This document addresses therapeutic apheresis, a procedure by which blood is removed from the body, separated into components, manipulated and returned to the individual. There are multiple pheresis procedures that are performed. The therapeutic apheresis procedures addressed in this document utilize devices approved by the United States (U.S.) Food & Drug Administration (FDA) and include the following subcategories: plasmapheresis/plasma exchange, cytapheresis (specifically, erythrocytapheresis, leukocytapheresis, platelet apheresis, red blood cell exchange and thrombocytapheresis), low-density lipid (LDL) apheresis, selective high-density lipid (HDL) delipidation and therapeutic apheresis and immunoadsorption (IA).

Medically Necessary:

I. Plasmapheresis or plasma exchange is considered medically necessary for any of the following conditions listed in alphabetical order below:
   1. Acute inflammatory demyelinating polyneuropathy (Guillain-Barre syndrome)
   2. Anti-glomerular basement membrane disease (Goodpasture's syndrome) when the individuals is dialysis-independent and there is evidence of diffuse alveolar hemorrhage (DAH)
   3. Anti-neutrophil cytoplasmic antibodies (ANCA)-associated rapidly progressive glomerulonephritis (granulomatosis with polyangiitis; Wegener’s granulomatosis)
   4. Atypical hemolytic uremic syndrome (aHUS) with Factor H autoantibodies or complement gene mutation
   5. Autoimmune hemolytic uremic syndrome- severe cold agglutin disease
   6. Catastrophic antiphospholipid syndrome (CAPS)
   7. Chronic inflammatory demyelinating polyneuropathy
   8. Cryoglobulinemia, mixed or symptomatic/severe
   9. H.E.L.L.P syndrome of pregnancy (hemolysis, elevated liver enzymes, low platelets)
   10. Hyperviscosity syndromes associated with monoclonal gammapathies (such as, multiple myeloma and Waldenström’s macroglobulinemia)
   11. Multiple myeloma cast nephropathy (acute renal failure secondary to multiple myeloma)
   12. Multiple sclerosis -acute CNS inflammatory demyelinating disease
   13. Myasthenia gravis that is moderate to severe or prior to thymectomy
   14. Neuromyelitis optica ([NMO], also known as Devic’s disease), acute disease (excluding maintenance therapy)
   15. Paraproteinemic demyelinating neuropathies associated with IgA, IgG or IgM monoclonal gammapathy of undetermined significance (MGUS) (excluding multiple myeloma)
Therapeutic Apheresis

16. Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection (PANDAS) exacerbation
17. Sydenham’s chorea
18. Systemic lupus erythematosus - for individuals with severe or life-threatening symptoms when conventional therapy has failed to prevent clinical deterioration
19. Thrombotic microangiopathy secondary to drugs or malignancy
20. Thrombotic Thrombocytopenic Purpura (TTP)
21. Transplantation when any of the following are met:
   a. Hematopoietic stem cell transplant – ABO incompatible
   b. Solid organ transplantation for any of the following:
      i. Heart transplantation recipients who are in the operating room experiencing a hyper-acute rejection episode
      ii. Liver transplantation from a live donor with ABO incompatibility
      iii. Renal transplant recipients who are post-transplant and experiencing recurrent focal and segmental glomerulosclerosis (FGS) or experiencing a humoral or antibody mediated rejection
      iv. Renal transplantation in highly sensitive kidney transplant candidates (high PRA protocols) to reduce the number of antibodies reactive against human lymphocyte antigens (HLA)
      v. Renal transplantation from a live donor with ABO incompatibility or positive cross-match, where a non-reactive live or cadaveric donor is unavailable
22. Voltage gated potassium channel antibodies
23. Wilson’s disease – fulminant

II. Low-density lipid apheresis is considered medically necessary for individuals with any of the following:
   1. Homozygous familial hypercholesterolemia;
   2. Severe, refractory heterozygous familial hypercholesterolemia who have failed a 6-month trial of diet therapy and maximum tolerated combination drug therapy AND who meet either of the following FDA-approved indications:
      a. Functional hypercholesterolemic heterozygotes with low-density lipoprotein (LDL) that is greater than 300 mg/dL; or
      b. Functional hypercholesterolemic heterozygotes with LDL that is greater than 200 mg/dL and documented coronary artery disease
   3. Liprotein (a) hyperlipoproteinemia

III. Cytapheresis:
   1. Phlebotomy (Erythrocytapheresis) is considered medically necessary as a treatment for any of the following:
      a. Hereditary hemochromatosis
      b. Polycythemia vera
      c. Symptomatic secondary polycythemia
      d. Porphyra cutanea tarda
   2. Leukocytapheresis is considered medically necessary for leukemias with leukostasis
   3. Thrombocytapheresis is considered medically necessary for essential thrombocytosis (symptomatic, when the platelet count is greater than 1,000,000/mm³)
4. Red blood cell exchange is considered **medically necessary** as treatment for any of the following:
   a. Babesiosis:
      i. Severe
      ii. In the high-risk population
   b. Severe malaria
   c. Sickle cell disease, acute:
      i. Acute stroke
      ii. Acute severe, chest syndrome
      iii. Multi-organ failure syndrome
      iv. Pre-procedure preparation (surgery or hematopoietic stem cell transplant)
      v. Pregnancy
   d. Sickle cell disease, chronic exchange or non-acute:
      i. Stroke prophylaxis (primary or secondary)
      ii. Iron overload

IV. Immunoadsorption is considered **medically necessary** for individuals with **either** of the following:
   1. Thrombotic Thrombocytopenic Purpura (TTP); or
   2. Moderate to severe rheumatoid arthritis in adult patients with long-standing disease who have failed or are intolerant to disease-modifying antirheumatic drugs such as methotrexate, hydroxychloroquine, sulfasalazine, gold, azathioprine, D-penicillamine, etanercept, infliximab and leflunomide.

**Investigational and Not Medically Necessary:**

I. Plasmapheresis or plasma exchange is considered **investigational and not medically necessary** the criteria above are not met and all other indications including, but not limited to:
   1. Acute disseminated encephalomyelitis
   2. Acute liver failure
   3. Amyloidosis, systemic
   4. Amyotrophic lateral sclerosis (ALS)
   5. Anti-glomerular basement membrane disease (Goodpasture's syndrome) when the individuals is dialysis-dependent and there is no evidence of diffuse alveolar hemorrhage (DAH)
   6. Aplastic anemia
   7. Autoimmune hemolytic anemia (AHA) –warm autoimmune hemolytic anemia (WAHA)
   8. Burn shock resuscitation
   9. Chronic fatigue syndrome
   10. Chronic focal encephalitis (Rasmussen encephalitis)
   11. Coagulation factor inhibitors, alloantibody and autoantibody
   12. Dermatomyositis
   13. Heart (cardiac) transplantation – for desensitization, positive cross-match due to donor specific HLA antibody or antibody mediated rejection
   14. Hemolytic Uremic Syndrome (aHUS), with MCP mutations
   15. Hemolytic Uremic Syndrome associated with infection (such as shiga toxin or Streptococcus pneumoniae)
   16. Henoch-Schonlein purpura
   17. Heparin induced thrombocytopenia
   18. Hypertriglyceridemic pancreatitis

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II. Low-density lipid apheresis is considered **investigational and not medically necessary** for all indications not meeting the criteria above including, but not limited to:
   1. Peripheral vascular disease (PVD)
   2. Phytic Acid Storage Disease (Refsum Disease)
   3. Sudden sensorineural hearing loss

III. Selective high-density lipid (HDL) delipidation and therapeutic apheresis is considered **investigational and not medically necessary** for all indications.

