INSTRUCTIONS FOR USE
This protocol provides assistance in interpreting UnitedHealthcare benefit plans. When deciding coverage, the enrollee specific document must be referenced. The terms of an enrollee's document (e.g., Certificate of Coverage (COC) or Evidence of Coverage (EOC)) may differ greatly. In the event of a conflict, the enrollee's specific benefit document supersedes this protocol. All reviewers must first identify enrollee eligibility, any federal or state regulatory requirements and the plan benefit coverage prior to use of this Protocol. Other Protocols, Policies and Coverage Determination Guidelines may apply. UnitedHealthcare reserves the right, in its sole discretion, to modify its Protocols, Policies and Guidelines as necessary. This protocol is provided for informational purposes. It does not constitute medical advice. This policy does not govern Medicare Group Retiree members.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

COMMERCIAL & MEDICAID COVERAGE RATIONALE

Therapeutic apheresis is medically necessary for treating or managing the following conditions/diagnoses:
- ABO incompatible heart transplantation in children less than 40 months of age (plasma exchange)
- ABO incompatible hematopoietic stem cell and bone marrow transplant (plasma exchange)
- ABO incompatible kidney transplantation (plasma exchange)
- Acute inflammatory demyelinating polyneuropathy (Guillain-Barré syndrome) (plasma exchange)
- ANCA-associated rapidly progressive glomerulonephritis (Wegener’s Granulomatosis) (plasma exchange)
- Anti-glomerular basement membrane disease (Goodpasture’s syndrome) (plasma exchange)
- Babesiosis (RBC exchange)
- Cardiac allograft rejection or prophylaxis of cardiac transplant rejection (photopheresis)
- Chronic inflammatory demyelinating polyneuropathy (plasma exchange)
- Cryoglobulinemia (plasma exchange)
- Cutaneous T-cell lymphoma; mycosis fungoides; Sézary syndrome, erythrodermic (photopheresis)
- Heterozygous or homozygous familial hypercholesterolemia (plasma exchange or selective adsorption)
- Focal segmental glomerulosclerosis, recurrent (plasma exchange)
- Graft-versus-host disease, skin, chronic (photopheresis)
- Hyperleukocytosis, leukostasis (leukocytapheresis)
- Hyperviscosity in monoclonal gammopathies, treatment of symptoms (plasma exchange)
- IgG/IgA, or IgM type of paraproteinemic polyneuropathy (plasma exchange)
- Lung allograft rejection (photopheresis)
- Multiple sclerosis (relapsing form with steroid resistant exacerbations) (plasma exchange)
- Myasthenia gravis (plasma exchange)
- Neuromyelitis optica (Devic’s syndrome) (plasma exchange)
- Renal transplantation, antibody mediated rejection (plasma exchange)
- Renal transplantation, desensitization, living or deceased donor recipients, positive crossmatch due to donor specific HLA antibody (plasma exchange)
- Rheumatoid arthritis, refractory (immunoabsorption)
- Sickle cell disease for one of the following:
  - Red blood cell exchange for treating acute stroke, acute chest syndrome, or multiorgan failure
  - Prophylaxis with red blood cell exchange for primary or secondary stroke prevention or for prevention of transfusional iron overload
- Thrombotic thrombocytopenic purpura (plasma exchange)

Therapeutic apheresis including plasma exchange, plasmapheresis, or photopheresis is **not medically necessary** for treating or managing the following conditions/diagnoses, including but not limited to:
- ABO incompatible solid organ transplantation, liver perioperative
- Acute disseminated encephalomyelitis
- Acute liver failure
- Age related macular degeneration
- Amyloidosis, systemic
- Amyotrophic lateral sclerosis
- Aplastic anemia; pure red cell aplasia
- Autoimmune hemolytic anemia; warm autoimmune hemolytic anemia; cold agglutinin disease
- Burn shock resuscitation
- Catastrophic antiphospholipid syndrome
- Chronic focal encephalitis (Rasmussen’s encephalitis)
• Coagulation factor inhibitors
• Cutaneous T-cell lymphoma; mycosis fungoides; Sézary syndrome, non-erythrodermic
• Dermatomyositis or polymyositis
• Dilated cardiomyopathy
• Graft-versus-host disease, skin, acute
• Graft-versus-host disease, non-skin, acute/chronic
• Hereditary hemochromatosis
• Hemolytic uremic syndrome
• High density lipoprotein (HDL) delipidation and plasma reinfusion
• Hyperleukocytosis, prophylaxis
• Hypertriglyceridemic pancreatitis
• Hyperviscosity in monoclonal gammopathies, prophylaxis for rituximab
• IgG/IgA or IgM type of paraproteinemic polyneuropathy treated with immunoabsorption
• Immune thrombocytopenic purpura
• Immune complex rapidly progressive glomerulonephritis
• Inclusion body myositis
• Inflammatory bowel disease
• Lambert-Eaton myasthenic syndrome
• Malaria
• Multiple myeloma type of paraproteinemic polyneuropathy
• Multiple sclerosis, chronic progressive or secondary progressive
• Myeloma cast nephropathy
• Nephrogenic systemic fibrosis
• Overdose, venoms, and poisoning
• Paraneoplastic neurologic syndromes
• Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS) and Sydenham’s chorea
• Pemphigus vulgaris
• Phytanic acid storage disease (Refsum’s disease)
• Polycythemia vera and erythrocytosis
• POEMS (polyneuropathy, organomegaly, endocrinopathy, M protein, and skin changes)
• Post transfusion purpura
• Psoriasis
• Red cell alloimmunization in pregnancy
• Rheumatoid arthritis, refractory, treated with plasma exchange
• Schizophrenia
• Sclerodema (progressive systemic sclerosis)
• Sepsis with multiorgan failure
• Stiff-person syndrome
• Systemic lupus erythematosus
• Thrombocytosis
• Thrombotic microangiopathy: drug-associated
• Thrombotic microangiopathy: hematopoietic stem cell transplant-associated
• Thyroid storm
• Wilson’s disease, fulminant

There is insufficient evidence to conclude that apheresis, plasma exchange, plasmapheresis, immunoadsorption, or photopheresis is beneficial for health outcomes such as decreased morbidity and mortality rates in patients with disorders other than those listed as medically necessary.

