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## Subject: Apheresis, Plasmapheresis and Plasma Exchange

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### DESCRIPTION:

#### Apheresis, Plasmapheresis, and Plasma Exchange

The terms apheresis, plasmapheresis, and plasma exchange (PE) are often used interchangeably. The American Society for Apheresis (ASFA) defines these procedures as follows:

**Apheresis:** A procedure in which blood of the individual or donor is passed through a medical device which separates out one or more components of blood and returns the remainder with or without extracorporeal treatment or replacement of the separated component.

**Plasmapheresis:** A procedure in which blood of an individual or the donor is passed through a medical device which separates out plasma from the other components of blood and the plasma is removed (ie, <15% of total plasma volume) without the use of replacement solution.

**Plasma exchange (PE):** A therapeutic procedure in which blood of the individual is passed through a medical device which separates out plasma from other components of blood; the plasma is removed and replaced with a replacement solution such as colloid solution (eg, albumin and/ or plasma) or a combination of crystalloid/colloid solution.

#### Low-Density Lipid (LDL) Apheresis

Low-density lipid (LDL) apheresis refers to the extracorporeal removal of circulating apo B-containing lipoproteins, including LDL, lipoprotein (a), and very low density lipoprotein (VLDL). There are multiple apheresis methods, including dextran sulphate cellulose adsorption, heparin-induced extracorporeal LDL cholesterol precipitation, immunoabsorption, and double filtration plasma pheresis of lipoproteins.

## **Therapeutic apheresis with selective HDL delipidation and plasma reinfusion**

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 body. 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 individual. 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.

## **POSITION STATEMENT:**

### **Apheresis, Plasmapheresis, and Plasma Exchange (36511-36514)**

**Apheresis, plasmapheresis, and plasma exchange meet the definition of medical necessity** for the following conditions:

#### **Autoimmune**

- Severe multiple manifestations of mixed cryoglobulinemia (MC) such as cryoglobulinemic nephropathy, skin ulcers, sensory motor neuropathy, and widespread vasculitis in combination with immunosuppressive treatment
- Catastrophic antiphospholipid syndrome (CAPS)

#### **Hematologic**

- ABO incompatible hematopoietic progenitor cell transplantation
- Hyperviscosity syndromes associated with multiple myeloma or Waldenström macroglobulinemia
- Idiopathic thrombocytopenic purpura in emergency situations
- Thrombotic thrombocytopenic purpura (TTP)
- Atypical hemolytic-uremic syndrome
- Sickle cell disease, acute or non-acute
- Post-transfusion purpura
- HELLP syndrome of pregnancy (a severe form of preeclampsia, characterized by hemolysis [H], elevated liver enzymes [EL], and low platelet [LP] counts)
- Myeloma with acute renal failure
- Familial hypercholesterolemia
- In conjunction with CAR T-cell therapy

#### **Neurologic**

- Acute inflammatory demyelinating polyneuropathy (Guillain-Barré syndrome [GBS])
- Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)

- Multiple sclerosis (MS), with acute fulminant central nervous system (CNS) demyelination
- Myasthenia gravis in crisis or as part of preoperative preparation
- Paraproteinemia polyneuropathy; IgA, IgG
- Wilson's disease, fulminant with hepatic failure/hemolysis

### Renal

- Antiglomerular basement membrane disease (Goodpasture syndrome)
- ANCA (antineutrophil cytoplasmic antibody)-associated vasculitis [eg, Wegener granulomatosis (also known as granulomatosis with polyangiitis [GPA]) with associated renal failure
- Dense deposit disease with factor H deficiency and/or elevated C3 Nephritic factor

### Transplantation

- Cardiac transplantation, for desensitization
- Hematopoietic stem cell transplantation, for ABO incompatibility
- Liver transplantation, for ABO incompatibility, or desensitization for living donor
- Renal transplantation, for any of the following:
  - ABO compatible/antibody mediated rejection
  - ABO compatible/living donor desensitization
  - ABO incompatible/living donor desensitization
  - ABO incompatible/antibody mediated rejection
  - Focal segmental glomerulosclerosis after renal transplant

Apheresis, plasmapheresis, and plasma exchange is considered **experimental or investigational** for all other conditions. There is insufficient evidence in the published medical literature to permit conclusions on safety, efficacy and long-term outcomes.

### Low-density Lipid (LDL) Apheresis (36516, S2120)

Low-density lipid (LDL) apheresis **meets the definition of medical necessity** for homozygous familial hypercholesterolemia as an alternative to plasmapheresis.