IV. Cytapheresis is considered **investigational and not medically necessary** for all indications not meeting the criteria above including, but not limited to:
   1. Dermatomyositis

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Therapeutic Apheresis

2. Hematopoietic stem cell transplant – ABO incompatible
3. Hyperleukocytosis, (asymptomatic)
4. Inclusion body myositis
5. Polymyositis
6. Psoriasis

V. Thrombocytapheresis is considered investigational and not medically necessary when the criteria above are not met and for all other indications.

VI. Immunoadsorption pheresis is considered investigational and not medically necessary for all indications not meeting the criteria above, including, but not limited to:
1. Autoimmune diseases other than rheumatoid arthritis
2. Chronic focal encephalitis (Rasmussen Encephalitis)
3. Coagulation factor inhibitors alloantibody and autoantibody
4. Cryoglobulinemia, symptomatic or severe
5. Immune thrombocytopenia, refractory
6. Multiple sclerosis – acute CNS inflammatory demyelinating disease
7. Paraneoplastic neurological syndromes
8. Paraproteinemic demyelinating neuropathies associated with IgA, IgG or IgM monoclonal gammopathy
9. Pemphigus vulgaris
10. Treatment of cancer

Rationale

Evidence in peer-reviewed, published medical literature and medical society guidelines support the clinical effectiveness and safety of therapeutic pheresis modalities for the indications listed in the policy statements. There is evidence for the accepted indications that the use of this procedure can result in an improvement in symptoms, primarily for acute self-limited conditions, and subsequently for an improvement in quality of life. Evidence is limited regarding the role of therapeutic apheresis to remove specific autoantibodies, proteins and complements in the pathogenesis of many other conditions.

The Guidelines on the Use of Therapeutic Apheresis in Clinical Practice (Sixth special issue) were updated by the American Society for Apheresis (ASFA) in 2013. Therapeutic apheresis is a general term which includes all apheresis based procedures used in a therapeutic manner. This involves the individual’s blood being passed through an external device which separates blood into components as treatment of a disease. Specific ASFA definitions for the therapeutic modalities addressed in this document are as follows (Schwartz, 2013):

Erythrocytapheresis: procedure in which blood of the patient or donor is passed through a medical device which separates RBCs from other components of blood, the RBCs are removed and replaced with crystalloid or colloid solution, when necessary.

Immunoadsorption: A therapeutic procedure in which plasma of the patient, after separation from the blood, is passed through a medical device which has the capacity to remove immunoglobulins by specifically binding them to the active component (e.g., Staphylococcal protein A) of the device.
Leukocytapheresis: A procedure in which blood of the patient or the donor is passed through a medical device which separates out white blood cells (e.g., leukemic blasts or granulocytes), collects the selected cells and returns remainder of the patient’s or the donor’s blood with or without addition of replacement fluid such as colloid and/or crystalloid solution. This procedure can be used therapeutically or in preparation of blood components.

Low-density lipid apheresis: The selective removal of low density lipoproteins from the blood with the return of the remaining components. A variety of instruments are available which remove LDL cholesterol based upon charge (dextran sulfate and polyacrylate), size (double-membrane filtration), precipitation at low pH (HELP), or immunoadsorption with anti-Apo B-100 antibodies.

Red blood cell (RBC) Exchange: A therapeutic procedure in which blood of the patient is passed through a medical device which separates RBCs from other components of blood, the RBCs are removed and replaced with donor RBCs alone and colloid solution.

Therapeutic plasma exchange (TPE): A therapeutic procedure in which blood of the patient 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 (e.g., albumin and/or plasma) or combination of crystalloid/collod solution.

Thrombocytapheresis: A therapeutic procedure in which blood of the patient is passed through a medical device which separates out platelets, removes the platelets and returns remainder of the patient’s blood with or without addition of replacement fluid such as colloid and/or crystalloid solution.

The ASFA utilizes categories and grade of recommendation for various indications. The four categories are (Schwartz, 2013):

- **Category I**: Disorders for which apheresis is accepted as first-line therapy, either as a primary standalone treatment or in conjunction with other modes of treatment.
- **Category II**: Disorders for which apheresis is accepted as second-line therapy, either as a standalone treatment or in conjunction with other modes of treatment.
- **Category III**: Optimum role of apheresis therapy is not established. Decision making should be individualized.
- **Category IV**: Disorders in which published evidence demonstrates or suggests apheresis to be ineffective or harmful. Institutional Review Board (IRB) approval is desirable if apheresis treatment is undertaken in these circumstances.

The Grading Recommendations include the following (Schwartz, 2013):

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Description</th>
<th>Methodological quality of supporting evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1A</td>
<td>Strong recommendation, high-quality evidence</td>
<td>Randomized controlled trials (RCTs) without important evidence from observational studies</td>
</tr>
</tbody>
</table>
# Medical Policy

## Therapeutic Apheresis

| Grade 1B | Strong recommendation, moderate quality evidence | RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies |
| Grade 1C | Strong recommendation, low-quality or very low-quality evidence | Observational studies or case series |
| Grade 2A | Weak recommendation, high quality evidence | RCTs without important limitations or overwhelming evidence from observational studies |
| Grade 2B | Weak recommendation, moderate-quality evidence | RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies |
| Grade 2C | Weak recommendation, low-quality or very low-quality evidence | Observational studies or case series |

### Plasma Pheresis and Plasma Exchange

The ASFA recommends plasmapheresis or plasma exchange as Categories I-II treatment options and the associated levels of evidence range with Grade 1A – 1C recommendations for the following indications (Schwarz, 2013):

- Acute inflammatory demyelinating polyneuropathy (Guillain-Barre Syndrome)
- ANCA-associated rapidly progressive glomerulonephritis (granulomatosis with polyangiitis; Wegner’s granulomatosis)
- Anti-glomerular basement membrane disease (Goodpasture's syndrome) when dialysis-independent and evidence of diffuse alveolar hemorrhage (DAH)
- Chronic inflammatory demyelinating polyneuropathy
- Focal segmental glomerulosclerosis that is recurrent in a transplanted kidney
- Hematopoietic stem cell transplant – ABO incompatible
- Hyperviscosity syndromes associated with monoclonal gammopathies
- Liver transplantation from a live donor with ABO incompatibility or positive cross-match
- Multiple sclerosis -acute CNS inflammatory demyelinating disease
- Myasthenia gravis, moderate to severe and pre-thymectomy
- Neuromyelitis optica (Devic’s syndrome) - acute
- Paraproteinemic demyelinating neuropathies associated with IgA or IgG monoclonal gammopathy of undetermined significance (MGUS) (excluding multiple myeloma)
- Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection (PANDAS) exacerbation

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• Renal transplantation in highly sensitive kidney transplant candidates (high PRA protocols) to reduce the number of antibodies reactive against human lymphocyte antigens (HLA)
• Renal transplantation from a live donor with ABO incompatibility or positive cross-match, where a non-reactive live or cadaveric donor is unavailable
• Renal transplant recipients who are post-transplant and experiencing a humoral or antibody mediated rejection
• Sydenham’s chorea
• Thrombotic microangiopathy, drug (ticlopidine) related
• Thrombotic Thrombocytopenic Purpura (TTP)
• Voltage gated potassium channel antibodies
• Wilson’s disease – fulminant

In addition to the above ASFA recommendations, published peer-reviewed literature and/or specialty medical societies support the use therapeutic apheresis when there is evidence that a targeted component(s) of the blood or plasma is readily removed with therapeutic apheresis and there is sufficient improvement in clinical symptoms without causing serious adverse effects.

