Medica Central Coverage Policy

Policy Name:	**Therapeutic Apheresis (TA) – Plasmapheresis, Plasma Exchange MP9627**
Effective Date:	**07/01/2025**

Important Information – Please Read Before Using This Policy

These services may or may not be covered by all Medica Central 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 Provider Service Center. Please use the Quick Reference Guide on the Provider Communications page for the appropriate phone number. https://mo-central.medica.com/Providers/SSM-employee-health-plan-for-IL-MO-OK-providers

Medica Central 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. Amyloidosis, systemic, dialysis related
3. Chronic inflammatory demyelinating polyradioculoneuropathy (CIDP)
4. Cryoglobulinemia, severe/symptomatic
5. Dilated idiopathic cardiomyopathy, NYHA II-IV
6. Encephalitis associated with N-methyl D-aspartate receptor antibodies
7. Focal segmental glomerulosclerosis
8. Multiple sclerosis, acute attack/relapse
9. Myasthenia gravis, acute/short term and long term treatment
10. Neuromyelitis optica spectrum disorders, acute attack or relapse (Devic's syndrome)

11. Renal transplantation, ABO compatible
    a. Antibody-mediated rejection or desensitization, or desensitization in living donor
12. Renal transplantation, ABO incompatible
    a. Antibody-mediated rejection
    b. Desensitizations, living donor
13. 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, primary or secondary progressive
3. Atopic (neuro) dermatitis (atopic eczema), recalcitrant
4. Immune thrombocytopenia, refractory
5. Paraneoplastic neurologic syndromes
6. Chronic acquired demyelinating polyneuropathies, IgG/IgA/IgM
7. Pemphigus vulgaris, severe
8. Thrombotic microangiopathy, infection associated: Shiga toxin-mediated (STEC-HUS)

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® Immunoadsorption 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. Focal segmental glomerulosclerosis, all types
3. Lipoprotein (a) hyperlipoproteinemia
4. Peripheral vascular disease
5. 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 AND DOUBLE FILTRATION PLASMAPHERESIS

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. Cryoglobulinemia (e.g.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).
4. Toxic epidermal necrolysis, refractory

HEMATOLOGIC

1. Autoimmune hemolytic anemia, severe cold agglutinin disease
2. Hyperviscosity in monoclonal gammopathies (e.g., treatment of symptoms; prophylaxis for rituximab)

HEPATIC

1. Acute liver failure requiring high volume apheresis

2. Erythropoietic protoporphyria, liver disease

METABOLIC

1. Familial hypercholesterolemia, all patients
2. Acute toxins, venoms, and poison, mushroom poisoning
3. Erythropoietic protoporphyria, liver disease
4. Refsum's disease (phytanic acid storage disease)
5. Systemic amyloidosis, dialysis related (e.g., ß2-microglobulin)
6. Thrombotic microangiopathy:
   a. Complement-mediated: Factor H autoantibodies
   b. Drug-associated: Ticlopidine
7. Thrombotic microangiopathy, thrombotic thrombocytopenis purpura
8. Thyroid storm
9. Vasculitis: Hepatitis B polyarteritis nodosa
10. Voltage-gated potassium channel antibody related diseases
11. Wilson's disease, fulminant

NEUROLOGICAL

1. Multiple sclerosis, acute attack/relapse
2. Acute disseminated encephalomyelitis, steroid refractory
3. Chronic inflammatory demyelinating polyradioculoneuropathy (CIDP)
4. Chronic acquired demyelinating polyneuropathies (e.g., IgG/IgA/IgM)
5. Lambert-Eaton myasthenic syndrome
6. Myasthenia gravis, acute/short term and long term treatment
7. Neuromyelitis optica spectrum disorders, acute attack or relapse (Devic's syndrome)
8. Pediatric autoimmune neuropsychiatric disorders associated with:
   a. Streptococcal infections (PANDAS), exacerbation
9. Steroid responsive encephalopathy associated with autoimmune thyroiditis (Hashimoto's encephalopathy)
10. 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. Vasculitis, ANCA-associated

   a. Microscopic polyangiitis
   b. Granulomatosis with polyangiitis
   c. Eosinophilic granulomatosis with polyangiitis
3. Myeloma cast nephropathy.
4. Focal segmental glomerulosclerosis, recurrent in kidney transplant

TRANSPLANTATION

1. Cardiac transplantation:
   a. Desensitization
   b. Rejection prophylaxis
2. Hematopoietic stem cell transplant (HSCT), major ABO incompatibility (ABOi)
   a. Major ABO incompatible, HPC(M)
   b. Major ABO incompatible, HPC(A)
3. Liver transplantation, desensitization, ABOi: living donor
4. Renal (kidney) transplantation, ABO compatible:
   a. Antibody mediated rejection
   b. Living donor desensitization
5. Renal (kidney) transplantation, ABO incompatible:
   a. Antibody mediated rejection
   b. Living donor desensitization/prophylaxis.

