

Policy Name:	Therapeutic Apheresis (TA) - Plasmapheresis, Plasma Exchange
Effective Date:	4/17/2023

Important Information - Please Read Before Using This Policy

These services may or may not be covered by all Medica plans. Coverage is subject to requirements in applicable federal or state laws. Please refer to the member's plan document for other specific coverage information. If there is a difference between this general information and the member's plan document, the member's plan document will be used to determine coverage. With respect to Medicare, Medicaid, and other government programs, this policy will apply unless these programs require different coverage. Members may contact Medica Customer Service at the phone number listed on their member identification card to discuss their benefits more specifically. Providers with questions may call the Medica Provider Service Center toll-free at 1-800-458-5512.

Medica coverage policies are not medical advice. Members should consult with appropriate health care providers to obtain needed medical advice, care, and treatment.

Coverage Policy

EXTRACORPOREAL COLUMN IMMUNOADSORPTION APHERESIS

Therapeutic apheresis (TA) employing extracorporeal immunoadsorption (ECI) is **COVERED** for the following indications:

1. Acute inflammatory demyelinating polyneuropathy (Guillain-Barre syndrome, acute), primary treatment
2. Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)
3. Cryoglobulinemia, severe/symptomatic
4. Dilated idiopathic cardiomyopathy, NYHA II-IV
5. Encephalitis associated with N-methyl D-aspartate receptor antibodies
6. Focal segmental glomerulosclerosis, recurrent in kidney transplant
7. Multiple sclerosis, acute attack/relapse
8. Myasthenia gravis, acute/short term and long term treatment
9. Neuromyelitis optica spectrum disorders, acute attack or relapse (Devic's syndrome)
10. Renal transplantation, ABO compatible
 - a. Antibody-mediated rejection or desensitization, or desensitization in living donor
11. Renal transplantation, ABO incompatible
 - a. Antibody-mediated rejection
 - b. Desensitizations, living donor
12. Voltage-gated potassium channel antibody-related diseases

TA employing ECI is investigative and unproven and therefore **NOT COVERED** for all other indications, including but not limited to treatment for

1. Coagulation factor inhibitors, alloantibody or autoantibody
2. Multiple sclerosis, chronic
3. Atopic (neuro) dermatitis (atopic eczema), recalcitrant
4. Immune thrombocytopenia, refractory
5. Paraneoplastic neurologic syndromes
5. Paraproteinemic demyelinating polyneuropathies, IgG/IgA/IgM
6. Pemphigus vulgaris, severe
7. Thrombotic microangiopathy, infection associated: Shiga toxin-mediated (STEC-HUS)
8. Renal transplantation, ABO compatible

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a. Desensitization, deceased donor

There is insufficient reliable evidence in the form of high quality peer-reviewed medical literature to establish the efficacy or effects on health care outcomes.

The investigative determination does not apply to HDE approved devices. HDE approved devices are covered for the following:

1. Excorim® Immunoabsorption System (H970004) for the treatment of individuals with hemophilia A and B who have Factor VIII or Factor IX inhibitor titers above 10 BU/ml.

EXTRACORPOREAL LOW-DENSITY LIPOPROTEIN APHERESIS

TA employing extracorporeal low-density lipoprotein apheresis is **COVERED** for the treatment of:

1. Familial hypercholesterolemia, refractory, either homozygous or heterozygous
2. Lipoprotein (a) hyperlipoproteinemia
3. Peripheral vascular disease
4. Phytanic acid storage disease (Refsum's disease).

TA employing extracorporeal low-density lipoprotein apheresis is investigative and unproven and **therefore NOT COVERED** for all other indications, including but not limited to:

1. Hypertriglyceridemic pancreatitis, severe, including prevention of relapse
2. Steroid-resistant focal segmental glomerulosclerosis in native kidney, recurrent in kidney transplant
3. Sudden sensorineural hearing loss

There is insufficient reliable evidence in the form of high quality peer-reviewed medical literature to establish the efficacy or effects on health care outcomes.

Note: This determination does not apply to devices that have been granted a Humanitarian Device Exemption (HDE) by the FDA. Medica considers an FDA-approved humanitarian device exemption (HDE) device medically necessary when all of the FDA-required criteria are met.

- LIPOSORBER® LA-15 System (H170002) has FDA HDE approval for the treatment of adult and pediatric patients with nephrotic syndrome associated with primary focal segmental glomerulosclerosis, when standard treatment options, including corticosteroid and/or calcineurin inhibitors treatments, are unsuccessful or not well tolerated and the patient has a glomerular filtration rate (GFR) greater than or equal to 60 ml/min/1.73m² or the patient is post renal transplantation.