Acute inflammatory demyelinating polyneuropathy (AIDP)/ Guillain-Barre Syndrome (GBS)
The American Academy of Neurology (AAN) (Cortese, 2011) published an updated evidence-based guideline on plasmapheresis in neurologic disorders. Plasmapheresis was recommended in the treatment of “AIDP/GBS severe enough to impair independent walking or to require mechanical ventilation (Level A). Plasmapheresis should be considered in the treatment of milder clinical presentations (Level B).” In a consensus statement by the American Association of Neuromuscular and Electrodiagnostic Medicine (AANEM) Committee (Donofrio, 2009), treatment of GBS in adults, particularly those who require an aid to walk (disability grade ≥ 2) within 2 weeks of the onset of symptoms with IVIG was recommended. The committee noted based on randomized trials, similar functional improvements in individuals treated with IVIG or plasmapheresis. Data did not support the combination of IVIG and plasmapheresis to treat GBS.

Atypical Hemolytic Uremic Syndrome (aHUS)
Atypical HUS is a rare genetic and chronic blood disease that can lead to renal failure and is associated with increased risk of stroke and death. Prompt diagnosis is essential, as aHUS is aggressive and treatment can be initiated for affected individuals. According to Loirat (2011), the diagnosis of aHUS relies on: 1) no associated disease; 2) investigations for Shiga toxin E. coli infection at onset of aHUS with no evidence of a Shiga-toxin/EHEC positive test (stool culture and polymerase chain reaction for Shiga-toxins; serology for anti-lipopolysaccharides antibodies); and 3) ADAMTS 13 (A Disintegrin-like And Metalloprotease with ThromboSpondin type 1 motif 13) determination as manifestations of aHUS and TTP may overlap. Frequent causes of aHUS involve complement regulatory abnormalities such as factor H mutations and MCP mutations. Plasma exchange can replace mutated circulating complement factors, specifically factor H. However, plasma exchange does not demonstrate similar efficacy for individuals with isolated MCP mutations, and plasma exchange is not recommended to treat MCP aHUS. Based on expert consensus opinion, plasma therapy has demonstrated efficacy as the first-line treatment for aHUS and should be started as early as possible, typically within 24 hours of presentation. (Ariceta, 2009; Lapeyraque, 2011; Loirat, 2011; Taylor 2010).

Autoimmune Hemolytic Uremic Syndrome – Severe Cold Agglutin Disease

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Individuals with autoimmune hemolytic anemia may be classified into warm or cold autoantibody types. Those with cold agglutinin disease (CAD) have IgM autoantibodies that target red blood cells when the temperatures are typically between 0–5 degrees Celsius. Avoiding exposure to cold temperatures is the primary treatment. However, for severe disease, immunosuppression with targeted therapy and anti-lymphoma chemotherapy may be used. Specialty input recommends use of plasmapheresis or plasma exchange to treat autoimmune hemolytic syndrome with severe cold agglutinin disease.

**Catastrophic Antiphospholipid Syndrome (CAPS)**

ASFA (Schwartz, 2013) defines CAPS as the acute onset of multiple thromboses in at least three organ systems over a period of days or weeks, in individuals with antiphospholipid antibodies. European Forum on Antiphospholipid Antibodies maintains a registry of individuals with CAPS due to the rarity of the disease. Data from the registry documented higher survival rates related to the increased frequency of combination therapy including anticoagulants, glucocorticoids and plasma exchange and/or intravenous immune globulin (Cervera, 2012). Specialty input recommends use of plasmapheresis or plasma exchange to treat CAPS.

**Cryoglobulinemia**

Cryoglobulins, single or mixed immunoglobulins may precipitate at low temperatures and can deposit in the vessels and tissues of the body. The increase of cryoglobulins can increase the viscosity of the circulating blood and may cause vasculitis and obstruct vessels, causing organ damage. Cryoglobulinemia involves the presence of cryoglobulins in the blood and typically occurs concomitantly with other conditions such as viral hepatitis, lymphoproliferative and autoimmune disorders. Treatment includes addressing the underlying concomitant disorder, suppression of the immune response, and plasmapheresis for severe or life-threatening complications.

**Hyperviscosity syndromes associated with monoclonal gammopathies**

The National Comprehensive Cancer Network® Clinical Practice Guidelines in Oncology (NCCN Guidelines®, 2013) on multiple myeloma recommend plasmapheresis as an adjunctive therapy for symptomatic hyperviscosity. The guideline also notes, “Institutions differ in their use of plasmapheresis for adjunctive treatment of renal dysfunction.” The recommendation to improve renal function by utilizing plasmapheresis is a category 2B recommendation.

**Multiple Myeloma Cast Nephropathy**

The formation of casts in the distal tubules of the kidneys is thought to be due to an increase in light chain concentrations typically seen with tumor progression (Schwartz, 2013). Primary therapy typically involves chemotherapy and intravenous fluid to increase the alkaline levels and to dissolve the light chains. The ASFA recommendation was a category II with a level of evidence 2B. However, specialty input recommended use of plasmapheresis or plasma exchange to treat multiple myeloma cast nephropathy.

**Multiple Sclerosis – Acute CNS inflammatory demyelinating disease**

The ASFA recommends the use of plasmapheresis or plasma exchange to treat acute CNS inflammatory demyelinating disease associated with multiple sclerosis (Schwartz, 2013). The AAN has a Level B recommendation for plasmapheresis as adjunctive treatment of exacerbations in relapsing forms of MS. Based on Level A evidence, the AAN states, “Plasmapheresis should not be offered for chronic progressive or secondary progressive MS” (Cortese, 2011).
PANDAS
Although ASFA (Schwartz, 2013) provides a Category I recommendation grade 1B level of evidence for plasmapheresis or plasma exchange as a treatment for PANDAS and Sydenham’s chorea, there is still conflicting information in the published literature. The AAN guideline on plasmapheresis in neurologic disorders (Cortese, 2011) stated there is “insufficient evidence to support or refute the use of plasmapheresis in the treatment of acute obsessive compulsive disorders (OCD) and tic symptoms in the setting of PANDAS.” Swedo and colleagues (2012) proposed a set of diagnostic criteria for Pediatric Acute-onset Neuropsychiatric Syndrome (PANS) as modified from PANDAS criteria. The authors noted this new set of criteria would need to be validated in large trials. In a retrospective review in a large metropolitan area, Gabbay (2008) reported significant over diagnosis of PANDAS and subsequent therapies that included plasma exchange.