**Apheresis is first-line therapy when treating or managing the following conditions/diagnoses:**
- Acute inflammatory demyelinating polyneuropathy (Guillain-Barré syndrome) (plasma exchange)
- ANCA-associated rapidly progressive glomerulonephritis (Wegener’s Granulomatosis) (plasma exchange)
- Anti-glomerular basement membrane disease (Goodpasture’s syndrome) (plasma exchange)
- Babesiosis (RBC exchange)
- Cardiac allograft rejection prophylaxis (photopheresis)
- Chronic inflammatory demyelinating polyneuropathy (plasma exchange)
- Cryoglobulinemia (plasma exchange)
- Cutaneous T-cell lymphoma; mycosis fungoides; Sézary syndrome, erythrodermic (photopheresis)
- Homozygous familial hypercholesterolemia (plasma exchange or selective adsorption)
- Hyperleukocytosis, leukostasis (leukocytapheresis)
- Hyperviscosity in monoclonal gammopathies, treatment of symptoms (plasma exchange)
- IgG/IgA, or IgM type of paraproteinemic polyneuropathy (plasma exchange)
- Myasthenia gravis (plasma exchange)
- Renal transplantation, antibody mediated rejection (plasma exchange)
- Renal transplantation, desensitization, living or deceased donor recipients, positive crossmatch due to donor specific HLA antibody (plasma exchange)
- Sickle cell disease for one of the following:
  - Red blood cell exchange for treating acute stroke or multiorgan failure
  - Prophylaxis with red blood cell exchange for primary or secondary stroke prevention or for prevention of transfusional iron overload
- Thrombotic thrombocytopenic purpura (plasma exchange)

**Apheresis is medically necessary for persons who are refractory to or intolerant of standard therapy for the following conditions/diagnoses where apheresis is second-line therapy:**
- ABO incompatible heart transplantation in children less than 40 months of age (plasma exchange)
- ABO incompatible hematopoietic stem cell and bone marrow transplant (plasma exchange)
- ABO incompatible kidney transplantation (plasma exchange)
- Cardiac allograft rejection (photopheresis)
- Focal segmental glomerulosclerosis, recurrent (plasma exchange)
- Heterozygous familial hypercholesterolemia (plasma exchange or selective adsorption)
- Graft-versus-host disease, skin, chronic (photopheresis)
- Lung allograft rejection (photopheresis)
• Multiple sclerosis (relapsing form with steroid resistant exacerbations) (plasma exchange)
• Neuromyelitis optica (Devic’s syndrome) (plasma exchange)
• Rheumatoid arthritis, refractory (immunoadsorption)
• Sickle cell disease, acute chest syndrome (red blood cell exchange)

**BENEFIT CONSIDERATION**

Some of the disorders for which apheresis is **not medically necessary** are serious, rare diseases. Coverage exists for some otherwise **not medically necessary** services that treat serious, rare diseases when certain conditions are met.

**MEDICARE COVERAGE RATIONALE**

Medicare covers apheresis when criteria are met. Refer to the National Coverage Determination for Apheresis (Therapeutic Pheresis) (110.14). Local Coverage Determinations for Nevada for Apheresis do not exist at this time (Accessed July 2016). The National Coverage Determination is as follows:

**Apheresis (Therapeutic Pheresis) (110.14)**

**Description**

Apheresis (also known as pheresis or therapeutic pheresis) is a medical procedure utilizing specialized equipment to remove selected blood constituents (plasma, leukocytes, platelets, or cells) from whole blood. The remainder is re-transfused into the person from whom the blood was taken.

For purposes of Medicare coverage, apheresis is defined as an autologous procedure, i.e., blood is taken from the patient, processed, and returned to the patient as part of a continuous procedure (as distinguished from the procedure in which a patient donates blood preoperatively and is transfused with the donated blood at a later date).

**Indications and Limitations of Coverage**

Apheresis is **covered** for the following indications:

• Plasma exchange for acquired myasthenia gravis;
• Leukapheresis in the treatment of leukemia;
• Plasmapheresis in the treatment of primary macroglobulinemia (Waldenstrom);
• Treatment of hyperglobulinemias, including (but not limited to) multiple myelomas, cryoglobulinemia and hyperviscosity syndromes;
• Plasmapheresis or plasma exchange as a last resort treatment of thrombotic thrombocytopenic purpura (TTP);
• Plasmapheresis or plasma exchange in the last resort treatment of life threatening rheumatoid vasculitis;
• Plasma perfusion of charcoal filters for treatment of pruritis of cholestatic liver disease;
• Plasma exchange in the treatment of Goodpasture's Syndrome;
• Plasma exchange in the treatment of glomerulonephritis associated with antiglomerular basement membrane antibodies and advancing renal failure or pulmonary hemorrhage;
• Treatment of chronic relapsing polyneuropathy for patients with severe or life threatening symptoms who have failed to respond to conventional therapy;
• Treatment of life threatening scleroderma and polymyositis when the patient is unresponsive to conventional therapy;
• Treatment of Guillain-Barre Syndrome; and
• Treatment of last resort for life threatening systemic lupus erythematosus (SLE) when conventional therapy has failed to prevent clinical deterioration.

Apheresis is **covered only** when performed in a hospital setting (either inpatient or outpatient) or in a nonhospital setting, e.g., a physician directed clinic when the following conditions are met:

- A physician (or a number of physicians) is present to perform medical services and to respond to medical emergencies at all times during patient care hours;
- Each patient is under the care of a physician; and
- All nonphysician services are furnished under the direct, personal supervision of a physician.

**Medicare covers extracorporeal photopheresis when criteria are met. Refer to the National Coverage Determination for Extracorporeal Photopheresis (110.4). Local Coverage Determinations for Nevada for Extracorporeal Photopheresis do not exist at this time. (Accessed July 2016). The National Coverage Determination is as follows:**

**Extracorporeal Photopheresis (110.4)**

Extracorporeal photopheresis is a medical procedure in which a patient's white blood cells are exposed first to a drug called 8-methoxypsoralen (8-MOP) and then to ultraviolet A (UVA) light. The procedure starts with the removal of the patient's blood, which is centrifuged to isolate the white blood cells. The drug is typically administered directly to the white blood cells after they have been removed from the patient (referred to as ex vivo administration) but the drug can alternatively be administered directly to the patient before the white blood cells are withdrawn. After UVA light exposure, the treated white blood cells are then re-infused into the patient.