For a current list of HDE-approved devices, refer to the FDA HDE Database at: <https://www.fda.gov/medical-devices/hde-approvals/listing-cdrh-humanitarian-device-exemptions>

STANDARD PLASMAPHERESIS / PLASMA EXCHANGE

NOTE: Clinical conditions have been listed by general disease groupings. Although it is recognized that disease grouping definitions are often fluid and overlapping, this format is intended to aid in application of the position statement.

TA employing standard plasmapheresis/plasma exchange methodology is **COVERED** for the following indications:

AUTOIMMUNE / RHEUMATIC

1. Hyperglobulinemias and macroglobulinemias producing hyperviscosity syndromes, including but not limited to multiple myeloma, cryoglobulinemia, and Waldenstrom's macroglobulinemia
2. Systemic lupus erythematosus, severe complications (e.g., cerebritis, diffuse alveolar hemorrhage)
3. Catastrophic antiphospholipid syndrome (CAPS).

HEMATOLOGIC

1. Autoimmune hemolytic anemia, severe cold agglutinin disease
2. Hyperviscosity in monoclonal gammopathies (e.g., treatment of symptoms; prophylaxis for rituximab)
3. Acquired thrombotic thrombocytopenic purpura (TTP), autoimmune.

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HEPATIC

1. Acute liver failure requiring high volume apheresis

METABOLIC

1. Factor H autoantibodies, thrombotic microangiopathy, complement related
2. Familial hypercholesterolemia, homozygous with small blood volume
3. Overdose, venoms, and poisoning: mushroom poisoning
4. Refsum's disease (phytanic acid storage disease)
5. Thrombotic microangiopathy:
 - a. Complement-mediated: Factor H autoantibodies
 - b. Drug-associated: Ticlopidine
6. Thyroid storm
7. Vasculitis: Hepatitis B virus-associated polyarteritis nodosa (HBC-PAN)
8. Voltage-gated potassium channel antibody related diseases
9. Wilson's disease, fulminant hepatic failure with hemolysis.

NEUROLOGICAL

1. Acute inflammatory demyelinating polyneuropathy (Guillain-Barre syndrome, acute), primary treatment
2. Multiple sclerosis, acute attack/relapse
3. Acute disseminated encephalomyelitis, steroid refractory
4. Multiple myeloma, severe/symptomatic cryoglobulinemia
5. Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)
6. Paraproteinemic demyelinating polyneuropathies (e.g., IgG/IgA/IgM)
7. Lambert-Eaton myasthenic syndrome
8. Myasthenia gravis, acute/short term and long term treatment
9. Neuromyelitis optica spectrum disorders, acute attack or relapse (Devic's syndrome)
10. Pediatric autoimmune neuropsychiatric disorders associated with:
 - a. Streptococcal infections (PANDAS), exacerbation
11. Steroid responsive encephalopathy associated with autoimmune thyroiditis (Hashimoto's encephalopathy)
12. Encephalitis associated with N-methyl D-aspartate receptor antibodies.

RENAL (other than transplant-related)

1. Anti-glomerular basement membrane disease (Goodpasture's syndrome):
 - a. When dialysis independent
 - b. With diffuse alveolar hemorrhage (DAH).
2. ANCA-associated vasculitis
 - a. When dialysis dependent or imminent
 - b. With diffuse alveolar hemorrhage (DAH)
3. Myeloma cast nephropathy.

TRANSPLANTATION

1. Cardiac transplantation, desensitization
2. Focal segmental glomerulosclerosis, recurrent, in transplanted kidney
3. Hematopoietic stem cell transplant (HSCT), major ABO incompatibility (ABOi)-
4. Liver transplantation, ABO incompatible: live donor desensitization
5. Renal transplantation, ABO compatible:
 - a. Antibody mediated rejection
 - b. Living donor desensitization
6. Renal transplantation, ABO incompatible:
 - a. Antibody mediated rejection

- b. Living donor desensitization.

All other applications of TA employing standard plasmapheresis/plasma exchange are considered investigative and unproven and therefore **NOT COVERED**. There is insufficient reliable evidence in the form of high quality peer-reviewed medical literature to establish the efficacy or effects on health care outcomes. Examples of applications that are considered investigative include, but are not limited to:

- 1.

AUTOIMMUNE / RHEUMATIC

1. Dermatomyositis, polymyositis, or inclusion body myositis
2. Neonatal lupus, cardiac
3. Pemphigus vulgaris, severe
4. Progressive systemic sclerosis (scleroderma)
5. Psoriasis, disseminated pustular
6. Rheumatoid arthritis, refractory
7. Toxic epidermal necrolysis, refractory

HEMATOLOGIC

1. Hemophagocytic lymphocytosis (HLA); macrophage activating syndrome
2. Warm autoimmune hemolytic anemia, severe
3. Coagulation factor inhibitors, alloantibody or autoantibody
4. Red cell alloimmunization in pregnancy, gestational age less than 20 weeks
5. Thrombocytopenic purpura (TP), other than thrombotic TP (e.g., Henoch-Schonlein purpura, post-transfusion purpura, refractory immune thrombocytopenia).