Sydenham’s chorea
Although ASFA (Schwartz, 2013) provides a Category I recommendation grade 1B level of evidence for plasmapheresis or plasma exchange as a treatment for Sydenham’s chorea, there is still conflicting information in the published literature. Sydenham’s chorea is an autoimmune neuropsychiatric disorder that manifests after an acute bout of rheumatic fever. Symptoms include rapid and jerky, involuntary movements that may affect the face, trunk and extremities, which may prevent independent activities of daily living. Chorea is usually treated with neuroleptics, valproic acid and corticosteroids. Sydenham’s chorea is thought to be an autoimmune disorder based on the presence of antibodies that react with neuronal tissue that control motor activity (Garvey, 2005; National Institute of Neurological Disorders and Stroke [NINDS], 2007). The AAN guideline (Cortese, 2011) noted there is “Insufficient evidence to support or refute the use of plasmapheresis in the treatment of Sydenham chorea.” The NINDS notes there is no specific treatment for Sydenham’s chorea.

Systemic Lupus Erythematosus (SLE) - Severe
Circulating autoantibodies and immune complexes along with complement deposition results in injury to the cell and tissue for individuals with SLE. Immunosuppressive agents and targeted therapies are used to treat SLE. Specialty input recommends therapeutic plasmapheresis or plasma exchange for those with severe or life-threatening symptoms and conventional therapies have failed to prevent clinical deterioration.

Thrombotic Microangiopathy (TMA)
TMA is a rare medical condition involving small blood vessel damage from blood clots, usually as a result of other complex and serious illnesses. There are various syndromes such as HUS and TTP that involve TMA as a component of the specific syndrome, but are classified separately based on additional clinical indications (Loriat, 2011).

Transplantation
Approximately 20% of individuals waiting for cadaveric renal transplantation have high cytotoxic antibody titers rendering them at high risk for hyperacute and acute allograft rejection. Plasma exchange and immunoadsorption have been utilized as a means of removing these antibodies prior to transplantation resulting in significant reductions in the level of antibodies. When used in individuals with recurrent FSGS, pheresis induced a decrease in urinary protein. Additionally, randomized controlled trials have been conducted establishing the efficacy of plasma exchange in the treatment of biopsy proven acute antibody mediated renal allograft rejection The literature on pheresis for the treatment of chronic rejection is limited to a few uncontrolled studies with modest and transient results.
Other Indications

Additional ASFA indications for plasma pheresis or plasma exchange were of lower levels of evidence and/or the optimum role of therapy could not be established; or the evidence demonstrated the therapy could be ineffective or harmful. These indications are listed by categories:

Plasmapheresis or plasma exchange treatment options with Category I-II recommendation and levels of evidence ranging from Grade 2A – 2C include the following indications (Schwartz, 2013):

- Acute disseminated encephalomyelitis
- Lambert-Eaton myasthenic syndrome
- Overdose of drugs or poisoning – mushroom
- Phytic acid storage disease (Refsum’s disease)

Plasmapheresis or plasma exchange treatment options with Category III recommendations and levels of evidence ranging from Grade 1B – 2C were provided for the following indications (Schwartz, 2013):

- Acute liver failure
- Aplastic anemia
- Autoimmune hemolytic anemia, warm (WAHA) when condition is severe
- Chronic focal encephalitis (Rasmussen encephalitis)
- Coagulation factor inhibitors with autoantibody
- Heart (cardiac) transplantation – desensitization, when there is a positive cross-match due to donor specific HLA antibody or antibody mediated rejection (AMR)
- Hemolytic Uremic Syndrome associated with infection (Streptococcus pneumonae)
- Henoch-Schonlein purpura
- Heparin induced thrombocytopenia
- Hypertriglyceridemic (HTG) pancreatitis
- Immune complex rapidly progressive glomerulonephritis
- Immunoglobulin A nephropathy – crescentic and chronic progressive
- Liver transplantation – desensitization from a deceased donor and for humoral rejection
- Lung transplantation – antibody mediated rejection
- Multiple sclerosis that is chronic progressive or secondary progressive multiple sclerosis
- Nephrogenic systemic fibrosis
- Overdose of drugs or poisoning – envenomation, natalizumab and PML
- Paraneoplastic syndromes
- Paraproteinemic demyelinating polyneuropathy associated with multiple myeloma
- Pemphigus vulgaris
- Post transfusion purpura
- Red cell alloimmunization in pregnancy, prior to intrauterine transfusion availability
- Scleroderma (progressive systemic sclerosis)
- Sepsis with multi-organ failure
- Stiff-person syndrome

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Therapeutic Apheresis

- Sudden sensorineural hearing loss
- Thyroid storm
- Toxic epidermal necrolysis, refractory

Plasmapheresis or plasma exchange treatment options with Category IV recommendations and levels of evidence ranging from Grade 1A – 2C were provided for the following indications (Schwartz, 2013):
- Amyloidosis, systemic
- Amyotrophic lateral sclerosis
- Coagulation factor inhibitors with alloantibody
- Dermatomyositis or Polymyositis
- Hemolytic Uremic Syndrome associated with infection (Shiga toxin)
- Immune thrombocytopenia, immune and refractory
- Inclusion body myositis
- POEMS syndrome
- Psoriasis
- Schizophrenia

Immune thrombocytopenia
Immune thrombocytopenia has a widely accepted abbreviation, ITP, and is also known as “immune thrombocytopenic purpura and idiopathic thrombocytopenic purpura.” The most recent name “immune thrombocytopenia” is based on an international work group to standardize the terminology and definitions of ITP (Neunert, 2011; Rodeghiero, 2009). The 2011 evidence-based practice guideline for ITP does not include any form of therapeutic apheresis as a recommended treatment (Neunert, 2011).

Lupus Nephritis
The ASFA lists the use of plasmapheresis or plasma exchange treatment options with a Category IV recommendation and level of evidence Grade 1B. This recommendation was based on a controlled study that showed no benefit of adding therapeutic plasmapheresis or plasma exchange to prednisone and cyclophosphamide for individuals with severe lupus nephritis (Schwartz, 2013). American College of Rheumatology (ACR) guidelines for screening, treatment and management of lupus nephritis do not include the use of plasmapheresis or plasma exchange as treatment modalities (Hahn, 2012). Similarly, the Joint European League Against Rheumatism and European Renal Association-European dialysis and Transplant Association (EULAR/ERA-EDTA) (Bertsias, 2012) do not include the use of plasmapheresis or plasma exchange as a recommended treatment for the management of adult or pediatric lupus nephritis.

