Medica Coverage Policy

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<th>Therapeutic Apheresis (TA) - Plasmapheresis, Plasma Exchange</th>
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Important Information - Please Read Before Using This Policy

These services may or may not be covered by all Medica plans. Please refer to the member’s plan document for 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 and Minnesota Health Care Programs, this policy will apply unless those 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 about this Medica coverage policy 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 APERHESIS**

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

1. Cryoglobulinemia, severe/symptomatic
2. Dilated idiopathic cardiomyopathy, NYHA II-IV
3. Renal transplantation, ABO compatible
   a. Antibody-mediated rejection or desensitization, living donor
4. Renal transplantation, ABO incompatible
   a. Antibody-mediated rejection
   b. Desensitization, living donor
5. Rheumatoid arthritis (RA), adult refractory.

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

1. Coagulation factor inhibitors, alloantibody or autoantibody*
2. Acute central nervous system inflammatory demyelinating disease (multiple sclerosis)
3. Atopic (neuro) dermatitis (atopic eczema), recalcitrant
4. Immune thrombocytopenia, refractory
5. Paraneoplastic neurologic syndromes
6. Paraproteinemic demyelinating polyneuropathies, IgG/IgA/IgM
7. Pemphigus vulgaris
8. Thrombotic microangiopathy: Shiga toxin-mediated, absence of severe neurologic symptoms
9. Renal transplantation, ABO compatible
   a. Desensitization, deceased donor
9. Renal transplantation, ABO incompatible
   a. Deceased donor, group A2/A2B into group B recipient.
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. 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 therefore NOT COVERED for all other indications, including but not limited to:
1. Steroid-resistant focal segmental glomerulosclerosis in native kidney
2. Sudden sensorineural hearing loss

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 (e.g., cerebritis, diffuse alveolar hemorrhage)
3. Catastrophic antiphospholipid syndrome.

HEMATOLOGIC
1. Autoimmune hemolytic anemia, life threatening cold agglutinin disease
2. Hyperviscosity in monoclonal gammopathies (e.g., treatment of symptoms; prophylaxis for rituximab)
3. Red cell alloimmunization in pregnancy, prior to intrauterine transfusion availability
4. Acquired thrombotic thrombocytopenic purpura (TTP), autoimmune.

METABOLIC
1. Atopic (neuro) dermatitis (atopic eczema), recalcitrant
2. Factor H autoantibodies
3. Familial hypercholesterolemia, homozygous with small blood volume
4. Overdose, venoms, and poisoning: mushroom poisoning
5. Progressive multifocal leukoencephalopathy associated with natalizumab
6. Refsum’s disease (phytanic acid storage disease)
7. Thrombotic microangiopathy:
   a. Complement-mediated: Factor H autoantibodies
   b. Drug-associated: Ticlopidine
8. Vasculitis: Hepatitis B virus-associated polyarteritis nodosa (HBC-PAN)
9. Voltage-gated potassium channel antibodies

NEUROLOGICAL
1. Acute inflammatory demyelinating polyneuropathy (Guillain-Barre syndrome, acute), primary treatment
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2. Acute central nervous system inflammatory demyelinating disease (multiple sclerosis)
3. Acute disseminated encephalomyelitis
4. Multiple myeloma
5. Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)
6. Paraproteinemnic demyelinating polyneuropathies (e.g., IgG/IgA/IgM)
7. Lambert-Eaton myasthenic syndrome
8. Myasthenia gravis (e.g., moderate to severe; pre-thymectomy)
9. Neuromyelitis optica spectrum disorders, acute (Devic’s syndrome)
10. Pediatric autoimmune neuropsychiatric disorders associated with severe:
   a. Streptococcal infections (PANDAS)
   b. Sydenham’s chorea (SC)
11. Steroid responsive encephalopathy associated with autoimmune thyroiditis (Hashimoto’s encephalopathy)

RENA L (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 rapidly progressive glomerulonephritis (Wegener’s granulomatosis):
   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, from bone marrow or peripheral blood
4. Liver transplantation, ABO incompatible: live donor desensitization
5. Renal transplantation, ABO compatible: Antibody mediated rejection or desensitization, living donor, including HLA antibody
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 therefore NOT COVERED.

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

HEMATOLOGIC
1. Aplastic anemia; including pure red cell aplasia
2. Hemophagocytic lymphocytosis (HLA); macrophage activating syndrome
3. Warm autoimmune hemolytic anemia
4. Coagulation factor inhibitors, alloantibody or autoantibody
5. Thrombocytopenic purpura (TP), other than thrombotic TP (e.g., Henoch-Schönlein purpura, post-transfusion purpura, refractory immune thrombocytopenia).