HEPATIC

1. Acute liver failure, standard-plasmapheresis/plasma exchange

METABOLIC

1. Atopic (neuro) dermatitis (atopic eczema), recalcitrant
2. Erythropoietic protoporphyria, liver disease
3. Hemolysis with elevated liver function tests and low platelet count (HELLP syndrome), antepartum or postpartum
4. Progressive multifocal leukoencephalopathy associated with natalizumab
5. Thrombotic microangiopathy when associated with:
 - a. Complement-mediated: complement factor gene mutations
 - b. Coagulation mediated: *THBD*, *DGKE*, and *PLG* mutations
 - c. Drug-associated:
 - i. Clopidogrel
 - ii. Gemcitabine
 - iii. Quinine
 - d. Hemolytic uremic syndrome (HUS) infection associated:
 - i. Shiga toxin-mediated (STEC-HUS), severe
 - ii. Streptococcus pneumonia-related (pHUS)
6. Thrombocytopenia and thrombosis, heparin induced
7. Overdose or poisoning, drug
8. Overdose, venoms, and poisoning: all indications *other than* mushroom poisoning (e.g., envenomation)
9. Pruritus due to hepatobiliary disease, treatment resistant
10. Vasculitis
 - e. Bechet's disease
 - f. Eosinophilic granulomatosis with polyangiitis (EGPA)
 - g. Idiopathic polyarteritis nodosa (PAN).

NEUROLOGICAL

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1. Amyotrophic lateral sclerosis (ALS) or progressive systemic sclerosis
2. Chronic focal encephalitis (Rasmussen's encephalitis)
3. Multiple sclerosis, chronic
4. Neuromyelitis optica spectrum disorders, maintenance
5. Paraneoplastic neurologic syndromes
6. Pediatric autoimmune neuropsychiatric disorders associated with severe Sydenham's chorea
7. Stiff-person syndrome
8. Functional psychotic disorders (e.g., schizophrenia)
9. Paraproteinemic demyelinating polyneuropathy, chronic acquired:
 - a. Multiple myeloma
 - b. Anti-MAG neuropathy
 - c. Multifocal motor neuropathy.

RENAL

1. Anti-glomerular basement membrane disease (Goodpasture's syndrome); when dialysis dependent with no diffuse alveolar hemorrhage (DAH)
2. Focal segmental glomerulosclerosis, steroid resistant in native kidney
3. Immunoglobulin A nephropathy, chronic progressive or crescentic
4. Nephrogenic systemic fibrosis.

TRANSPLANTATION

1. Liver transplant, ABO incompatible for either:
 - a. Desensitization, deceased donor
 - b. Living donor, antibody-mediated rejection, including ABO and HLA
2. Lung transplantation, antibody-mediated rejection or desensitization
3. Heart (Cardiac): Transplant antibody-mediated rejection
4. Renal transplant, ABO compatible, for deceased donor desensitization
5. Hematopoietic stem cell transplant (HSCT)-associated, including thrombotic microangiopathy, or HLA desensitization, or major/minor ABO incompatibility with pure RBC aplasia
6. Thrombotic microangiopathy, transplantation associated.

MISCELLANEOUS

1. Burn shock resuscitation
2. Cardiomyopathy / dilated idiopathic; NYHA II-IV
3. Complex regional pain syndrome
4. Acute liver failure, standard plasmapheresis/plasma exchange
5. Amyloidosis, systemic
6. Hypertriglyceridemic pancreatitis, severe, including prevention of relapse
7. POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, skin changes)
8. Sepsis / septic shock with multi-organ failure
9. Sensorineural hearing loss, sudden
10. All disorders not listed.

Note: This determination does not apply to devices that have been granted a Humanitarian Device Exemption (HDE) by the FDA. Medica considers an FDA-approved humanitarian device exemption (HDE) device medically necessary when all of the FDA-required criteria are met.

- The Plasma Delipidation System (PDS-2™ System) (H190001) has FDA HDE approval to reduce coronary artery atheroma in adult patients with homozygous familial hypercholesterolemia (HOFH) who are either inadequately responsive to or intolerant of maximal therapy for HOFH, including the latest medications and other device therapies approved by the FDA.