**Indications and Limitations of Coverage**

**Nationally Covered Indications**

- The Centers for Medicare & Medicaid Services (CMS) has determined that extracorporeal photopheresis is **reasonable and necessary** under §1862(a)(1)(A) of the Social Security Act (the Act) under the following circumstances:
  1. Effective April 8, 1988, Medicare provides coverage for:
  2. Palliative treatment of skin manifestations of cutaneous T-cell lymphoma that has not responded to other therapy.
  3. Effective December 19, 2006, Medicare also provides coverage for: Patients with acute cardiac allograft rejection whose disease is refractory to standard immunosuppressive drug treatment; and patients with chronic graft versus host disease whose disease is refractory to standard immunosuppressive drug treatment.
  4. Effective April 30, 2012, Medicare also provides coverage for: Extracorporeal photopheresis for the treatment of bronchiolitis obliterans syndrome (BOS) following lung allograft transplantation only when extracorporeal photopheresis is provided under a clinical research study that meets the following conditions: The clinical research study meets the requirements specified below to assess the effect of extracorporeal photopheresis for the treatment of BOS.
following lung allograft transplantation. The clinical study must address one or more aspects of the following question:

Prospectively, do Medicare beneficiaries who have received lung allografts, developed BOS refractory to standard immunosuppressive therapy, and received extracorporeal photopheresis, experience improved patient-centered health outcomes as indicated by:

a. improved forced expiratory volume in one second (FEV1);
b. improved survival after transplant; and/or,
c. improved quality of life?

The required clinical study must adhere to the following standards of scientific integrity and relevance to the Medicare population:

a. The principal purpose of the research study is to test whether extracorporeal photopheresis potentially improves the participants’ health outcomes.
b. The research study is well supported by available scientific and medical information or it is intended to clarify or establish the health outcomes of interventions already in common clinical use.
c. The research study does not unjustifiably duplicate existing studies.
d. The research study design is appropriate to answer the research question being asked in the study.
e. The research study is sponsored by an organization or individual capable of successfully executing the proposed study.
f. The research study is in compliance with all applicable Federal regulations concerning the protection of human subjects found at 45 CFR Part 46. If a study is regulated by the Food and Drug Administration (FDA), it must also be in compliance with 21 CFR parts 50 and 56.
g. All aspects of the research study are conducted according to appropriate standards of scientific integrity (see http://www.icmje.org).
h. The research study has a written protocol that clearly addresses, or incorporates by reference, the standards listed here as Medicare requirements for coverage with evidence development.
i. The clinical research study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Trials of all medical technologies measuring therapeutic outcomes as one of the objectives meet this standard only if the disease or condition being studied is life threatening as defined in 21 CFR § 312.81(a) and the patient has no other viable treatment options.
j. The clinical research study is registered on the ClinicalTrials.gov website by the principal sponsor/investigator prior to the enrollment of the first study subject.
k. The research study protocol specifies the method and timing of public release of all pre-specified outcomes to be measured including release of outcomes if outcomes are negative or study is terminated early. The results must be made public within 24 months of the end of data collection. If a report is planned to be published in a peer-reviewed journal, then that initial release may be an abstract that meets the requirements of the International Committee of Medical Journal Editors (http://www.icmje.org).
l. The research study protocol must explicitly discuss subpopulations affected by the treatment under investigation, particularly traditionally underrepresented groups in clinical
studies, how the inclusion and exclusion criteria effect enrollment of these populations, and a plan for the retention and reporting of said populations on the trial. If the inclusion and exclusion criteria are expected to have a negative effect on the recruitment or retention of underrepresented populations, the protocol must discuss why these criteria are necessary.

m. The research study protocol explicitly discusses how the results are or are not expected to be generalizable to the Medicare population to infer whether Medicare patients may benefit from the intervention. Separate discussions in the protocol may be necessary for populations eligible for Medicare due to age, disability or Medicaid eligibility.

Consistent with section 1142 of the Act, the Agency for Healthcare Research and Quality supports clinical research studies that CMS determines meet the above-listed standards and address the above-listed research questions.

Any clinical study under which there is coverage of extracorporeal photopheresis for this indication pursuant to this national coverage determination (NCD) must be approved by April 30, 2014. If there are no approved clinical studies on this date, this NCD will expire and coverage of extracorporeal photopheresis for BOS will revert to the coverage policy in effect prior to the issuance of the final decision memorandum for this NCD.

**Nationally Non-Covered Indications**

All other indications for extracorporeal photopheresis not otherwise indicated above as covered remain non-covered.

**For Medicare and Medicaid Determinations Related to States Outside of Nevada:**

Please review Local Coverage Determinations that apply to other states outside of Nevada.

http://www.cms.hhs.gov/mcd/search

**Important Note:** Please also review local carrier Web sites in addition to the Medicare Coverage database on the Centers for Medicare and Medicaid Services’ Website.

**DESCRIPTION OF SERVICES**

Therapeutic apheresis is a procedure in which the blood of a patient is passed through an extracorporeal medical device which separates components of blood to treat a disease. Therapeutic apheresis is a general term which includes all apheresis based procedures such as plasma exchange, plasmapheresis, red blood cell exchange, leukocytapheresis, photopheresis, and other procedures. Therapeutic apheresis does not include stem cell collection or harvesting for use in bone marrow/stem cell transplantation.

During plasma exchange (also called plasmapheresis) the plasma is removed and replaced with a replacement solution such as colloid solution (e.g., albumin and/or plasma) or combination of crystalloid/colloid solution. During plasmapheresis, the plasma is removed (i.e., less than 15% of total plasma volume) without the use of a replacement solution. During red blood cell exchange or erythrocytapheresis, the blood of the patient is passed through a medical device which separates red blood cells from other components of blood, the red blood cells are removed, and replaced with either donor red blood cells alone and/or colloid solution. Leukocytapheresis is a procedure in which the
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). The device collects the selected cells and returns the remainder of the patient’s or the donor’s blood with or without addition of replacement fluid such as colloid and/or crystalloid solution (Szczepiorkowski et al. 2010).

Photopheresis (also known as extracorporeal photopheresis or extracorporeal photochemotherapy) is a therapeutic apheresis procedure in which buffy coat (the upper, lighter portion of the blood clot occurring when coagulation is delayed or when blood has been centrifuged) is separated from patient’s blood, is treated extracorporeally with a photoactive compound (e.g., psoralens) and exposed to ultraviolet A light. After this process, the product is reinfused to the patient.

Selective adsorption is a process where the patient's plasma is passed over a specific adsorption column that removes constituents implicated in the individual’s disease. The treated plasma is reinfused into the patient without the addition of allogeneic plasma or albumin. This may also be referred to as component-specific apheresis, or selective immunoadsorption. One type of affinity column (Prosorba) uses staph protein A to remove circulating immune complexes and immunoglobulins. However, the Prosorba column is no longer being marketed. Another type of column (Liposorber LA-15) selectively targets and removes LDL cholesterol from the plasma.

This policy does not address the injection of platelets or plasma into other body parts such as bones, joints, tendons etc.

Therapeutic apheresis is usually done in an outpatient facility and usually requires several hours to complete. In some clinical situations, plasma exchange may be performed daily for at least 1 week.