**Low-density lipid (LDL) apheresis meets the definition of medical necessity** for heterozygous familial hypercholesterolemia (FH), when **ALL** of the following are met:

- Failed diet therapy and maximum tolerated combination drug therapy **AND** meets **ONE** of the following FDA-approved indications:
  - Functional hypercholesterolemic heterozygotes with LDL  $\geq 300$  mg/dL, **OR**
  - Functional hypercholesterolemic heterozygotes with LDL  $\geq 200$  mg/dL **AND** documented coronary artery disease\*

\* **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 is considered **experimental or investigational** for all other conditions, including but not limited to treatment of preeclampsia, nonfamilial hypercholesterolemia, nephrotic syndrome, sudden sensorineural hearing loss, severe diabetic foot ulcerations, peripheral artery disease, and non–arteritic acute anterior ischemic optic neuropathy. There is insufficient to clinical evidence to determine the impact of this procedure on health outcomes.

Therapeutic apheresis with selective high-density lipoprotein (HDL) delipidation and plasma reinfusion (**0342T**) is considered **experimental or investigational**, for all indications, including but not limited to acute coronary syndrome. The available clinical evidence does not support clinical value.

## BILLING/CODING INFORMATION:

### CPT Coding:

36511	Therapeutic apheresis; for white blood cells
36512	Therapeutic apheresis; for red blood cells
36513	Therapeutic apheresis; for platelets
36514	Therapeutic apheresis; for plasma pheresis
36516	Therapeutic apheresis; with extracorporeal immunoadsorption, selective adsorption or selective filtration and plasma reinfusion
0342T	Therapeutic apheresis with selective HDL delipidation and plasma reinfusion <b>(investigational)</b>

### HCPCS Coding:

S2120	Low density lipoprotein (LDL) apheresis using heparin-induced extracorporeal LDL precipitation
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### ICD-10 Diagnosis Codes That Support Medical Necessity for 36511-36514:

C88.0	Waldenstrom macroglobulinemia
C88.2	Heavy chain disease
D47.3	Essential (hemorrhagic) thrombocythemia
D57.00-D57.819	Sickle-cell disorders
D58.8	Other specified hereditary hemolytic anemias
D59.3	Hemolytic-uremic syndrome
D69.49	Other primary thrombocytopenia
D69.51	Posttransfusion purpura
D69.59	Other secondary thrombocytopenia
D75.1	Secondary polycythemia
D89.1	Cryoglobulinemia
G35	Multiple sclerosis
G60.9	Hereditary and idiopathic neuropathy, unspecified

G61.0	Guillain-Barre syndrome
G61.81	Chronic inflammatory demyelinating polyneuritis
G70.01	Myasthenia gravis with (acute) exacerbation
M30.1	Polyarteritis with lung involvement [Churg-Strauss]
M31.0	Hypersensitivity angiitis
M31.1	Thrombotic microangiopathy
M31.30	Wegener's granulomatosis without renal involvement
M31.31	Wegener's granulomatosis with renal involvement
O14.10	Severe pre-eclampsia, unspecified trimester
O14.12	Severe pre-eclampsia, second trimester
O14.13	Severe pre-eclampsia, third trimester
O14.20	HELLP syndrome (HELLP), unspecified trimester
O14.22	HELLP syndrome (HELLP), second trimester
O14.23	HELLP syndrome (HELLP), third trimester
O90.89	Other complications of the puerperium, not elsewhere classified

### ICD-10 Diagnosis Codes That Support Medical Necessity for 36516, S2120:

E78.01	Familial hypercholesterolemia
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### REIMBURSEMENT INFORMATION:

Refer to section entitled [POSITION STATEMENT](#).

### PROGRAM EXCEPTIONS:

**Federal Employee Program (FEP):** Follow FEP guidelines.

**State Account Organization (SAO):** Follow SAO guidelines.

#### Medicare Advantage products:

The following National Coverage Determination (NCD) was reviewed on the last guideline reviewed date: APHERESIS (Therapeutic Pheresis) (110.14), located at cms.gov.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at [Coverage Protocol Exemption Request](#)

### DEFINITIONS:

**Familial hypercholesterolemia (FH):** A recessive genetic disorder caused by a defect on chromosome 19 that makes the liver incapable of metabolizing (or removing) excess LDL. The result is very high LDL levels which can lead to premature cardiovascular disease. There are two forms of FH. If inherited from one parent, the result is heterozygous FH (HeFH). HeFH occurs in 1 in 200 to 500 people worldwide. If

inherited from both parents, it is much more severe in its consequences. This form of FH is called homozygous FH (HoFH). It is very rare, occurring in about 1 in 160,000 to one million people worldwide.