Phytic Acid Storage Disease (Refsum’s disease)
Refsum Disease, or phytic acid storage disease, is a rare genetic disease where individuals lack the enzyme to break down phytic acid found in certain foods. This excess phytic acids accumulate in the brain, blood and other tissues, with can cause blindness and arrhythmias in the heart. Avoidance of foods such as dairy products, beef, lamb, and fatty fish (e.g., tuna, cod and haddock) is the primary treatment. When there is excessive buildup of phytic acid, plasma exchange has been utilized with some improvement in symptoms, but vision and hearing problems persisted (National Institute of Neurological Disorders and Stroke, 2011).
Stiff Person (Man) Syndrome
Also known as Stiff-Man Syndrome, the classic features of this syndrome include painful muscular spasms associated with muscular stiffness, often times impairing the ability to walk. This syndrome is a rare, chronic but usually not progressive disorder. Published literature includes case reports with mixed results (Schwartz, 2013).

Lipid apheresis – Low- and High-density
Low-density apheresis
Low-density lipoprotein apheresis describes a variety of technologies used to acutely remove low-density lipoprotein (LDL) from the plasma. The individual initially undergoes an apheresis procedure to isolate the plasma. The low-density lipoproteins are then selectively removed from the plasma by either immunoadsorption, heparin-induced extracorporeal LDL precipitation (also referred to as HELP), or dextran sulfate adsorption. In immunoadsorption, polyclonal antihuman apoB antibodies from sheep selectively bind and remove LDL. (ApoB is the protein moiety of low-density lipoprotein). In HELP, LDL and other particles containing ApoB are precipitated by heparin at an acidic pH. Dextran sulfate adsorption removes LDL by binding the positively charged apoB to dextran sulfate particles bound to cellulose. LDL apheresis is a selective procedure in which only pathogenic low-density lipoproteins are removed. The plasma is then returned to the individual. Examples of two LDL-apheresis systems currently FDA-approved for use in the United States are the Heparin-Induced Extracorporeal LDL Cholesterol Precipitation (H.E.L.P.) system (B. Braun Medical Inc., Bethlehem, PA) and the LipoSorber® system (Kaneka Pharma America Corporation, New York, NY).

The ASFA recommends low density lipoprotein (LDL) apheresis as Categories I-II treatment options and the associated level of Grade 1A (strong recommendation, high-quality evidence) (Schwartz, 2013).

Familial hypercholesterolemia is an autosomal, co-dominant inherited disorder of lipoprotein metabolism that features mutations in the LDL-receptor gene. Due to reduced or absent LDL receptors, low-density lipoprotein cholesterol (LDLc) is not effectively cleared by the liver, resulting in very high plasma concentration in the circulating blood. LDLc deposits be found in the tendons (tendon xanthomas), arterial walls, along with an early onset of atherosclerosis and an increased risk of premature coronary heart disease (CHD). The estimated frequency is 1:500 for heterozygotes, and 1:1,000,000 for homozygotes. The USA Make Early Diagnosis to Prevent Early Death (MEDPED) Program uses the following diagnostic criteria for familial hypercholesterolemia (Castro-Oros, 2010; Robinson, 2013):

- Family with clinical suspicions of familial hypercholesterolemia:
  - Age < 20 years old (yo.), total cholesterol (TC) > 270 mg/dL
  - Age 20 - 29 yo., TC > 290 mg/dL
  - Age 30 - 39 yo., TC > 340 mg/dL
  - Age ≥ 40 yo., TC > 360 mg/dL.

Individuals with homozygous hypercholesterolemia are treated aggressively to prevent or slow the progression of cardiovascular disease (CVD) due to the prolonged high lipid level exposure since birth (Robinson, 2013). Statins and other agents along with diet and lifestyle modifications are recommended to lower TC. LDL apheresis may be used to selectively lower LDLc to optimal levels.
**Medical Policy**

**Therapeutic Apheresis**

*High-density lipid apheresis*

Autologous apheresis with selective HDL delipidation and infusion of selected preβ-HDL is being investigated as a method to reduce atherosclerosis in individuals at high-risk for cardiovascular disease (CVD). The selective removal of cholesterol from HDL (α-HDL), also called delipidation, involves exposing the plasma to organic solvents in the proprietary collection device and the process of returning the resulting small form of HDL (β-HDL). A randomized, placebo-controlled study examined the safety of an investigational device called LS PDS-2 (Lipid Sciences Plasma Delipidation System-2; Life Sciences, CA) that does not have U.S. Food & Drug Administration approval at this time. A total of 28 individuals with acute coronary syndrome (ACS) who were scheduled for diagnostic cardiac catheterization were enrolled and 26 participants completed all of the treatments and visits. Treatment involved HDL selected apheresis once every 7 days, for a total of 7 treatments. Fourteen individuals randomized to the treatment arm completed the 7-week selective HDL delipidation treatment period and 12 individuals assigned to the control arm completed the placebo treatment period. Preβ-HDL was evaluated by electrophoresis and quantitative analysis. On average, preβ-HDL was increased by 28 times in post-delipidated plasma compared to baseline volume. Intravascular ultrasound (IVUS) of the target vessel was performed and a nonsignificant reduction in the volume of the atheroma was reported in the delipidated group versus the placebo group. Fifteen of the participants had 1 or more adverse events, with a total of 38 reported adverse events. Hypotension was the most common adverse event. The authors noted limitations to the study included a small sample size and majority of the participants on the trial were also on statin therapy. Additionally, the authors noted “It is not clear whether acute regression of atherosclerotic burden will be associated with decreased clinical cardiovascular events. Additional clinical trials are required” (Waksman, 2010).

At this time, there is a lack of published evidence from large trials to demonstrate the improved net clinical health outcome with therapeutic apheresis combined with selective HDL delipidation. The 2013 ASFA guidelines do not address HDL lipid apheresis.

*Cytapheresis*

*Erythrocytapheresis*

The ASFA recommends erythrocytapheresis with Category I and the associated Grade 1B level of evidence (strong recommendations, moderate quality evidence) treatment options were listed for the following indications (Schwartz, 2013):

- Hereditary hemochromatosis
- Polycythemia vera

The ASFA notes management of individuals with low risk polycythemia vera (PV) include maintaining hematocrit ≤45% with phlebotomy and low dose aspirin. Individuals with high risk are treated with phlebotomy and other cytoreductive agents. Cytapheresis is recommended to correct hyperviscosity as an alternative to emergent large-volume phlebotomy (Schwartz, 2013).