CLINICAL EVIDENCE

The American Society for Apheresis (ASFA) (Schwartz, 2013 et al.) has reviewed therapeutic apheresis outcomes and published practice guidelines. The guidelines included analysis based on the quality of the evidence as well as the strength of recommendation derived from the evidence. Disorders were placed into the four ASFA categories:

- 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. IRB approval is desirable if apheresis treatment is undertaken in these circumstances.

The ASFA recognized that categories alone are difficult to translate into clinical practice. Thus, the ASFA adopted a grade of recommendation system to assign recommendation grades for therapeutic apheresis to enhance the clinical value of ASFA categories. The grading recommendations used by the ASFA are adopted from Guyatt et al. 2006, Szczepiorkowski et al. 2010 and Schwartz et al. 2013:

- Grade 1A: Strong recommendation, high-quality evidence
- Grade 1B: Strong recommendation, moderate quality evidence
- Grade 1C: Strong recommendation, low-quality or very low-quality evidence
- Grade 2A: Weak recommendation, high quality evidence
- Grade 2B: Weak recommendation, moderate quality evidence
- Grade 2C: Weak recommendation, low-quality or very low-quality evidence

Therapeutic apheresis is considered to be proven for the following indications based on the ASFA’s assignment of category I or II with grade 1A or 1B for these indications:
- ABO incompatible hematopoietic stem cell and bone marrow transplant (plasma exchange)
- ABO incompatible kidney transplantation (plasma exchange)
- Acute inflammatory demyelinating polyneuropathy (Guillain-Barré syndrome) (plasma exchange)
- ANCA-associated rapidly progressive glomerulonephritis (Wegener’s Granulomatosis) (plasma exchange)
- Anti-glomerular basement membrane disease (Goodpasture’s syndrome) (plasma exchange)
- Babesiosis (RBC exchange)
- Cardiac allograft rejection or prophylaxis of cardiac transplant rejection (photopheresis)
- Chronic inflammatory demyelinating polyradiculoneuropathy (plasma exchange)
- Cryoglobulinemia (plasma exchange)
- Cutaneous T-cell lymphoma; mycosis fungoides; Sézary syndrome, erythrodermic (photopheresis)
- Heterozygous or homozygous familial hypercholesterolemia (plasma exchange or selective adsorption)
- Graft-versus-host disease, skin, chronic (photopheresis)
- Hyperleukocytosis, leukostasis (leukocytapheresis)
- Hyperviscosity in monoclonal gammopathies, treatment of symptoms (plasma exchange)
- Multiple sclerosis, acute central nervous system inflammatory demyelinating disease unresponsive to steroids (plasma exchange)
- Myasthenia gravis (plasma exchange)
- Paraproteinemic polyneuropathies, IgG/IgA (plasma exchange)
- Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS) and Sydenham’s chorea (plasma exchange)
- Renal transplantation, antibody mediated rejection (plasma exchange)
- Renal transplantation, desensitization, living donor, positive crossmatch due to donor specific HLA antibody (plasma exchange)
- Thrombotic thrombocytopenic purpura (plasma exchange)

Therapeutic apheresis is considered to be medically necessary for the following indications based on a review of the evidence:
- ABO incompatible heart transplantation in patients less than 40 months of age (plasma exchange) (Rao, 2004; West, 2001)
- Focal segmental glomerulosclerosis recurrent (plasma exchange) (Yokoyama, 1998; Garcia 2006)
- Lung allograft rejection (photopheresis) (Morrell, 2009; Benden, 2008; Salerno, 1999)
• Paraproteinemic polyneuropathies, IgM (plasma exchange)
• Rheumatoid arthritis, refractory (immunoadsorption) (Furst, 2002)

Therapeutic apheresis is considered to be **not medically necessary** for the following indications based on the ASFA’s assignment of grade 1C or 2A for these indications:
• Hyperviscosity in monoclonal gammopathies, prophylaxis for rituximab
• Wilson’s disease, fulminant (plasma exchange)

Therapeutic apheresis is considered to be **not medically necessary** for the following indications based on the ASFA’s assignment of grade 2B or 2C with any category, a category IV assignment, or a category III with grade 1A or 1B assignment for these indications:
• ABO incompatible solid organ transplantation, liver perioperative
• Acute disseminated encephalomyelitis
• Acute liver failure
• Age related macular degeneration
• Amyloidosis, systemic
• Amyotrophic lateral sclerosis
• Aplastic anemia; pure red cell aplasia
• Autoimmune hemolytic anemia: warm autoimmune hemolytic anemia; cold agglutinin disease
• Burn shock resuscitation
• Catastrophic antiphospholipid syndrome
• Chronic focal encephalitis (Rasmussen’s Encephalitis)
• Coagulation factor inhibitors
• Cutaneous T-cell lymphoma; mycosis fungoides; Sézary syndrome, non-erythrodermic
• Dermatomyositis or polymyositis
• Dilated cardiomyopathy
• Graft-versus-host disease, skin, acute
• Graft-versus-host disease, non-skin, acute/chronic
• Hereditary hemochromatosis
• Hemolytic uremic syndrome
• Hyperleukocytosis, prophylaxis
• Hypertriglycerideremic pancreatitis
• Immune thrombocytopenic purpura
• Immune complex rapidly progressive glomerulonephritis
• Inclusion body myositis
• Inflammatory bowel disease
• Lambert-Eaton myasthenic syndrome
• Malaria
• Multiple sclerosis, chronic progressive
• Myeloma cast nephropathy
• Nephrogenic systemic fibrosis
• Overdose, venoms, and poisoning
• Paraneoplastic neurologic syndromes
• Paraproteinemic polyneuropathies, multiple myeloma
- Paraproteinemic polyneuropathies, IgG/IgA or IgM treated with immunoadsorption
- Pemphigus vulgaris
- Phytanic acid storage disease (Refsum’s disease)
- Polycythemia vera and erythrocytosis
- POEMS (polyneuropathy, organomegaly, endocrinopathy, M protein, and skin changes)
- Post transfusion purpura
- Psoriasis
- Red cell alloimmunization in pregnancy
- Renal transplantation, High Panel Reactive Antibody (PRA); cadaveric donor
- Rheumatoid arthritis, refractory, treated with plasma exchange
- Schizophrenia
- Scleroderma (progressive systemic sclerosis)
- Sepsis with multiorgan failure
- Stiff-person syndrome
- Systemic lupus erythematosus
- Thrombocytosis
- Thrombotic microangiopathy: drug-associated
- Thrombotic microangiopathy: hematopoietic stem cell transplant-associated
- Thyroid storm

