-approved indications: (All LDL levels represent the best achievable LDL level after a program of diet and drug therapy.)

1. Functional hypercholesterolemic heterozygotes with LDL  $\geq$  300 mg/dL
2. Functional hypercholesterolemic heterozygotes with LDL  $\geq$  200 mg/dL AND documented coronary artery disease.\*

LDL apheresis is considered **investigational** for all other uses, including use in preeclampsia.

\*For definitions of maximum tolerated drug therapy and documented coronary artery disease, please see Policy Guidelines.

#### **Policy Guideline**

Maximum tolerated drug therapy is defined as a trial of drugs from at least two separate classes of hypolipidemic agents such as bile acid sequestrants, HMG-CoA reductase inhibitors, fibric acid derivatives, or niacin/nicotinic acids.

Documented coronary artery disease 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.

LDL apheresis represents a chronic, lifelong therapy. Frequency of LDL apheresis varies, but typically averages about once every two weeks to obtain an interapheresis level of LDL cholesterol at less than 120 mg/dL. Patients with homozygous FH may be treated more frequently. Patients are simultaneously treated with diet and drug therapy.

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Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced

procedures. **Some of this Protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

## References

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

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11. Medical Advisory Secretariat. Low density lipoprotein apheresis: an evidence-based analysis. Ontario Health Technology Assessment Series. 2007; 7(5).
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