Specialty input recommends use of erythrocytapheresis to treat symptomatic secondary polycythemia vera and porphyria cutanea tarda. Porphyria is a group of rare disorders where he process of heme production is affected. Porphyria cutanea tarda is the most common type of porphyria.
Erythrocytapheresis with Categories II – and the associated Grade 1B level of evidence (weak recommendation, low-quality or very low-quality evidence – moderate-quality of evidence) treatment option was listed for the following indication (Schwartz, 2013):

- Malaria

Erythrocytapheresis with Category III recommendations were provided for the following indications (Schwartz, 2013):

- Overdose of drugs or poisoning – tacrolimus

**Leukocytapheresis**

Leukocytapheresis with Category I recommendations were provided for the following indications (Schwartz, 2013):

- Hyperleukocytosis - leukostasis

Leukocytapheresis with Category III recommendations were provided for the following indications (Schwartz, 2013):

- Hyperleukocytosis – prophylaxis
- Psoriasis

Leukocytapheresis with Category IV recommendations were provided for the following indications (Schwartz, 2013):

- Dermatomyositis or Polymyositis
- Inclusion body myositis

**RBC exchange**

The ASFA recommends RBC exchange with Category I-II and the associated Grade 1C level of evidence (strong recommendations, low-quality or very low-quality evidence) treatment options were listed for the following indications (Schwartz, 2013):

- Babesiosis, severe
- Sickle cell disease, acute:
  - Acute stroke
  - Acute severe, chest syndrome
- Sickle cell disease, non-acute:
  - Stroke prophylaxis
  - Iron overload

Additional indications were recommended by specialty input using RBC exchange for the following indications:

- Babesiosis in the high-risk population
- Severe malaria
- Sickle cell disease
  - Multi-organ failure syndrome
  - Pre-procedure preparation for hematopoietic stem cell transplant or surgery
  - Pregnancy
  - Primary or secondary stroke prophylaxis

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**Thrombocytapheresis**
Thrombocytapheresis with Category II with “weak recommendation, low-quality or very low-quality evidence” or Category III recommendations were provided for the following indications (Schwartz, 2013):
- Thrombocytosis – symptomatic, prophylactic or secondary

**Immunoadsorption Pheresis**
Immunoadsorption pheresis with Category II 2b recommendations were provided for the following indications (Schwartz, 2013):
- Cryoglobulinemia, symptomatic or severe

Immunoadsorption pheresis with Category III recommendations were provided for the following indications (Schwartz, 2013):
- Acute CNS inflammatory demyelinating disease, associated with multiple sclerosis
- Chronic focal encephalitis (Rasmussen Encephalitis)
- Coagulation factor inhibitors alloantibody and autoantibody
- Immune thrombocytopenia, refractory
- Paraneoplastic neurological syndromes
- Paraproteinemic demyelinating neuropathies associated with IgA, IgG or IgM monoclonal gammopathy
- Pemphigus Vulgaris

The American College of Rheumatology (ACR) 2002 Update of the Rheumatoid Arthritis Guidelines note use of Staphylococcal protein A immunoadsorption column, “should be considered only for patients with refractory rheumatoid arthritis in whom treatment with several disease modifying anti-rheumatic drugs (DMARDs) has failed.” This recommendation was based on the improvement in 31.9% of the participants treated with the immunoadsorption column compared to 11.4% who received sham treatment in a randomized, multi-center trial (Felson, 1999).

The peer-reviewed medical literature supports the clinical effectiveness and safety of immunoadsorption for the indications listed in the policy statements. Most studies to date have supported the use of this procedure for individuals with hemolytic uremic syndrome and TTP resulting in a reduction of symptoms. Furthermore, the safety and efficacy of immunoadsorption has been well established in individuals with HUS, TTP, in post kidney transplant recipients with recurrent focal and segmental glomerulosclerosis (FGS). Additional research is needed to support the use of immunoadsorption in other immune-related disorders.

There are ongoing clinical trials investigating the use of the various forms of therapeutic apheresis modalities for multiple indications. Based on the data from the published studies and specialty consensus input, therapeutic apheresis modalities are considered medically necessary for selected indications. Conditions where data on efficacy, clinical utility and safety are lacking, or are conflicting are considered investigational and not medically necessary.

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**Background/Overview**

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Description of Pheresis Techniques
Applications of pheresis can be broadly subdivided into three general categories: acute-self limited diseases, acute, fulminant exacerbations of chronic diseases, and chronic diseases. In self-limited diseases and acute exacerbations of chronic diseases, therapeutic apheresis is used to acutely lower the circulating pathogenic substance. In chronic diseases, there is ongoing production of pathogenic autoantibodies. Because therapeutic apheresis does not address the underlying pathology, and due to the phenomenon of rebound antibody production, its use in most chronic diseases has been less effective than in acute, self-limiting diseases. For this reason, chronic conditions are not amenable to pheresis treatment. As an example, individuals with chronic progressive or relapsing-remitting multiple sclerosis are unlikely to benefit from pheresis treatment. However, individuals with an acute central nervous system inflammatory demyelinating disease (including the rare proportion of individuals with multiple sclerosis who suffer from this condition) have been found to have a reduction of symptoms.

Cytapheresis is another subtype of therapeutic apheresis in which the white blood cells are isolated and retained (leukapheresis or lymphocytopheresis) or red blood cells are isolated and retained (erythrocytapheresis).

Protein A column pheresis (extracorporeal immunoabsorption [ECI]) consists of highly purified protein A bonded to a silica matrix. Plasma is collected from the individual in a pheresis procedure and then is passed over the column (Prosurba®, Fresenius Medical Care, Lexington, MA). Circulating immune complexes and specific immunoglobulins bind to the protein A column and are thus selectively removed from the plasma. The plasma is returned to the individual, thus eliminating the need for a plasma exchange. Pathogenic levels of immunoglobulins and circulating immune complexes are associated with a number of diseases such as idiopathic thrombocytopenic purpura, hemolytic uremic syndrome, and red cell aplasia.

The goal of pheresis is the removal of harmful plasma components. Theoretically, decreasing the concentration of the harmful plasma component, will improve the course of the disease. Abnormal components potentially removed with apheresis include toxins, metabolic substances, and plasma components, such as complement or antibodies. Therefore, diseases thought to be caused by these abnormal constituents might best be treated with this form of therapy. Diseases benefiting from these procedures are largely autoimmune or neurological disorders. Pheresis techniques are not intended to be curative treatments for most indications. Rather, they are used to address related symptoms. Depending on the indication, alternative treatments, such as pharmacologic therapy, may be available.

Pheresis procedures are typically performed in outpatient settings, including blood banks, dialysis centers, hospital clinics and physician’s offices. Reinfusion with human plasma may cause anaphylaxis and bleeding complications, and though rare, may require replacement clotting factors. Therefore, pheresis procedures should be performed by appropriately-trained clinicians in a setting that can respond to medical emergencies at all times.

Definitions
Antibodies: Immunoglobulins (a specialized immune protein) produced as a result of the introduction of an antigen into the body.

Autoimmune disease: An illness occurring when the body tissues are attacked by its own immune system; as a result, individuals with these diseases frequently have unusual antibodies circulating in their blood that target their own body tissues.
Bullous pemphigoid: A disease characterized by tense blistering eruptions of the skin, generally caused by antibodies abnormally accumulating in a layer of the skin.

Cerebritis: Inflammation of the brain.

Cryoglobulinemia: The presence of abnormal proteins called cryoglobulins that, by definition, have the unusual properties of precipitating from the blood serum when it is chilled and re-dissolving upon rewarming.

Guillain-Barre: A condition that usually occurs after an infection; the signs and symptoms include loss of sensation in the arms and legs and increasing weakness.

Heterozygotes: A person possessing two different forms of a particular gene, one inherited from each parent.

Homozygotes: A person who has two identical forms of a particular gene, one inherited from each parent.