**Guillain-Barre syndrome:** an acute demyelinating neuropathy whose severity is graded on a scale of 1-5. Plasma exchange is reserved for those with grades 3-5 disease who do not initially respond to prednisone.

**HELLP syndrome of pregnancy:** a severe form of preeclampsia, characterized by hemolysis [H], elevated liver enzymes [EL], and low platelet [LP] counts).

**Myasthenia gravis:** an autoimmune disease with autoantibodies directed against the postsynaptic membrane of the muscle end plate. Clinically, the disease is characterized by fatigable weakness of voluntary muscles. Initial treatment focuses on the use of cholinesterase inhibitors to overcome the postsynaptic blockade. Immunosuppressant drugs including corticosteroids and azathioprine are also effective. Plasma exchange has been used as a short-term therapy in individuals with acute exacerbations associated with severe weakness.

**Post-transfusion purpura:** a rare disorder characterized by an acute severe thrombocytopenia occurring about 1 week after a blood transfusion in association with a high titer of anti-platelet alloantibodies.

**Rapidly progressive glomerulonephritis (RPGN) including Goodpasture's syndrome:** a general term describing the rapid loss of renal function in conjunction with the finding of glomerular crescents on renal biopsy specimens. There are multiple etiologies of RPGN including vasculitis, the deposition of anti-glomerular basement membrane (GBM) antibodies as seen in Goodpasture's syndrome, or the deposition of immune complexes as seen in various infectious diseases or connective tissue diseases. RPGN may also be idiopathic. Because many cases of RPGN represent an immune-mediated disease of acute onset, RPGN was an early focus of PE research.

**Thrombotic thrombocytopenic purpura (TTP)—Hemolytic uremic syndrome (HUS):** Once considered distinct syndromes, TTP and HUS are now considered different manifestations of the same disease process, i.e., thrombotic microangiopathy. The classic signs and symptoms include fever, thrombocytopenia, microangiopathic hemolytic anemia, neurologic abnormalities, and renal involvement. TTP-HUS may be seen in association with other conditions, such as pregnancy or HIV infection. PE has become the primary treatment for TTP-HUS, although a rationale for its effectiveness is unknown. PE is performed daily until a response is noted; the length of treatment averages about once a month, with increasing intervals between PE treatments.

## RELATED GUIDELINES:

[Extracorporeal Photopheresis, 01-90919-02](#)

## OTHER:

None applicable

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## COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Medical Policy and Coverage Committee on 01/27/22.

## GUIDELINE UPDATE INFORMATION:

11/15/00	Medical Coverage Guideline developed.
04/15/01	Revised to include coverage information for ECI.
08/28/02	Revised to include ICD-9 diagnosis code for a covered indication for 36521; Add clarification for ICD-9 diagnosis codes that support medical necessity for 36520.
01/01/03	HCPCS coding update.
04/15/03	Reviewed; revised to include additional covered indication.
05/15/07	Medical Coverage Guideline archived.
02/15/15	Medical Coverage Guideline returned to active status. Revised MCG title, description section, position statement, CPT, HCPCS, ICD9, and ICD10 coding; Medicare Advantage program exception, and definitions. Updated references and reformatted guideline.
10/01/15	Revision; updated ICD9 coding section.
02/15/16	Scheduled review. Maintained position statement, revised program exceptions section, and updated references.
10/01/16	ICD-10 coding update: deleted code E78.0; added code E78.01.
11/17/16	Unscheduled revision. Deleted ICD10 code G70.00.
03/15/17	Scheduled review. Maintained position statement. Updated references. Reformatted guideline.
07/15/17	Revision: Revised description section, coverage for low-density lipoprotein (LDL) apheresis, and definitions section. Updated references.

01/01/18	Annual CPT/HCPCS coding update: deleted 36515; revised 36516.
03/15/18	Revision: added CAR T-cell therapy as a covered indication. Updated references.
04/26/18	Revision: updated related guidelines.
03/15/20	Scheduled review, Revised description. Added coverage statements to position statement for sickle cell disease, Wilson’s disease, and certain conditions associated with heart, liver, kidney, and stem cell transplantation. Revised ICD10 coding section and updated references.
08/15/20	Unscheduled review. Maintained position statement and updated references.
07/15/21	Revision: minor update to position statement for selective high-density lipoprotein (HDL) delipidation and plasma reinfusion when used for acute coronary syndrome. Updated references.
02/15/22	Scheduled review. Revised description, maintained position statement, and updated references.
05/23/23	Update to Program Exceptions section.