MEDICAL POLICY

MEDICAL POLICY DETAILS	
Medical Policy Title	**Plasmapheresis, Plasma Exchange, and Apheresis**
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Product Disclaimer	• *Services are contract dependent; if a product excludes coverage for a service, it is not covered, and medical policy criteria do not apply.* • *If a commercial product (including an Essential Plan or Child Health Plus product), medical policy criteria apply to the benefit.* • *If a Medicaid product covers a specific service, and there are no New York State Medicaid guidelines (eMedNY) criteria, medical policy criteria apply to the benefit.* • *If a Medicare product (including Medicare HMO-Dual Special Needs Program (DSNP) product) covers a specific service, and there is no national or local Medicare coverage decision for the service, medical policy criteria apply to the benefit.* • *If a Medicare HMO-Dual Special Needs Program (DSNP) product DOES NOT cover a specific service, please refer to the Medicaid Product coverage line.*

POLICY STATEMENT

I. Based upon our criteria and assessment of the peer reviewed literature, plasmapheresis with plasma exchange has been medically proven to be effective and, therefore, is considered **medically appropriate** for the following conditions:
   A. ABO-incompatible hematopoietic progenitor cell transplants;
   B. acute fulminant central nervous system (CNS) demyelination associated with multiple sclerosis or other conditions, such as transverse myelitis, etc.;
   C. autoantibodies to neutrophil cytoplasmic antigens (ANCA)-associated vasculitis (e.g., Wegener's granulomatosis) with associated renal failure (serum Cr greater than 5.8 mg/dl);
   D. chronic inflammatory demyelinating polyneuropathy (CIDP) for patients with severe or life-threatening symptoms who have failed to respond to conventional therapy with prednisone or intravenous immunoglobulins (IVIg);
   E. cryoglobulinemia, multiple manifestations of mixed, severe type (e.g., cryoglobulinemic nephropathy, skin ulcers, sensory motor neuropathy, widespread vasculitis);
   F. Guillain-Barré syndrome (GBS):
      1. severity grade 1-2 within two weeks of onset; grades 1-2 disease defined by the following: minor symptoms of neuropathy, but capable of manual work (grade 1), ability to walk without support, but incapable of manual work (grade 2); or
      2. severity grade 3-5 within four weeks of onset; grades 3-5 disease defined by the following: ability to walk five meters with assistance (grade 3), confinement to a bed or chair-bound (grade 4), or requiring assisted ventilation for at least part of the day or night (grade 5); or
      3. children less than 10 years of age with severe GBS.;
   G. HELLP (hemolysis [H], elevated liver enzymes [EL], and low platelet [LP]counts) syndrome of pregnancy;

H. hemolytic uremic syndrome (HUS), atypical;
I. hyperviscosity syndromes associated with multiple myeloma, Waldenstrom's macroglobulinemia, or other conditions;
J. idiopathic thrombocytopenic purpura in emergency situations only;
K. IgA and IgG paraproteinemia with polyneuropathy;
L. myasthenia gravis in crisis or as part of a pre-operative preparation of a patient with Myasthenia gravis;
M. N-methyl-d- aspartate receptor antibody encephalitis;
N. post-transfusion purpura;
O. progressive renal failure due to anti-basement membrane antibodies (e.g., Goodpasture's syndrome)**;**
P. solid organ transplant: prior to transplant, as a treatment for patients at high-risk of antibody-mediated rejection (AMR), or following transplant as a treatment of AMR;
Q. progressive, multi-focal leukoencephalopathy associated with natalizumab; or
R. thrombotic thrombocytopenic purpura (TTP).

II. Based upon our criteria and assessment of the peer-reviewed literature, plasmapheresis with plasma exchange has not been medically proven to be effective and, therefore, is considered **investigational** for the following conditions:
A. amyotrophic lateral sclerosis;
B. asthma;
C. bullous pemphigoid;
D. chronic fatigue syndrome;
E. cryoglobulinemia, other than mixed, severe type as mentioned above;
F. Guillain-Barré syndrome in children less than 10 years of age with mild or moderate forms;
G. inclusion body myositis;
H. multiple sclerosis (chronic progressive or relapsing remitting);
I. neuromyelitis optica;
J. paraneoplastic syndromes, including Eaton-Lambert myasthenic syndrome;
K. paraproteinemic polyneuropathy, including monoclonal gammopathy of undetermined significance (MGUS);
L. pemphigus;
M. polymyositis and dermatomyositis**;**
N. rapidly progressive glomerulonephritis, excluding those related to anti-basement membrane immunoglobulins (e.g., Goodpasture's syndrome);
O. regional enteritis (Crohn's disease);
P. rheumatoid arthritis;
Q. scleroderma (systemic sclerosis);
R. stiff-person syndrome;
S. systemic lupus erythematosus; or
T. all other indications, unless listed in Policy Statement I.

