Prior Authorization Review Panel

MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.

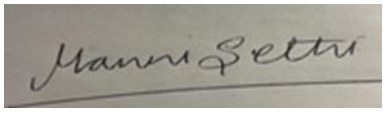
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Plan: AmeriHealth Caritas Pennsylvania Community HealthChoices & Keystone First Community HealthChoices	Submission Date: 8/1/2026
Policy Number: CCP.1238	Effective Date: 10/1/2016 Revision Date: 7/1/2026
Policy Name: Lipoprotein Apheresis	

Type of Submission:	Type of Policy:
☐ New Policy	☒ Prior Authorization Policy
☒ Revised Policy*	☐ Base Policy
☐ Annual Review- no revisions	☐ Experimental/Investigational Policy
	☐ Statewide PDL
	☐ Other:

*All revisions to the policy must be highlighted using track changes throughout the document.

Please provide any clarifying information for the policy below:

Name of Authorized Individual (Please type or print):	Signature of Authorized Individual:
Manni Sethi, MD, MBA, CHCQM	

Keystone First
Community HealthChoices

Lipoprotein Apheresis

Clinical Policy ID: CCP.1238

Recent review date: 7/2026

Next review date: 11/2027

Policy contains: Familial hypercholesterolemia; HELP; Liposorber; low-density lipoprotein apheresis; primary focal segmental glomerulosclerosis.

Keystone First Community HealthChoices has developed clinical policies to assist with making coverage determinations. Keystone First Community HealthChoices' clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation are considered by Keystone First Community HealthChoices, on a case by case basis, when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. Keystone First Community HealthChoices' clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. Keystone First Community HealthChoices' clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Keystone First Community HealthChoices will update its clinical policies as necessary. Keystone First Community HealthChoices' clinical policies are not guarantees of payment.

Coverage policy

Low-density lipoprotein apheresis, using heparin-induced extracorporeal precipitation or dextran sulfate adsorption, is clinically proven and, therefore, may be medically necessary for treating severe familial hypercholesterolemia when there is an inadequate response to, or intolerance of, maximum drug therapy (a six-month trial of ≥ two hypolipidemic agent classes) and one of the following criteria (American College of Cardiology [Blumenthal, 2026]; National Lipid Association [Ahmad, 2026]):

- Homozygous familial hypercholesterolemia with low-density lipoprotein cholesterol ≥ 500 mg/dL
- Heterozygous familial hypercholesterolemia with low-density lipoprotein cholesterol ≥ 300 mg/dL
- Heterozygous familial hypercholesterolemia with low-density lipoprotein cholesterol ≥ 70 mg/dL and documented coronary artery disease or peripheral artery disease
- Heterozygous familial hypercholesterolemia with lipoprotein(a) ≥ 60 mg/dL (or > 130 nmol/L) and documented coronary artery disease or peripheral artery disease

Low-density lipoprotein apheresis is clinically proven and, therefore, may be medically necessary for treating primary focal segmental glomerulosclerosis recurring after kidney transplantation (American Heart Association [Gianos, 2024]).

High-density lipoprotein apheresis is investigational/not clinically proven and, therefore, not medically necessary.

Limitations

All other uses of low-density lipoprotein apheresis are investigational/not clinically proven and, therefore, not

medically necessary.

The frequency of low-density lipoprotein apheresis considered medically necessary varies, but typically averages about once every two weeks in members with heterozygous familial hypercholesterolemia to obtain an intrapheresis low-density lipoprotein cholesterol (low-density lipoprotein-C) level ≤ 120 mg/dL. It may be medically necessary to treat members with homozygous familial hypercholesterolemia more frequently (Ahmad, 2026).

In members for whom low-density lipoprotein apheresis may be medically necessary, a minimum body weight of 15 kg is recommended because of the large extracorporeal blood volume (approximately 400 mL) required for this procedure (Ahmad, 2026; Gianos, 2024).

Alternative covered services

- Lifestyle management
- Intensive lipid-lowering drug treatment
- Surgery for members with severe familial hypercholesterolemia — Ileal bypass and liver transplantation
- For treatment of focal segmental glomerulosclerosis — corticosteroids, cyclophosphamide, or cyclosporine in members refractory to prednisone therapy, plasmapheresis, and renal transplantation

Background

Familial hypercholesterolemia is a congenital metabolic disorder resulting in severe elevations of blood cholesterol levels (Youngblom, 2025). Left untreated, it can lead to early development of atherosclerosis and coronary heart disease. Total cholesterol concentrations in patients with heterozygous familial hypercholesterolemia typically range from 350 to 550 mg/dL, and in homozygous familial hypercholesterolemia range from 650 to 1,000 mg/dL. Long-term intensive cholesterol-lowering drug therapy significantly reduces or removes the excess lifetime risk of coronary heart disease, lowering the level of risk to that of the general population. Some remain intolerant of or refractory to cholesterol-lowering therapy and require adjunct therapy (Youngblom, 2025).