Immune complex: A combination of an antibody (immunoglobulin), and an antigen (the target that the antibody is attacking).

Immune thrombocytopenic purpura: A condition in which antibodies destroy the cells in the body that is responsible for blood clotting (platelets).

Immunoglobulin: A protein produced by plasma cells and lymphocytes; immunoglobulins are an essential part of the body's immune system which attach to foreign substances, such as bacteria, and assist in destroying them.

Myocarditis: Inflammation of the heart muscle.

Nephritis: Inflammation of the kidney.

Pemphigus vulgaris: An autoimmune disease of the skin, with blistering.

Polymyositis: A chronic inflammatory disease of muscle that begins when white blood cells spontaneously invade muscles, which may result in severe muscle pain, tenderness and weakness.

PRA: Panel reactive antibodies.

Pure red cell aplasia: A condition where an individual has an inability to produce red blood cells.

Regional enteritis: Also called Crohn’s disease, a chronic inflammatory disease of the intestine primarily in the small and large intestines but which can occur anywhere in the digestive system between the mouth and the anus.

Scleroderma: A disease of connective tissue resulting in formation of scar tissue in the skin and at times other organs of the body.

Segmental glomerulosclerosis: An illness that occurs when scar tissue forms in some of the glomeruli (structures involved in the filtration of blood) of the kidney.

Vasculitis: A general term for a group of uncommon diseases characterized by inflammation of the blood vessels.
Waldenström’s macroglobulinemia: A disease where abnormal white blood cells produce excessive amounts of antibodies; bleeding and enlarged liver and spleen may be seen.

### Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

**Plasmapheresis, plasma exchange**

**When services are Medically Necessary:**

<table>
<thead>
<tr>
<th>CPT</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>36514</td>
<td>Therapeutic apheresis; for plasma pheresis</td>
</tr>
</tbody>
</table>

**ICD-9 Procedure**

- **99.71** Therapeutic plasmapheresis

**ICD-9 Diagnosis**

- **273.1** Monoclonal paraproteinemia
- **273.2** Other paraproteinemias (cryoglobulinemia)
- **273.3** Macroglobulinemia (Waldenström’s)
- **357.0** Acute infective polyneuritis [Guillain-Barre]
- **357.81** Chronic inflammatory demyelinating polyneuritis [CIDP]
- **392.0-392.9** Rheumatic chorea [Sydenham’s chorea]
- **446.6** Thrombotic microangiopathy (TTP)
- **580.4** Acute glomerulonephritis with lesion of rapidly progressive glomerulonephritis
- **582.4** Chronic glomerulonephritis with lesion of rapidly progressive glomerulonephritis
- **583.4** Nephritis and nephropathy with lesion of rapidly progressive glomerulonephritis
- **642.50-642.54** Severe pre-eclampsia (H.E.L.L.P syndrome)

**ICD-10 Procedure**

- **6A550Z3** Pheresis of plasma, single
- **6A551Z3** Pheresis of plasma, multiple

**ICD-10 Diagnosis**

- **C88.0** Waldenström macroglobulinemia
- **D47.2** Monoclonal gammopathy [MGUS]
- **D89.1** Cryoglobulinemia
- **G61.0** Guillain-Barre syndrome
- **G61.81** Chronic inflammatory demyelinating polyneuritis [CIDP]
- **I02.0-I02.9** Rheumatic chorea [Sydenham’s chorea]
- **M31.1** Thrombotic microangiopathy [TTP]
- **N01.0-N01.9** Rapidly progressive nephritic syndrome

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When services may be Medically Necessary when criteria are met:
For the procedure codes listed above for the following diagnosis codes

<table>
<thead>
<tr>
<th>ICD-9 Diagnosis</th>
<th>[For dates of service prior to 10/01/2015]</th>
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</thead>
<tbody>
<tr>
<td>034.0-034.1</td>
<td>Streptococcal sore throat and scarlet fever [when specified as causing PANDAS]</td>
</tr>
<tr>
<td>203.00-203.02</td>
<td>Multiple myeloma</td>
</tr>
<tr>
<td>275.1</td>
<td>Disorders of copper metabolism [Wilson’s disease]</td>
</tr>
<tr>
<td>279.49</td>
<td>Autoimmune disease, not elsewhere classified [when specified as PANDAS]</td>
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<tr>
<td>283.0</td>
<td>Autoimmune hemolytic anemias</td>
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<tr>
<td>283.11</td>
<td>Hemolytic-uremic syndrome</td>
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<tr>
<td>289.81</td>
<td>Primary hypercoagulable state [when specified as antiphospholipid antibody syndrome]</td>
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<td>300.3</td>
<td>Obsessive-compulsive disorders [when specified as PANDAS]</td>
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<tr>
<td>323.81</td>
<td>Other causes of encephalitis and encephalomyelitis [voltage gated potassium channel (VGKC) antibody syndrome]</td>
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<tr>
<td>336.0</td>
<td>Syringomyelia and syringobulbia [Morvan’s disease; VGKC antibody syndrome]</td>
</tr>
<tr>
<td>340</td>
<td>Multiple sclerosis</td>
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<tr>
<td>341.0</td>
<td>Neuromyelitis optica</td>
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<tr>
<td>341.8-341.9</td>
<td>Other/unspecified demyelinating disease of central nervous system</td>
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<td>357.3</td>
<td>Polyneuropathy in malignant disease [limbic encephalopathy, VGKC antibody syndrome]</td>
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<td>358.00-358.01</td>
<td>Myasthenia gravis</td>
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<tr>
<td>446.21</td>
<td>Goodpasture's syndrome</td>
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<tr>
<td>446.4</td>
<td>Wegener’s granulomatosis</td>
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<td>582.1</td>
<td>Chronic glomerulonephritis with lesion of membranous glomerulonephritis</td>
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<tr>
<td>583.81</td>
<td>Nephritis and nephropathy in diseases classified elsewhere [due to Goodpasture's syndrome]</td>
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<tr>
<td>584.5-584.9</td>
<td>Acute kidney failure</td>
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<td>585.1-585.9</td>
<td>Chronic kidney disease</td>
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<tr>
<td>586</td>
<td>Renal failure, unspecified</td>
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<td>710.0</td>
<td>Systemic lupus erythematosus</td>
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<tr>
<td>996.81</td>
<td>Complications of transplanted organ, kidney</td>
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<tr>
<td>996.82</td>
<td>Complications of transplanted organ, liver</td>
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<tr>
<td>996.83</td>
<td>Complications of transplanted organ, heart</td>
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<tr>
<td>V42.0-V42.1</td>
<td>Organ or tissue replaced by transplant, kidney, heart</td>
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<tr>
<td>V42.81</td>
<td>Bone marrow transplant</td>
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<table>
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<tr>
<td>B95.0-B95.1</td>
<td>Streptococcus group A/B, as the cause of diseases classified elsewhere [PANDAS]</td>
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<tr>
<td>C90.00-C90.02</td>
<td>Multiple myeloma</td>
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<td>Autoimmune hemolytic anemias</td>
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<td>D59.3</td>
<td>Hemolytic uremic syndrome</td>
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<tr>
<td>D68.61</td>
<td>Antiphospholipid syndrome</td>
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<tr>
<td>D89.89</td>
<td>Other specified disorders involving the immune mechanism, not elsewhere classified</td>
</tr>
</tbody>
</table>
Therapeutic Apheresis