III. Based upon our criteria and assessment of the peer reviewed literature, low-density lipoprotein (LDL) apheresis has been medically proven to be an effective treatment option and, therefore, is considered **medically appropriate** for severely hypercholesteremic patients with LDL consistently greater than:
A. 300 mg/dl despite maximal drug therapy; or
B. 200 mg/dl despite maximal drug therapy and documented coronary artery disease (defined as a history of myocardial infarction, coronary artery bypass surgery [CABG], percutaneous transluminal angioplasty [PTCA], other coronary revascularization procedure, or progressive angina, as documented by exercise or non-exercise stress test).

IV. Based upon our criteria and assessment of the peer-reviewed literature, therapeutic apheresis (e.g., erythrocytapheresis) has been medically proven to be effective and, therefore, is considered **medically appropriate** in the treatment regimen of patients with hyperviscosity syndrome due to primary or secondary polycythemia, when therapeutic phlebotomy is contraindicated.

IV. Based upon our criteria and assessment of the peer-reviewed literature, rheopheresis has not been medically proven to be effective as a treatment for the dry form of age-related macular degeneration, and, therefore, is considered **investigational**.

V. Based upon our criteria and assessment of the peer-reviewed literature, therapeutic apheresis with selective high-density lipoprotein (HDL) delipidation and plasma reinfusion has not been medically proven to be effective and, therefore, is considered **investigational** for all indications, including, but not limited to, acute coronary syndrome.

Refer to Corporate Medical Policy #7.02.02 Allogeneic Hematopoietic Stem Cell Transplantation

Refer to Corporate Medical Policy #11.01.03 Experimental or Investigational Services

This policy does not address protein immunoadsorption therapy/extracorporeal immunoadsorption where plasma is collected in an apheresis procedure and filtered through protein A columns.

POLICY GUIDELINE

Patients receiving plasma exchange as a treatment of CIDP should meet the diagnostic criteria for CIDP, as established by the American Academy of Neurology AIDS Task Force.

DESCRIPTION

Although often used interchangeably, the terms “therapeutic apheresis,” “plasmapheresis,” and “plasma exchange” carry different meanings when used properly.

Apheresis
Apheresis is a general term describing the removal of blood from a subject. A portion of the blood is separated and retained while the rest is returned to the donor.

HDL Apheresis
Therapeutic apheresis with selective HDL delipidation and plasma reinfusion is a procedure in which plasma is removed 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 alpha HDL to pre-beta-like HDL. The plasma with pre-beta-like HDL is then reinfused to the patient. The pre-beta-like HDL is a form of HDL that enhances cholesterol transport to the liver and is thought to reduce atherosclerosis development and burden.

LDL Apheresis (low-density lipoprotein apheresis)
LDL is removed from the plasma during LDL apheresis. The patient initially undergoes an apheresis procedure to isolate the plasma. The LDLs are then selectively removed from the plasma by column adsorption or precipitation. The LDL-depleted plasma and erythrocytes are then returned to the patient’s circulation. The procedure usually takes about two to four hours and must be repeated every one to three weeks.

Plasmapheresis
The most common form of apheresis is plasmapheresis, which involves the extraction of plasma from withdrawn blood followed by retransfusion of the formed elements into the donor. It may be done for therapeutic purposes or for the collection of plasma components. Other methods of apheresis are leukapheresis or lymphocytapheresis, in which the white blood cell is isolated and retained, and peripheral stem cell collection, in which the stem cells are isolated and retained for an upcoming autologous bone marrow transplant.

Plasma Exchange (PE)
Plasma Exchange is frequently done in conjunction with plasmapheresis. The plasma is isolated, then discarded and replaced with a substitution fluid such as albumin. Plasma exchange is a non-specific therapy, as the entire plasma is discarded.

The proposed benefits of plasmapheresis are based on the fact that circulating substances, such as toxins or autoantibodies, can accumulate in the plasma. It is hypothesized that removal of these factors can be therapeutic in certain

situations. Because plasmapheresis does not address underlying pathology, and due to the phenomenon of rebound antibody production, its use in chronic diseases has been more controversial than in acute, self-limited diseases.