The ASFA considers that apheresis as an accepted first-line therapy for the following conditions:
- Acute inflammatory demyelinating polyneuropathy (Guillain-Barré syndrome) (plasma exchange)
- ANCA-associated rapidly progressive glomerulonephritis (Wegener’s Granulomatosis) (plasma exchange)
- Anti-glomerular basement membrane disease (Goodpasture’s syndrome) (plasma exchange)
- Babesiosis (RBC exchange)
- Cardiac allograft rejection prophylaxis (photopheresis)
- Chronic inflammatory demyelinating polyneuropathy (plasma exchange)
- Cryoglobulinemia (plasma exchange)
- Cutaneous T-cell lymphoma; mycosis fungoides; Sézary syndrome, erythrodermic (photopheresis)
- Homozygous familial hypercholesterolemia (plasma exchange or selective adsorption)
- Hyperleukocytosis, leukostasis (leukocytapheresis)
- Hyperviscosity in monoclonal gammopathies, treatment of symptoms (plasma exchange)
- IgG/IgA, or IgM type of paraproteinemic polyneuropathy (plasma exchange)
- Myasthenia gravis (plasma exchange)
- Renal transplantation, antibody mediated rejection (plasma exchange)
- Sickle cell disease: red blood cell exchange for acute stroke
- Thrombotic thrombocytopenic purpura (plasma exchange)

The ASFA considers that apheresis as an accepted second-line therapy for the following conditions:
- ABO incompatible heart transplantation in children less than 40 months of age (plasma exchange)
• ABO incompatible hematopoietic stem cell and bone marrow transplant (plasma exchange)
• ABO incompatible kidney transplantation (plasma exchange)
• Cardiac allograft rejection (photopheresis)
• Heterozygous familial hypercholesterolemia (plasma exchange or selective adsorption)
• Graft-versus-host disease, skin, chronic (photopheresis)
• Lung allograft rejection (photopheresis)
• Multiple sclerosis (relapsing form with steroid resistant exacerbations) (plasma exchange)
• Neuromyelitis optica (Devic’s syndrome) (plasma exchange)
• Rheumatoid arthritis, refractory (immunoadsorption)
• Sickle cell disease: red blood cell exchange for acute chest syndrome

**National Comprehensive Cancer Network (NCCN)**
Guidelines issued by NCCN for acute myeloid leukemia indicate that leukapheresis is not recommended in the routine management of patients with a high WBC in acute promyelocytic leukemia (APL). However, in life threatening cases with leukostasis that is not responsive to other modalities, leukapheresis can be considered with caution (NCCN, 2016).

**National Institute for Health and Clinical Excellence (NICE)**
NICE published a report for Extracorporeal Photopheresis for Crohn's Disease in February 2009. The report assessed the efficacy and safety of ECP for Crohn's disease. According to NICE, the evidence base consisted primarily of 1 case-series study with 28 patients. The results of the study indicated that ECP leads to improved quality of life, reduction in bowel motion frequency and abdominal cramps, reduced steroid use, and reduction in inflammatory markers. Two of the 28 patients included in the study discontinued treatment due to adverse events. NICE recommended that ECP should not be used outside the context of research for Crohn’s disease.

The National Institute of Neurological Disorders and Stroke information page for Devic’s syndrome states that relapses and attacks are often treated with corticosteroid drugs and plasma (National Institutes of Health (NIH), 2016).

**Sickle Cell Disease**
Red blood cell exchange or erythrocytapheresis is being increasingly used for transfusion therapy in sickle cell disease (SCD). Many of the studies performed to evaluate this therapy are retrospective studies with small patient population.

Hulbert et al. (2006) conducted a retrospective cohort study of 137 children with sickle cell anemia (SCA) and strokes to test the hypothesis that exchange transfusion at the time of stroke presentation more effectively prevents second strokes than simple transfusion. Children receiving simple transfusion had a 5-fold greater relative risk of second stroke than those receiving exchange transfusions. Interpretation of these findings is limited due to the retrospective design of the study.

Velasquez et al. (2009) retrospectively reviewed red cell exchange (RCE) for the management of acute chest syndrome (ACS) in 44 patients with sickle cell disease. Clinical Respiratory Score (CRS) was assigned retrospectively to assess respiratory distress (0 = no distress, > 6 = severe). Median admission CRS of 2, progressed to 4 before RCE and declined to 2 within 24 hr afterwards. Median day of RCE
was day 2 (IQR 1-3) and the main indication was worsening respiratory distress. No patient developed venous thrombosis, alloantibodies or other complications from RCE. According to the authors, RCE appears to be a safe and effective treatment for patients with sickle cell disease and ACS. The small study population limits the validity of the conclusion of this study.

Turner et al. (2009) evaluated the efficacy of exchange transfusion (XC) versus simple transfusion (ST) for treatment of sickle cell anemia acute chest syndrome (ACS). Twenty patients who received XC for ACS were compared with 20 patients who received ST. Cohorts were similar with regard to age; sex; prior ACS episodes; echocardiogram results; and antibiotic, bronchodilator, and hydroxyurea use. Maximum temperature recorded was higher in the XC group, but lactate dehydrogenase (LDH), WBCs, and indirect bilirubin were comparable. Admission Hb levels were higher for XC (XC 8.6 g/dL vs. ST 7.4 g/dL, p = 0.02) and XC had higher peak Hb levels during hospitalization. No differences were demonstrable in postprocedure length of stay (XC 5.6 days vs. ST 5.9 days) or total length of stay (XC 8.4 days vs. ST 8.0 days). A total of 10.3 +/- 3.0 units were transfused for XC compared to 2.4 +/- 1.2 units for ST. Based on postprocedure length of stay or total length of stay, the authors could not detect a difference in the efficacy of XC compared to ST in populations despite red blood cell product usage fourfold higher in the XC group. According to the authors, there is a need for an adequately powered, randomized trial to examine the true risk-benefit ratio of XC in ACS.

Liem et al. (2004) evaluated 8 sickle cell patients with 9 episodes of acute chest syndrome (ACS) who received a manual, double-volume exchange transfusion. Six patients with SCD seen during a routine clinic visit were used as controls. The mean number of hospitalization days was 6, with an average of 2 days in the intensive care unit. All patients recovered without complication. Sickle cell patients with ACS had a higher WBC and ANC at baseline but lower sVCAM-1 levels compared to controls. TNF-alpha, IL-1alpha, IL-1beta, and IL-8 levels were not significantly different from controls. WBC, ANC, platelet, and sVCAM-1 measurements were significantly decreased immediately post-exchange in patients with ACS; however, this effect was not persistent as levels trended towards pre-exchange values by 24 hr post-exchange. Due to wide inter-individual variability, a consistent pattern was not seen for TNF-alpha, IL-1alpha, IL-1beta, or IL-8. The authors concluded that in sickle cell patients with ACS, a manual, double-volume exchange transfusion lowers WBC, ANC, platelets, and sVCAM-1 levels, but the effect is short-lived.