Familial hypercholesterolemia impacts women through life differently than men. Although cholesterol-lowering therapy is equally effective at diminishing cardiovascular risk in both sexes, women have higher untreated and treated low-density lipoprotein cholesterol levels, resulting in part from sex-specific hormonal and genetic determinants of lipoprotein metabolism. Women receive less intensive treatment, experience off-treatment periods due to family planning, and may experience premature atherosclerotic cardiovascular disease (Klevmoen, 2023; Zimodro, 2024).

Apheresis is the extracorporeal process of removing one or more blood constituents from whole blood and returning the remainder to the circulation. Therapeutic apheresis (also called blood component therapy) removes the abnormal pathogenic component, which, theoretically, should improve the disease course. Depending on clinical use, apheresis may be performed as a one-time-only treatment or several times per week for several weeks. For some, it may be a lifelong commitment.

Low-density lipoprotein apheresis involves the selective extracorporeal removal of low-density lipoproteins, lipoprotein(a) particles, very low-density lipoproteins, or high-density lipoproteins from either whole blood or plasma using a series of membrane filtering devices (Feingold, 2026). It is used for disorders with marked hyperlipidemia.

Selective removal of the low-density lipoproteins can occur through several processes. The U.S. Food and Drug Administration (2026) has approved two Class III devices for removal of low-density lipoproteins from the plasma

of high-risk patients for whom a lipid-lowering diet and maximum drug therapy have been ineffective or not tolerated:

- Dextran-sulfate adsorption, which selectively binds apolipoprotein B-containing lipoproteins (low-density lipoprotein, lipoprotein(a) particles, and very low-density lipoproteins). Marketed as the Liposorber LA-15 system (Kaneka Pharma America Corp., New York, New York)
- Heparin-induced extracorporeal low-density lipoprotein precipitation, which selectively precipitates out apolipoprotein B-containing lipoproteins from plasma at a given pH level in the presence of heparin. Marketed as HELP (B. Braun Avitum AG, Melsungen, Germany)

Approval for Liposorber was extended as a Humanitarian Use Device for adult and pediatric renal transplantation recipients with nephrotic syndrome associated with primary focal segmental glomerulosclerosis (U.S. Food and Drug Administration, 2013, 2018).

Selective high-density lipoprotein apheresis involves selective removal of cholesterol from high-density lipoprotein, converting the major alpha high-density lipoprotein to pre-beta-like high-density lipoprotein, which is then re-infused to the patient. The pre-beta-like high-density lipoprotein enhances cholesterol transport to the liver and is thought to reduce atherosclerosis development and burden. No extracorporeal apheresis device for high-density lipoprotein apheresis has been approved for clinical use.

Findings

Guidelines

Updated professional guidelines reflect advances in managing dyslipidemia, particularly new lipoprotein-lowering drugs. Low-density lipoprotein apheresis plays an important role in lowering low-density lipoprotein cholesterol, lipoprotein(a), and atherosclerotic cardiovascular disease risk in patients with severe familial hypercholesterolemia. It is safe and effective for use in patients as young as 2 years of age and in pregnant and lactating women. Since low-density lipoprotein apheresis imposes a high treatment burden on patients and health systems, guidelines recommend optimizing pharmacologic treatment outcomes, reserving low-density lipoprotein apheresis for those inadequately controlled with drug therapy.

A 2026 guideline update from the National Lipid Association confirmed the benefits of low-density lipoprotein apheresis in reducing concentrations of low density lipoprotein cholesterol and lipoprotein(a) in patients with familial hypercholesterolemia, including during pregnancy. Observational studies suggest low-density lipoprotein apheresis may reduce the incidence of atherosclerotic cardiovascular disease events. Indications may apply to children as young as 2 years, but a minimum body weight of 15 kg is recommended to accommodate the blood volume requirements of the procedure. Current indications for lipoprotein apheresis are (Ahmad, 2026):

- Homozygous familial hypercholesterolemia with low-density lipoprotein cholesterol ≥ 500 mg/dL
- Heterozygous familial hypercholesterolemia with low-density lipoprotein cholesterol ≥ 300 mg/dL
- Heterozygous familial hypercholesterolemia with low-density lipoprotein cholesterol ≥ 70 mg/dL and documented coronary artery disease or peripheral artery disease
- Heterozygous familial hypercholesterolemia with lipoprotein(a) ≥ 60 mg/dL (or > 130 nmol/L) and documented coronary artery disease or peripheral artery disease

The American Society for Apheresis recommends low-density lipoprotein apheresis for severe familial hypercholesterolemia (Connelly-Smith, 2023).

The Writing Committee for the American College of Cardiology recommends low-density lipoprotein apheresis in selected patients with severe hypercholesterolemia whose low density lipoprotein cholesterol is inadequately controlled with drug therapy. The indications for use align with those of the National Lipid Association (Blumenthal, 2026).