All other applications of TA employing standard plasmapheresis/plasma exchange and double filtration plasmapheresis 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:

AUTOIMMUNE / RHEUMATIC

1. Idiopathic inflammatory myopathies
   a. Anti-synthetase-syndrome
   b. Clinically amyopathic dermatomyositis
   c. Immune-mediated necrotizing myopathies
2. Immune checkpoint inhibitors, immune-related adverse events (i.e., oncologic drug-related biomarker proteins)
3. Immune thrombocytopenia, refractory
4. Neonatal lupus, cardiac
5. Pemphigus vulgaris, severe

6. Progressive systemic sclerosis (scleroderma)
7. Psoriasis, disseminated pustular

HEMATOLOGIC

1. Hemophagocytic lymphocytosis (HLA)
2. Warm autoimmune hemolytic anemia, severe
3. Coagulation factor deficiency and inhibitors, alloantibody or autoantibody
4. Red cell alloimmunization pregnancy, complications, hemolytic disease of the fetus and newborn
5. Post-transfusion purpura
6. Sickle cell disease, acute; other than acute stroke and severe acute chest syndrome
7. Immune thrombotic thrombocytopenia, vaccine-induced, refractory

HEPATIC

1. Acute liver failure standard TPE
2. Acute fatty liver of pregnancy

METABOLIC

1. Age related macular degeneration, dry/high risk
2. Atopic (neuro) dermatitis (atopic eczema), recalcitrant
3. Autoimmune dysautonomia
4. Progressive multifocal leukoencephalopathy associated with natalizumab
5. Thrombotic microangiopathy when associated with:
    a. Complement-mediated: complement factor gene mutations
6. Coagulation mediated thrombotic microangiopathy: *THBD*, *DGKE*, and *PLG* mutations
    a. Drug-associated:
        i. Clopidogrel
        ii. Gemcitabine
        iii. Quinine
    b. Thrombotic microangioplasty, infection associated:
        i. Shiga toxin-mediated (STEC-HUS), severe
        ii. Streptococcus pneumonia-related (pHUS)
7. Thrombotic microangioplasty, pregnancy associated:
    a. Pregnancy associated, severe
    b. Extremely preterm preeclampsia, severe
8. Thrombocytopenia and thrombosis, heparin induced

a. Pre-procedure; TPE/IA
b. Refractory or with thrombosis; TPE

9. Overdose or poisoning, drug
10. Acute toxins, venoms, and poisoning: all indications *other than* mushroom poisoning (e.g., envenomation)
11. Pruritus due to hepatobiliary disease, treatment resistant
12. Vasculitis, other
    a. Bechet's disease
    b. Kawasaki disease
    c. Multisystem inflammatory syndrome in children

NEUROLOGICAL

1. Alzheimer's disease
2. Chronic focal encephalitis (Rassmussen's encephalitis)
3. Multiple sclerosis, chronic primary or secondary progressive
4. Neuromyelitis optica spectrum disorders, maintenance
5. Paraneoplastic autoimmune retinopathies
6. Paraneoplastic neurologic syndromes
7. Paraneoplastic neurologic syndromes
8. Pediatric autoimmune neuropsychiatric disorders associated with sever Sydenham's chorea
9. Stiff-person syndrome
10. Paraproteinemic demyelinating polyneuropathy, chronic acquired:
    a. Anti-myelin-associated glycoprotein -(MAG) neuropathy
    b. Chronic ataxic neuropathy, ophthalmoplegia, immunoglobulin M (IgM) paraprotein, cold agglutinins, and disialosyl antibodies (CANOMAD/CANDA)

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. Immunoglobin A (IgA) nephropathy, chronic progressive or crescentic
4. Nephrogenic systemic fibrosis.
5. Vasculitis, IgA
    a. Crescentic rapidly progressive glomerulonephritis
    b. Severe extra-renal manifestations

TRANSPLANTATION

1. Heart (Cardiac): Transplant antibody-mediated rejection
2. Hematopoietic stem cell transplant, HLA desensitization, or ABO incompatibility, with pure RBC aplasia –
3. Intestine: -
   a. Antibody mediated rejection
   b. Desensitization
4. Liver transplant, ABOi for either:
   a. Desensitization, deceased donor
   b. Antibody-mediated rejection, including ABO and HLA
5. Lung transplantation:
   a. Antibody-mediated rejection
   b. Desensitization
6. Thrombotic microangiopathy, transplantation associated.

MISCELLANEOUS

1. Burn shock resuscitation
2. Cardiomyopathy / dilated idiopathic; NYHA II-IV
3. Complex regional pain syndrome
4. Hypertriglyceridemic pancreatitis, severe, including prevention of relapse
5. Sepsis / septic shock with multi-organ failure
6. Sensorineural hearing loss, sudden
7. 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 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 (TPE)*** 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 plasmaphersis and plasma exchange are often used interchangeably. Double filtration plasmapheresis (DFPP) is a type of therapeutic plasma exchange, but it is a more selective form, using two filters to remove specific large molecules from the plasma while minimizing the loss of other proteins, making it a more targeted treatment option compared to standard plasmapheresis. Plasma filters of different mean pore sizes exist, which allow targeting preferred portions of plasma components mainly determined by molecular weight and three-dimensional structure. With this differential approach, DFPP can be used for elimination of autoantibodies, immune complexes, or lipoproteins.

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 absorption and immunoadsorption 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 immunoadsorption (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.

Medica Central Coverage Policy

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