Wahl et al. (2012) compared alloimmunization rates between patients receiving simple or exchange chronic transfusions with erythrocytapheresis (ECP). Data were retrospectively collected for 45 sickle cell disease (SCD) patients (n=23 simple, n=22 ECP) on a chronic transfusion program to determine the rate of antibody formation (antibodies formed per 100 units transfused). The 45 patients received 10,949 units and formed six new alloantibodies during the study period; therefore, the overall alloimmunization rate was 0.055 alloantibodies per 100 U. The ECP group received significantly more blood. The rate of antibody formation (auto plus allo) was 0.040 antibodies per 100 U in the ECP group and 0.171 antibodies per 100 U in the simple transfusion group. The alloantibodies formed per 100 units was 0.013 in the ECP group and 0.143 in the simple transfusion group. The authors concluded that chronic ECP should be considered in patients requiring optimal management of HbS levels and iron burden. The authors stated that concerns about increased alloimmunization with ECP may be unjustified.
The National Heart, Lung, and Blood Institute (NHLBI) published a clinical guideline for the management of sickle cell disease (SCD) that includes the following recommendations (National Heart, Lung, and Blood Institute, 2002):

- Automated erythrocytapheresis is safe and is being used fairly often because it prevents iron overload, despite concerns about increased red cell utilization and venous access.
- Children with ischemic stroke should undergo acute evaluation with computed tomography (CT) scanning followed by intravenous hydration and exchange transfusion. In most cases this should be followed by chronic transfusion. For prevention of strokes, children (2 to 16 years of age) with SCD should be screened for stroke risk using transcranial Doppler (TCD). Chronic transfusion should be strongly considered in those with confirmed abnormal TCD. Chronic transfusion is also an option for stroke prevention in adults.
- Simple transfusions or exchange transfusions decrease the proportion of sickle red cells and are indicated for the treatment of acute chest syndrome (ACS). The main indication for transfusion therapy is poor respiratory function. The goal is to prevent progression of ACS to acute respiratory failure.
- Leading causes of death in SCD, such as acute chest syndrome, stroke, sepsis, and acute multiorgan failure often are accompanied by a falling hemoglobin level. Transfusions can improve tissue oxygenation and perfusion and are indicated in seriously ill patients to potentially limit areas of vaso-occlusion. Controlled clinical trials to evaluate transfusions in most life-threatening situations have not been performed, so medical practice is based mainly on clinical observations. However, limited studies indicate that aggressive transfusion regimens may improve recovery of organ function and survival in instances of acute multiorgan failure.

**Professional Societies**

**American Society for Apheresis (ASFA)**

According to the ASFA, red blood cell (RBC) exchange is an option for patients with acute ischemic stroke, acute chest syndrome (ACS), or multi organ failure. RBC exchange is also recommended as a prophylaxis for primary or secondary stroke. According to ASFA, advantages of RBC exchange over simple transfusion (S-Tx) through randomized controlled clinical trials have not been documented. The ASFA states that long-term RBC exchange has the distinctive advantage of preventing or markedly reducing transfusional iron accumulation, but is associated with significantly higher (1.5 to 3 times higher) blood requirements than S-Tx. Increased blood donor exposure can potentially increase rates of viral transmission and RBC alloimmunization. Strategies to reduce the risk of alloimmunization include the use of racially- and partial phenotypically-matched RBC (Schwartz, 2013).

**Desensitization for Renal Transplants**

Plasmapheresis has been used prior to renal transplants in highly sensitized patients to remove human leukocyte antigen (HLA) antibodies. Desensitization protocols use high dose intravenous immunoglobulin (IVIG) or low dose IVIG with plasmapheresis to convert a positive crossmatch to a negative crossmatch and allow for transplantation. Plasmapheresis may continue after the transplant or be reserved for post-transplant treatment of acute antibody mediated rejection (AMR). Clinical trials have demonstrated that living or deceased donor kidney recipients treated with plasmapheresis and IVIG have beneficial outcomes.

Yuan et al. (2010) evaluated the efficacy of plasmapheresis plus low-dose intravenous immunoglobulin in highly sensitized patients waiting for a deceased-donor renal transplant. Thirty-five
highly sensitized patients (HLA class I panel reactive antibody greater than 50%) received plasmapheresis, plus low-dose intravenous immunoglobulin treatment. In 25 patients (group 1), a positive T- and/or B-cell cytotoxicity crossmatch became negative by plasmapheresis plus low-dose intravenous immunoglobulin treatment. Two patients did not receive renal transplants due to persistent positive crossmatch. Eight patients already had a negative crossmatch before desensitization. During the same time, 32 highly sensitized patients (group 2), without desensitization, had a negative crossmatch and received deceased-donor renal transplants. Group 1 showed a numerically higher rate of acute rejection (32.0% vs 21.9%) and antibody-mediated rejection (20.0% vs 9.4%), but the difference was not statistically significant. Comparable mean serum creatinine levels at 24 months were observed. No difference in Kaplan-Meier graft survival was found between group 1 and group 2 after follow-up of 52 +/- 26 months. The authors concluded that desensitization with plasmapheresis plus low-dose intravenous immunoglobulin enables successful deceased-donor renal transplant in highly sensitized patients with a positive crossmatch. Antibody-mediated rejection occurred predominantly in recipients with donor-specific antibodies of high titers.

Meng et al. (2009) determined the percentage of panel reactivity and specificity of anti-HLA immunoglobulin (Ig) G antibodies in 73 presensitized renal allograft recipients who underwent cadaveric renal transplantation compared with 81 unsensitized recipients who received cadaveric renal transplantation (control group). Sensitized patients had higher rates of graft rejection and graft loss. A total of 20 out of the 73 patients received pre-transplantation plasmapheresis (PP) and/or immunoadsorption (IA) and of these, 10 achieved negative panel reactive antibodies (PRAs). Graft rejection rate was 18% in unsensitized group, 41% in non-PP and/or IA sensitized group, and 20% in PP and/or IA sensitized group. Graft loss rate was 5% in unsensitized group, 21% in non-PP and/or IA sensitized group, and 15% in PP and/or IA sensitized group (20% positive PRA at transplant and 10% negative PRA at transplant). The authors concluded that pre-transplant PRA preparations might improve the access of presensitized patients to renal donors.