A scientific statement by the American Heart Association supports low-density lipoprotein apheresis as safe and effective for lowering low density lipoprotein levels in patients with familial hypercholesterolemia, including patients as young as 2 years with homozygous familial hypercholesterolemia, pregnant or breastfeeding women with severe atherosclerotic cardiovascular disease and/or familial hypercholesterolemia, and patients as young as 2 years with refractory focal segmental glomerulosclerosis. A minimum body weight of 15 kg is recommended because of the large extracorporeal blood volume (approximately 400 mL) required for this procedure. Preeclampsia and clinical atherosclerotic cardiovascular disease with low density lipoprotein cholesterol levels above goal in the absence of familial hypercholesterolemia remain off-label uses with limited evidentiary support (Gianos, 2024).

Evidence review

Several systematic reviews and meta-analyses have examined the safety and efficacy of low-density lipoprotein apheresis for familial hypercholesterolemia. The evidence for the impact of lipoprotein apheresis on atherosclerotic cardiovascular disease outcomes is derived from prospective and retrospective observational studies showing a consistent benefit across various cohorts when using major adverse cardiovascular events as primary end points. With repeated sessions or a single session, lipoprotein apheresis can significantly reduce lipoprotein(a) and low density lipoprotein cholesterol levels by approximately 65% to 85% (Gianos, 2024). Reductions in inflammatory markers (e.g., C-reactive protein), circulating enzymes, and hemostasis have been reported (Hatami, 2025, 2026; Razi, 2026).

Alothman (2022) conducted a systematic review and meta-analysis of seven studies of 194 children with homozygous familial hypercholesterolemia. Low-density lipoprotein apheresis dramatically reduced cholesterol levels, but also imposed a high treatment burden on patients, with most reporting it to be tiring, painful, uncomfortable, and time-consuming, compromising educational attainment. The review noted inadequate psychological support for these patients.

Gu (2024) conducted a systematic review of 25 seminal studies on treatments for homozygous familial hypercholesterolemia. Low-density lipoprotein apheresis reduced low-density lipoprotein cholesterol levels by around 40% compared to baseline based on the best available evidence from five observational studies. However, these studies were considered at high to very high risk of bias and limited by confounding, with the largest study including only 30 patients. In contrast, high-quality evidence from randomized controlled trials demonstrated that monoclonal antibody therapy using evinacumab, evolocumab, and alirocumab reduced low-density lipoprotein cholesterol by 49%, 31%, and 36%, respectively, compared to placebo in trials totaling 184 patients. While low-density lipoprotein apheresis is effective, the authors concluded that it places a significant burden on patients and healthcare systems. They recommend that combinations of newer pharmacologic agents be considered and individualized for patients with homozygous familial hypercholesterolemia to optimize treatment outcomes.

In pediatric kidney transplant recipients, recurrent focal segmental glomerulosclerosis is a significant cause of graft failure. Hayes (2026) synthesized results from eight studies of 25 total participants who received low-density lipoprotein apheresis following kidney transplant. Median follow-up duration was eight months (interquartile range six to 24 months). All studies had a moderate to high risk of bias. The complete and partial remission rates were 0.36 (95% confidence interval 0.13 to 0.61) and 0.37 (95% confidence interval 0.14 to 0.62), respectively. Secondary outcomes of median serum albumin, estimated glomerular filtration rate values, and urine protein–creatinine ratio also improved after treatment.

An international registry study of children with homozygous familial hypercholesterolemia compared the long-term outcomes of participants who initiated high-frequency lipoprotein apheresis in childhood (lipoprotein apheresis group) and those who only received lipid-lowering drugs (pharmacotherapy-only group), matched by sex and untreated plasma low density lipoprotein cholesterol concentrations (n = 125 per group). Lipoprotein apheresis was associated with greater mean reductions in plasma cholesterol concentrations between baseline and final follow-up (P < .0001), longer atherosclerotic cardiovascular disease-free survival, and longer cardiovascular death-free survival. However, outcomes in the pharmacotherapy-only group trended toward a lower rate of cardiovascular death and a lower median age at coronary artery bypass grafting (Reijman, 2024).

In 2024, we reordered and condensed the findings section and updated the references.

In 2025, we updated the references with no policy changes warranted.

In 2026, we updated the references and modified coverage criteria to align with updated 2026 guideline recommendations from the American College of Cardiology and the National Lipid Association.

References

On May 28, 2026, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were “blood component removal” (MeSH); “hyperlipoproteinemia type II” (MeSH), “therapeutic apheresis,” and “lipoprotein apheresis." We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

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Policy updates

6/2016: initial review date and clinical policy effective date: 10/2016

6/2017: Policy references updated.

7/2017: Policy references updated.

7/2018: Policy references updated.

7/2019: Policy references updated. Policy ID changed.

7/2020: Policy references updated.

7/2021: Policy references updated.

7/2022: Policy references updated.

7/2023: Policy references updated.

7/2024: Policy references updated.

7/2025: Policy references updated.

7/2026: Policy references updated. Coverage modified.

Related codes

Below are the most commonly submitted codes for the service(s)/item(s) subject to this policy CCP.1238. This is not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and bill accordingly.

Code	Code description
S2120	Low density lipoprotein (LDL) apheresis using heparin-induced extracorporeal LDL precipitation
36516	Therapeutic apheresis; with extracorporeal immunoadsorption, selective adsorption or selective filtration and plasma reinfusion