Rheopheresis
Rheopheresis is a technique in which the blood is removed from the patient, and the red cells are separated from the plasma. The plasma then undergoes a filtration process in which high molecular weight proteins, lipoproteins, and free radicals are removed. The filtered plasma is recombined with the red blood cells and returned to the patient. Rheopheresis has been proposed as a treatment of the dry form of age-related macular degeneration, as it has the potential to improve microcirculation and ocular blood flow by reducing the blood viscosity.

RATIONALE

Plasmapheresis is a procedure and, therefore, not subject to FDA approval; however, the plasma exchange systems, such as the Haemonetics Therapeutic Plasma Exchange Set (Haemonetics Corp.), and data systems and plasmapheresis data systems, such as the Plasmapheresis Data System III 1.0 (Medserve, Inc.), that are used in the procedure have been approved by the FDA.

Published clinical trials substantiate the beneficial effect of plasmapheresis on health outcomes for acute fulminant CNS demyelination and paraproteinemic polyneuropathies. Based on the literature, plasmapheresis is a widely accepted component in the management of acute rejection, with most experience related to kidney transplantation due to its higher volume and use in living donors. It is accepted as standard therapy for transplant recipients at high risk for antibody-mediated rejection (AMR). As a treatment for AMR, plasmapheresis is often used in combination with IVIG or anti-CD20 therapy.

Published clinical trials have not provided evidence to support the efficacy and safety of plasmapheresis over current treatment options for the indications listed as investigational in this policy. The available literature reflects studies involving small numbers of subjects, indicating that plasmapheresis may be beneficial in treating patients with severe, resistant pemphigus vulgaris or bullous pemphigoid, i.e., those who are not responding to standard therapy or who require unacceptably high doses of steroids or immunosuppressants. However, two systematic reviews (N. Khumalo et al., 2005 and G. Kirtschig et al., 2004) identified no benefit from the addition of plasmapheresis to the treatment regimens of patients with bullous pemphigoid.

Two lipid apheresis systems (for LDL apheresis) have received FDA approval: the Liposorber LA-15 system (Kaneka Pharma America Corp.) and the H.E.L.P. (Heparin-induced Extracorporeal Lipoprotein Precipitation) system (Hogan & Hartson). Clinical trials substantiate that LDL apheresis leads to lowering of total cholesterol and LDL cholesterol in severely hypercholesteremic patients.

HDL Therapeutics, a Florida based cardiovascular medical devices company, received FDA clearance for its PDS-2 (Plasma Delipidation System) in 2020. The system is designed to reduce plaque buildup in the coronary arteries (e.g., coronary artery atheroma), which is found in the plasma of adult patients with homozygous familial hypercholesterolemia (HoFH) a life-threatening genetic condition that causes high levels of cholesterol and can be life threatening. Data on therapeutic apheresis with selective HDL delipidation and plasma reinfusion is limited to one randomized, controlled trial (RCT) on safety and feasibility (Waksman et al., 2010). This RCT reported improvements in intermediate outcomes; however, data are insufficient to determine the impact of therapeutic apheresis with selective HDL delipidation and plasma reinfusion on health outcomes.

Although the outcome data from the few small studies investigating rheopheresis as a treatment for the dry form of age-related macular degeneration are promising, larger, well-designed studies with long-term outcomes are necessary, to determine its overall safety and efficacy, as well as to define the role of this treatment modality.

CODES

- *Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.*
- *CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.*

- *Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.*
- *Code Key: Experimental/Investigational = (E/I), Not medically necessary/ appropriate = (NMN).*

Codes

Code	Description
36511	Therapeutic apheresis, for white blood cells
36512	for red blood cells
36513	for platelets
36514	for plasma pheresis
36516	with extracorporeal immunoadsorption, selective adsorption or selective filtration and plasma reinfusion
0342T **(E/I)**	Therapeutic apheresis with selective HDL delipidation and plasma reinfusion

HCPCS Codes

Code	Description
S2120	Low density lipoprotein (LDL) apheresis using heparin-induced extracorporeal LDL precipitation

ICD10 Codes

Code	Description
	Multiple diagnosis codes

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*Key Article

CMS COVERAGE FOR MEDICARE PRODUCT MEMBERS

There is currently a National Coverage Determination (NCD)110.14 for apheresis. Please refer to the following NCD website for Medicare Members: [http://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=82&ncdver=1&CoverageSelection=Both&ArticleType=All&PolicyType=Final&s=New+York+-+Upstate&CptHcpcsCode=36514&bc=gAAAABAAAAAA&] accessed 01/04/24.