Montgomery et al. (2011b) used mathematical simulations verified by actual data from several national kidney-paired donation (KPD) programs to evaluate which donor/recipient phenotypes are likely to benefit from each transplant modality. They found that pairs that are easy to match are likely to receive compatible kidneys in a KPD. Those who are hard to match may be better served by desensitization with high-dose IVIg or plasmapheresis and low-dose IVIg. The phenotype which is both hard to match and hard to desensitize due to board and strong HLA reactivity are most likely to be transplanted by a hybrid modality utilizing desensitization after identifying a more immunologically favorable donor in a KPD. The authors state that recent outcomes from desensitization in which starting donor-specific antibody strength is low have been very good. For broadly sensitized patients with a high-strength cross-match, searching for a better donor in a KPD pool can facilitate a safer and more successful desensitization treatment course.

Beimler et al. (2009) reported on the effectiveness of a single pre-transplant plasma exchange session in rendering a positive complement-dependent cytotoxicity-XM negative and, in combination with anti-B-lymphocyte antigen (CD20) therapy, allowing successful renal transplantation in two sensitized deceased-donor kidney allograft recipients. In a third patient with high donor-specific reactivity, the therapy was unsuccessful. Plasma exchange treatments were continued during the post-transplant period until stable allograft function was achieved. Both patients showed good graft outcome at 27 and 21 months after transplantation with serum creatinine values of 1.60 and 1.25 mg/dL, respectively.
Montgomery et al. (2011a) used a protocol that included plasmapheresis and the administration of low-dose intravenous immune globulin to desensitize 211 human leukocyte antigen (HLA)-sensitized patients who underwent live-donor renal transplantation (treatment group). The rates of death were compared between the group undergoing desensitization treatment and two carefully matched control groups of patients on a waiting list for kidney transplantation who continued to undergo dialysis (dialysis-only group) or who underwent either dialysis or HLA-compatible transplantation (dialysis-or-transplantation group). In the treatment group, Kaplan-Meier estimates of patient survival were 90.6% at 1 year, 85.7% at 3 years, 80.6% at 5 years, and 80.6% at 8 years, as compared with rates of 91.1%, 67.2%, 51.5%, and 30.5%, respectively, for patients in the dialysis-only group and rates of 93.1%, 77.0%, 65.6%, and 49.1%, respectively, for patients in the dialysis-or-transplantation group. The authors concluded that live-donor transplantation after desensitization provided a significant survival benefit for patients with HLA sensitization, as compared with waiting for a compatible organ. By 8 years, this survival advantage more than doubled. According to the authors, plasmapheresis does not result in a durable reduction in HLA antibody unless the patient undergoes transplantation within several days after the last treatment. This factor accounts for the paucity of reports of protocols that use plasmapheresis to desensitize patients who are on the waiting list for a transplant from a deceased donor.

**Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS) and Sydenham’s chorea**

Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS) and Sydenham’s Chorea (SC) are pediatric post-infectious autoimmune neuropsychiatric disorders. Both share an array of neuropsychiatric symptoms and both may have a shared etiopathogenesis. Because of the possible role of antineuronal antibodies in the pathogenesis, antibody removal by therapeutic plasma exchange (TPE) may be effective. However, the mechanism for the benefit of TPE is not clear, as there is a lack of relationship between therapeutic response and the rate of antibody removal (Szczepiorkowski, 2010).

Eighteen patients were entered into a randomized controlled trial designed to determine if intravenous immunoglobulin or plasma exchange would be superior to prednisone in decreasing the severity of chorea. Mean chorea severity for the entire group was significantly lower at the 1-month follow-up evaluation (overall 48% improvement). Although the between-group differences were not statistically significant, clinical improvements appeared to be more rapid and robust in the intravenous immunoglobulin and plasma exchange groups than in the prednisone group (mean chorea severity scores decreased by 72% in the intravenous immunoglobulin group, 50% in the plasma exchange group, and 29% in the prednisone group). According to the authors, larger studies are required to confirm these clinical observations and to determine if these treatments are cost-effective for this disorder (Garvey, 2005).

Studies failed to provide convincing evidence that plasma exchange is effective for treating pediatric autoimmune neuropsychiatric disorders associated with streptococcus infection and Sydenham chorea. Additional studies are needed to determine if plasma exchange is a useful for treating these conditions.

**High Density Lipoprotein (HDL) Delipidation**

Low levels of HDL are associated with increased risk of cardiovascular disease. Researchers posit that plasma selective delipidation converts alpha-HDL to pre-beta-like HDL, the most effective form of
HDL for lipid removal from arterial plaques. However, there is a paucity of clinical evidence regarding HDL delipidation for various cardiac disease indications, including acute coronary syndrome (ACS). A search of the peer-reviewed medical literature identified one placebo-controlled RCT (n=28) (Waksman et al., 2010). This study sought to determine whether serial autologous infusions of selective HDL delipidated plasma are feasible and well tolerated in patients with ACS. Patients undergoing cardiac catheterization were randomized to either 7 weekly HDL selective delipidated or control plasma apheresis/reinfusions. Patients underwent intravascular ultrasound (IVUS) evaluation of the target vessel. All reinfusion sessions were tolerated well by all patients. The levels of prebeta-like HDL and alphaHDL in the delipidated plasma converted from 5.6% to 79.1% and 92.8% to 20.9%, respectively. The IVUS data demonstrated a numeric and non-significant trend toward regression in the total atheroma volume in the delipidated group compared with an increase of total atheroma volume in the control group. Study results demonstrated that serial autologous infusions of selective HDL delipidated plasma is clinically feasible and well tolerated. Study limitations included small study population and lack of appropriate blinding methods. The study may not have been sufficiently powered to detect differences between treatment and controls. Additional well-designed studies are necessary to determine the ability of HDL delipidation and plasma reinfusion to improve patient-relevant clinical outcomes, such as the reduction of cardiovascular events and increased overall survival.

**Inflammatory Bowel Disease**

Leukocytapheresis is an extracorporeal therapy for ulcerative colitis. A large-scale, prospective, observational study was performed by Yokoyama et al. (2014) which enrolled patients from 116 medical facilities in Japan with active ulcerative colitis treated with leukocytapheresis. Out of 847 patients, 623 were available for efficacy analysis. 80.3% of the patients had moderate to severe disease activity, and 67.6% were steroid refractory. As concomitant medications, 5-aminosalicylic acids, corticosteroids, and thiopurines were administered to 94.8%, 63.8%, and 32.8% of the patients, respectively. In addition, infliximab and tacrolimus were concomitantly used in 5.8% and 12.3%, respectively. Intensive leukocytapheresis (≥4 leukocytapheresis sessions within the first 2 weeks) was used in >70% of the patients. Adverse events were seen in 10.3% (87/847), which were severe in only 5 patients (0.6%). Any concomitant medications did not increase the incidence of adverse events. The authors concluded that leukocytapheresis, including intensive procedure, is a safe and effective therapeutic option for active ulcerative colitis. However, this study did not translate research data into clinical guidelines that can be used to improve physician decision-making and patient care.