For a current list of HDE-approved devices, refer to the FDA HDE Database at: <https://www.fda.gov/medical-devices/hde-approvals/listing-cdrh-humanitarian-device-exemptions>

Note: See also related Medica coverage policy; *Extracorporeal Photopheresis (Photochemotherapy)*

Description

Apheresis is a collective term applied to the separation of whole blood into its individual components. The term **cytapheresis** is used when the intent is to separate a single cellular component from the patient's whole blood (e.g., leukocytes, platelets). The term **plasmapheresis** is used when the intent is to separate the plasma from the patient's whole blood or to selectively remove a circulating biochemical from the plasma. Plasmapheresis can be performed with or without the use of selective membrane or column filtering devices. It is suggested that in specified acute or chronic, and often systemic, disorders the plasma contains the harmful constituents (e.g., autoimmune complexes, cytokines) that are thought to contribute to patient deterioration. The focus of this policy is methods of plasmapheresis, including both therapeutic plasma exchange and plasma perfusion.

Therapeutic **plasma exchange** involves removing a large volume of plasma and replacing it with an equivalent volume of replacement fluid. The cellular/plasma-substitute suspension is then reinfused. The method of removal, separation, and reinfusion is similar to the techniques used for kidney dialysis. Examples of replacement fluid include fresh frozen plasma, a plasma substitute, or a combination of albumin, calcium, and normal saline. In current practice, the terms plasmapheresis and plasma exchange are often used interchangeably.

Plasma perfusion is a multiphase separation method in which a patient's plasma is isolated from the cellular components and subsequently passed through a filtration medium in the form of an adsorption column or a series of membranes. After unwanted plasma components are removed, the filtered plasma is reinfused along with the patient's cellular components. Two systems used currently are low-density lipoprotein column adsorption and immunoabsorption using a protein A selection column.

- **Extracorporeal affinity low-density lipoprotein (LDL) apheresis** uses a series of membrane filtering devices which selectively remove LDL from the patient's plasma, while preserving the level of high-density lipoprotein. The patient's cells are resuspended in the LDL-depleted plasma and reinfused. This therapy is intended to prevent the development and/or slow the progression of atherosclerotic cardiovascular disease. A variety of methodologies are available, including but limited to double filtration plasmapheresis, HELP-apheresis, polyacrylate whole blood adsorption.
- **Extracorporeal immunoabsorption (ECI) apheresis.** A therapeutic procedure in which plasma of the patient, after membrane based or centrifugal separation from the blood, is passed through a medical device (adsorber column) which has a capacity to remove immunoglobulins by binding them to select ligands on the backing matrix surface (membranes or beads) of the adsorber column. Several systems have been designed to selectively remove pathogenic substances, to avoid some of the adverse effects of TPE and to improve the efficiency of removal of a particular substance. ECI is not used extensively in the United States.

Therapeutic apheresis (TA) has become a tool in the management of certain diseases. The American Society for Apheresis has categorized the appropriateness of apheresis for various clinical applications. The categories range from I (currently accepted first-line therapy through) IV (application considered ineffective or harmful). TA is rarely considered a curative therapy. The true benefit of apheresis, usually coupled with medication and/or other standard therapies, is thought to be the temporary elimination of the harmful by-products of disease-related metabolism. It is suggested that this allows the body's normal immune response to function, which in turn results in improved organ function. As therapeutic apheresis is not curative, multiple treatment sessions are often administered. The therapy can be administered in either an outpatient or inpatient setting.

FDA Approval

Therapeutic apheresis is a procedure, and therefore is not regulated by the FDA.

Multiple membrane apheresis devices (including filters) have received FDA premarket approval. In 1996 the FDA granted market clearance for the use of apheresis systems by "blood banks, hospitals, and clinics for use with therapeutic plasma exchange." Several apheresis systems have been approved, however the FDA does not approve specific indications for plasma exchange.

Prior Authorization

Prior authorization is not required. However, services with specific coverage criteria may be reviewed retrospectively to determine if criteria are being met. Retrospective denial may result if criteria are not met.

Coding Considerations

Use the current applicable CPT/HCPCS code(s). The following codes are included below for informational purposes only, and are subject to change without notice. Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement.

CPT Codes:

- **36514** - Therapeutic apheresis; for plasmapheresis
- **36516** - Therapeutic apheresis; with extracorporeal selective adsorption or selective filtration and plasma reinfusion
- **S2120** - Low density lipoprotein (LDL) apheresis using heparin-induced extracorporeal LDL precipitation.

Original Policy Effective Date:	1/1/2005
Re-Review Date(s):	9/1/2006 8/1/2009 8/1/2012 5/20/2015 10/23/2017 – administrative update; HDE-approved devices added 5/16/2018 6/18/2019 – administrative update; code update 1/16/2020 2/13/2020 – administrative update; format 6/3/2021 – administrative update; HDE information added 2/15/2023

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