HEPATIC
1. Acute liver failure requiring high volume apheresis

METABOLIC
1. Erythropoietic porphyria, liver disease
2. Hemolysis with elevated liver function tests and low platelet count (HELLP syndrome), antepartum or postpartum
3. Monoclonal gammopathies with hyperviscosity
4. Thrombotic microangiopathy when associated with:
   a. Complement-mediated:
      i. complement factor gene mutations
      ii. membrane cofactor protein (MCP) mutations
      iii. THBD mutation
   b. Drug-associated:
      i. Clopidogrel
      ii. Gemcitabine
      iii. Quinine
      iv. Calcineurin inhibitors
   c. Shiga toxin-mediated (i.e., with or without severe neurologic symptoms, Streptococcus pneumonia)
2. Thrombocytopenia, heparin induced
3. Overdose or poisoning, drug
4. Overdose, venoms, and poisoning: all indications other than mushroom poisoning (e.g., invenomation)
5. Pruritus due to hepatobiliary disease, treatment resistant
6. Thyroid storm
7. Vasculitis
   a. Behcet’s disease
   b. Eosinophilic granulomatosis with polyangiitis (EGPA)
   c. Idiopathic polyarteritis nodosa (PAN).

NEUROLOGICAL
1. Amyotrophic lateral sclerosis (ALS) or progressive systemic sclerosis
2. Acute inflammatory demyelinating polyneuropathy (Guillain-Barre syndrome, acute), following intravenous immune globulin
3. Chronic focal encephalitis (Rasmussen’s encephalitis)
4. Multiple sclerosis, chronic progressive
5. Neuromyelitis optica spectrum disorders, maintenance
6. Paraneoplastic neurologic syndromes
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. ANCA-associated rapidly progressive glomerulonephritis (Wegener’s granulomatosis); when dialysis independent
2. Anti-glomerular basement membrane disease (Goodpasture’s syndrome); when dialysis independent with no diffuse alveolar hemorrhage (DAH)
4. Immunoglobulin A nephropathy, chronic progressive or crescentic
5. Immune complex rapidly progressive glomerulonephritis

**TRANSPANTATION**
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) for either: Transplant antibody-mediated rejection.
4. Renal transplant, ABO compatible, for deceased donor desensitization
5. Renal transplant, ABO incompatible, deceased donor due to A2/A2B into B recipient
6. Hematopoietic stem cell transplant (HSCT)-associated, including thrombotic microangiopathy or HLA desensitization.

**MISCELLANEOUS**
1. Burn shock resuscitation
2. Cardiomyopathy / dilated idiopathic; NYHA II-IV
3. Complex regional pain syndrome
4. Acute liver failure
5. Amyloidosis, systemic
6. Hypertriglyceridemic pancreatitis
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: See also related MTAC position statement, *Extracorporeal Photopheresis (Photochemotherapy)* and *OncoSorb® (UltraPheresis™) for Non-Hematologic Cancer.*
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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 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.

- **Extracorporeal immunoabsorption (ECI) protein A column apheresis** uses a polycarbonate column that contains highly purified protein A which is bound to a silica matrix. Protein A is derived from certain strains of the bacterium *Staphylococcus aureus*. Protein A binds to and removes immunoglobulins and circulating immune complexes that are thought to contribute to the symptoms characteristic of rheumatoid arthritis, idiopathic thrombocytopenia purpura, and hemolytic uremic syndrome.

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.

In the mid-1990s, two lipid apheresis systems received FDA approval. These are the Liposorber® LA-15 System (Kaneka America Corp.) and the H.E.L.P. system (B. Braun Medical Inc.).
The PROSORBA® Column was originally approved in 1987 for extracorporeal column immunoadsorption treatment of idiopathic thrombocytopenic purpura (ITP). In 1999, it was FDA approved for the therapeutic reduction of the signs and symptoms of moderate to severe RA in adults and for the removal of immunoglobulin G (IgG) and IgG-containing immune complexes in patients with ITP. In 2006 production of PROSORBA columns was discontinued and are no longer available in the United States. The Excorim® Immunoadsorption System received an HDE in April 1998 for the treatment of patients with hemophilia A and B who have Factor VIII or Factor IX inhibitor titers above 10 Bethesda Units/ml (BU/ml).

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
36515 - Therapeutic apheresis; with extracorporeal immunoadsorption and plasma reinfusion
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

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