**Professional Societies**

**American Academy of Neurology (AAN)/MS Council for Clinical Practice**

In 2002, the Therapeutics and Technology Assessment Subcommittee of the AAN and the MS Council for Clinical Practice Guidelines issued a report on disease-modifying therapies in MS. The subcommittee concluded that "on the basis of consistent class I, II, and III studies, plasma exchange is of little or no value in the treatment of progressive MS." The AAN guideline also states that on the basis of a single small Class I study, it is considered possible that plasma exchange may be helpful in the treatment of severe acute episodes of demyelination in previously non-disabled individuals (Type C recommendation - possibly effective, ineffective, or harmful for the given condition in the specified population) (Goodin, 2002).
A 2011 guideline from the AAN assessed the role of plasmapheresis in the treatment of neurologic disorders. According to the guideline, plasmapheresis is established as effective for severe acute inflammatory demyelinating polyneuropathy (AIDP)/Guillain-Barré syndrome (GBS) and in the short-term management of chronic inflammatory demyelinating polyneuropathy. Plasmapheresis is probably effective and should be considered for mild AIDP/GBS, as second-line treatment of steroid-resistant exacerbations in relapsing forms of multiple sclerosis (MS), and for neuropathy associated with immunoglobulin A or immunoglobulin G gammopathy. Plasmapheresis is probably effective for acute fulminant demyelinating CNS disease but it is not possible to determine if plasmapheresis is more or less effective in patients with different demyelinating disease. There is insufficient evidence to support or refute the use of plasmapheresis for myasthenia gravis, pediatric autoimmune neuropsychiatric disorders associated with streptococcus infection, and Sydenham chorea (Cortese et al. 2011).

**European Federation of Neurological Societies (EFNS)**

In a 2005 guideline for the treatment of multiple sclerosis relapses, the EFNS states that patients with inflammatory demyelination, including patients with MS, who have not responded to treatment with methylprednisolone may benefit from plasma exchange treatment, but only about one-third of treated patients are likely to respond. This treatment regimen should probably be restricted to a subgroup of patients with severe relapses (level B recommendation). A randomized, controlled study specifically addressing the effect of plasma exchange in patients with severe relapses of MS not responding to methylprednisolone treatment would be desirable (Sellenbjerg et al. 2005).

**Additional Search Terms**

photoimmune therapy, photoimmunotherapy

**U.S. FOOD AND DRUG ADMINISTRATION (FDA)**

Devices for therapeutic apheresis are regulated by the FDA as Class II or III devices depending on whether they rely on centrifugation or filtration of blood. Devices that separate blood cells from plasma by filtration are Class III devices that are subject to the most extensive regulations enforced by the FDA.

Additional information, regarding product code LKN (separator, automated, blood cell and plasma, therapeutic), can be obtained from the U.S. Food and Drug Administration (FDA) [website]: Center for Devices and Radiological Health at the following Web sites: [http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm). Accessed July 2016.

The FDA has granted premarket approval (PMA) to one extracorporeal photopheresis (ECP) device, the UVAR Photopheresis System (Therakos, Inc., Exton, PA, USA). This system is currently only approved for the palliative treatment of skin manifestations resulting from cutaneous T-cell lymphoma (CTCL), which are unresponsive to other treatments. Therakos now markets a second generation of the system under the name UVAR XTS. The UVAR XTS system utilizes the photoactive drug, UVADEX (8-methoxsalen), also manufactured by Therakos and approved by FDA for the same indication.

UVADEX was granted Orphan Drug Status "for use in conjunction with the UVAR photopheresis [system] to treat diffuse systemic sclerosis" in June 1993 and "for use in conjunction with the UVAR photopheresis system to treat graft versus host disease [GVHD]" in October 1998. In addition, UVADEX was granted Orphan Drug Status "for the prevention of acute rejection of cardiac allografts" in May 1994. See the following Web sites for more information:

Additional Medical Products

APPLICABLE CODES

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Coverage Determination Guidelines may apply.

<table>
<thead>
<tr>
<th>CPT® Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>36511</td>
<td>Therapeutic apheresis; for white blood cells</td>
</tr>
<tr>
<td>36512</td>
<td>Therapeutic apheresis; for red blood cells</td>
</tr>
<tr>
<td>36513</td>
<td>Therapeutic apheresis; for platelets</td>
</tr>
<tr>
<td>36514</td>
<td>Therapeutic apheresis; for plasma pheresis</td>
</tr>
<tr>
<td>36515</td>
<td>Therapeutic apheresis; with extracorporeal immunoadsorption and plasma reinfusion</td>
</tr>
<tr>
<td>36516</td>
<td>Therapeutic apheresis; with extracorporeal selective adsorption or selective filtration and plasma reinfusion</td>
</tr>
<tr>
<td>36522</td>
<td>Photopheresis, extracorporeal</td>
</tr>
<tr>
<td>0342T</td>
<td>Therapeutic apheresis with selective HDL delipidation and plasma reinfusion</td>
</tr>
</tbody>
</table>

*CPT® is a registered trademark of the American Medical Association.

<table>
<thead>
<tr>
<th>HCPCS Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>S2120</td>
<td>Low density lipoprotein (ldl) apheresis using heparin-induced extracorporeal ldl precipitation</td>
</tr>
</tbody>
</table>
REFERENCES


**PROTOCOL HISTORY/REVISION INFORMATION**

<table>
<thead>
<tr>
<th>Date</th>
<th>Action/Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>07/28/2016</td>
<td></td>
</tr>
<tr>
<td>07/23/2015</td>
<td></td>
</tr>
<tr>
<td>08/28/2014</td>
<td></td>
</tr>
<tr>
<td>01/23/2014</td>
<td></td>
</tr>
<tr>
<td>02/28/2013</td>
<td></td>
</tr>
<tr>
<td>07/26/2012</td>
<td></td>
</tr>
<tr>
<td>10/27/2011</td>
<td></td>
</tr>
<tr>
<td>01/28/2011</td>
<td></td>
</tr>
<tr>
<td>06/24/2010</td>
<td></td>
</tr>
<tr>
<td>06/26/2009</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Corporate Medical Affairs Committee</td>
</tr>
</tbody>
</table>

The foregoing Health Plan of Nevada/Sierra Health & Life Operations protocol has been adopted from an existing UnitedHealthcare coverage determination guideline that was researched, developed and approved by the UnitedHealthcare Coverage Determination Committee.