Low density lipid apheresis

When services may be Medically Necessary when criteria are met:

CPT
36516  Therapeutic apheresis; with extracorporeal selective adsorption or selective filtration and plasma reinfusion

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

ICD-9 Diagnosis  [For dates of service prior to 10/01/2015]
272.0  Pure hypercholesterolemia
**Therapeutic Apheresis**

<table>
<thead>
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<th>ICD-10 Diagnosis</th>
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<tr>
<td>E78.0</td>
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_Cytapheresis and therapeutic phlebotomy_

**When services are Medically Necessary:**

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<td>Therapeutic apheresis; for white blood cells</td>
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<tr>
<td>36512</td>
<td>Therapeutic apheresis; for red blood cells [red blood cell exchange]</td>
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<td>36513</td>
<td>Therapeutic apheresis; for platelets</td>
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<td>99195</td>
<td>Therapeutic phlebotomy</td>
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<td>Therapeutic leukopheresis</td>
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<tr>
<td>99.73</td>
<td>Therapeutic erythrocytapheresis</td>
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<td>99.74</td>
<td>Therapeutic plateletpheresis</td>
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<td>238.4</td>
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<td>275.01</td>
<td>Hereditary hemochromatosis</td>
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<th>[For dates of service on or after 10/01/2015]</th>
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<tbody>
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<td>6A550Z0</td>
<td>Pheresis of erythrocytes, single</td>
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<tr>
<td>6A550Z1</td>
<td>Pheresis of leukocytes, single</td>
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<tr>
<td>6A550Z2</td>
<td>Pheresis of platelets, single</td>
</tr>
<tr>
<td>6A551Z0</td>
<td>Pheresis of erythrocytes, multiple</td>
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<tr>
<td>6A551Z1</td>
<td>Pheresis of leukocytes, multiple</td>
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<tr>
<td>6A551Z2</td>
<td>Pheresis of platelets, multiple</td>
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<table>
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<tr>
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<th>[For dates of service on or after 10/01/2015]</th>
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<tbody>
<tr>
<td>D45</td>
<td>Polycythemia vera</td>
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<tr>
<td>E80.1</td>
<td>Porphyria cutanea tarda</td>
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<tr>
<td>E83.110</td>
<td>Hereditary hemochromatosis</td>
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**When services may be Medically Necessary when criteria are met:**

For the procedure codes listed above for the following diagnosis codes

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<tr>
<th>ICD-9 Diagnosis</th>
<th>[For dates of service prior to 10/01/2015]</th>
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</thead>
<tbody>
<tr>
<td>084.0-084.9</td>
<td>Malaria</td>
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<tr>
<td>088.82</td>
<td>Babesiosis</td>
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<td>203.00-208.92</td>
<td>Leukemias</td>
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<tr>
<td>238.71</td>
<td>Essential thrombocytopenia (thrombocytosis)</td>
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<tr>
<td>277.1</td>
<td>Disorders of porphyrin metabolism [when specified as porphyria cutanea tarda]</td>
</tr>
<tr>
<td>282.60-282.69</td>
<td>Sickle-cell disease</td>
</tr>
</tbody>
</table>

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Therapeutic Apheresis

ICD-10 Diagnosis

For dates of service on or after 10/01/2015
B50.0-B54          Malaria
B60.0              Babesiosis
C90.00-C95.92      Leukemias
D47.3              Essential (hemorrhagic) thrombocytopenia
D57.00-D57.819     Sickle-cell disorders
D75.1              Secondary polycythemia
O99.011-O99.03     Anemia complicating pregnancy, childbirth and the puerperium

Immunoadsorption pheresis

When services are Medically Necessary:

CPT
36515  Therapeutic apheresis; with extracorporeal immunoadsorption and plasma reinfusion

ICD-9 Procedure
99.76  Extracorporeal immunoadsorption

ICD-9 Diagnosis
446.6  Thrombotic microangiopathy (TTP)

ICD-10 Procedure
6A550Z3  Pheresis of plasma, single
6A551Z3  Pheresis of plasma, multiple

ICD-10 Diagnosis
M31.1  Thrombotic microangiopathy [TTP]

When services may be Medically Necessary when criteria are met:
For the procedure codes listed above for the following diagnosis codes

ICD-9 Diagnosis
714.0-714.9  Rheumatoid arthritis, other inflammatory polyarthropathies

ICD-10 Diagnosis
M05.00-M05.9  Rheumatoid arthritis with rheumatoid factor
M06.00-M06.09  Rheumatoid arthritis without rheumatoid factor
M06.80-M06.9  Other specified and unspecified rheumatoid arthritis

Plasmapheresis, lipid apheresis, immunopheresis, cytapheresis

When services are Investigational and Not Medically Necessary:

Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. The member’s contract benefits in effect on the date that services are rendered must be used. Medical Policy, which addresses medical efficacy, should be considered before utilizing medical opinion in adjudication. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

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For the procedure codes listed above for plasmapheresis, lipid apheresis, immunopheresis, leukocytapheresis, thrombocytapheresis and red blood cell exchange when criteria are not met or for all other diagnoses not listed, or when the code describes a procedure indicated in the Position Statement section as investigational and not medically necessary.

When services are also Investigational and Not Medically Necessary:

**CPT**

0342T Therapeutic apheresis with selective HDL delipidation and plasma reinfusion

**ICD-9 Diagnosis**

*For dates of service prior to 10/01/2015*

All diagnoses

**ICD-10 Procedure**

*For dates of service on or after 10/01/2015*

For the following codes when specified as apheresis with selective HDL delipidation and plasma reinfusion:

6A550Z3 Pheresis of plasma, single
6A551Z3 Pheresis of plasma, multiple

**ICD-10 Diagnosis**

*For dates of service on or after 10/01/2015*

All diagnoses

**References**

Peer Reviewed Publications:


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Government Agency, Medical Society, and Other Authoritative Publications:


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Websites for Additional Information

   - Resfum Disease. Updated September 27, 2011.

Index

Adacolumn
Apheresis, therapeutic
Cellsorba®
Cytapheresis
Immunoadsorption
LDL apheresis
Lipsorb®
Pheresis
Plasma Exchange
Plasmapheresis
Prosorba®
Protein A column
Selective HDL delipidation

The use of specific product names is illustrative only. It is not intended to be a recommendation of one product over another, and is not intended to represent a complete listing of all products available.

Document History

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Therapeutic Apheresis

erythrocytapheresis. Revised leukocytapheresis medically necessary criteria. Added medically necessary indications for red blood cell (RBC) exchange. Revised investigational and not medically necessary statements. Updated Rationale, Background, Coding and Reference sections


Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. The member’s contract benefits in effect on the date that services are rendered must be used. Medical Policy, which addresses medical efficacy, should be considered before utilizing medical opinion in adjudication. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

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