LOUISIANA BLUE

Plasma Exchange (PE)

Policy # 00249
Original Effective Date: 03/19/2010
Current Effective Date: 01/13/2025

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Note: Hematopoietic Cell Transplantation for Autoimmune Diseases is addressed separately in medical policy 00050.

Note: Immunoglobulin Therapy is addressed separately in medical policy 00170.

When Services Are Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider plasma exchange (PE) to be **eligible for coverage**** for the conditions listed below:

AUTOIMMUNE DISEASES

- Severe symptomatic cryoglobulinemia (MC) with manifestations such as cryoglobulinemic nephropathy, skin ulcers, sensory motor neuropathy, widespread vasculitis;
- Catastrophic antiphospholipid syndrome

HEMATOLOGIC CONDITIONS

- ABO-incompatible (ABOi) hematopoietic stem cell transplantation, major ABOi hematopoietic cells;
- Hyperviscosity syndromes associated with multiple myeloma or Waldenström's macroglobulinemia;
- Idiopathic thrombocytopenic purpura (ITP) in emergency situations;
- Thrombotic thrombocytopenic purpura (TTP);
- Atypical hemolytic uremic syndrome (HUS);
- Post-transfusion purpura;
- HELLP syndrome of pregnancy (a severe form of preeclampsia, characterized by hemolysis [H], elevated liver enzymes [EL], and low platelet [LP] counts);
- Myeloma with acute renal failure

NEUROLOGIC CONDITIONS

- Acute inflammatory demyelinating polyneuropathy (Guillain-Barré syndrome); primary treatment;
- Chronic acquired demyelinating polyneuropathy
  - IgG/IgA/IgM related
- Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP);
- Multiple sclerosis (MS), with acute fulminant central nervous system (CNS) demyelination;
- Myasthenia gravis in crisis or as part of preoperative preparation;
- Neuromyelitis optica spectrum disorders (NMOSD), acute attack/relapse (excluding maintenance therapy) when there has been an inadequate response to or failure of medical therapy;
- N-methyl-D-aspartate receptor antibody encephalitis;
- Paraproteinemia polyneuropathy; immunoglobulin A, G, M;
- Progressive multifocal leukoencephalopathy associated with natalizumab
- Voltage-gated potassium channel disorders (neuromyotonia, limbic encephalitis, Morvan syndrome)

RENAL DISEASES

- Anti-glomerular basement membrane (GBM) disease (Goodpasture syndrome);
- Anti-neutrophil cytoplasmic antibody (ANCA)–associated vasculitis (eg, Microscopic polyangiitis, granulomatous polyangiitis, renal limited vasculitis, rapidly progressive glomerulonephritis) with associated renal failure or diffuse alveolar hemorrhage;
- Dense deposit disease with factor H deficiency and/or elevated C3 nephritic factor.

TRANSPLANTATION

- Solid organ transplantation:
  - Kidney (ABO compatible and ABO incompatible)
    - Antibody mediated rejection
    - Desensitization/prophylaxis, living donor
  - Heart (desensitization/rejection prophylaxis);
  - Liver, ABO incompatible living donor, desensitization;
- Hematopoietic stem cell transplantation, ABO incompatible
  - Major ABO incompatible, second line therapy
- Renal transplantation: antibody-mediated rejection; human leukocyte antigen (HLA) desensitization;
- Focal segmental glomerulosclerosis after renal transplant.

MISCELLANEOUS/OTHER

- Wilson disease, fulminant;
- Familial hypercholesterolemia, homozygous or severe, refractory heterozygous, second line therapy.

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers plasma exchange (PE) to be **investigational*** in all other conditions, including, but not limited to, the following:

- Acute disseminated encephalomyelitis;
- Acute inflammatory demyelinating polyneuropathy (Guillain-Barré syndrome) in children <10 years old with mild or moderate forms (e.g. ambulatory children with mild, non-progressive disease);
- Acute liver failure; except indications noted as eligible for coverage (e.g. Wilson disease);
- Amyotrophic lateral sclerosis;
- Anti-neutrophil cytoplasmic antibody (ANCA)–associated vasculitis (eg, Microscopic polyangiitis granulomatous polyangiitis, renal limited vasculitis, rapidly progressive glomerulonephritis) without associated renal failure or diffuse alveolar hemorrhage;
- Aplastic anemia;
- Asthma;
- Autoimmune hemolytic anemia; warm autoimmune hemolytic anemia; cold agglutinin disease;
- Chronic fatigue syndrome;
- Coagulation factor inhibitors;
- Cryoglobulinemia, except for severe symptomatic cryoglobulinemia (MC) with manifestations as noted above;
- Dermatomyositis and polymyositis;
- Focal segmental glomerulosclerosis (other than transplant);
- Heart transplant rejection treatment;
- Hemolytic uremic syndrome (HUS), typical (diarrheal-related);
- Idiopathic thrombocytopenic purpura, refractory or nonrefractory;
- Inclusion body myositis;
- Lambert-Eaton myasthenic syndrome (LEMS);
- Multiple sclerosis (MS) with chronic progressive or relapsing remitting course;
- Neuromyelitis optica spectrum disorders (NMOSD), except when refractory to glucocorticoids;
- Mushroom poisoning;
- Myasthenia gravis with anti-MuSK antibodies;
- Overdose and poisoning (other than mushroom poisoning);
- Paraneoplastic syndromes;
- Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS);
- Pemphigus vulgaris;
- Phytanic acid storage disease (Refsum disease);

- POEMS (polyneuropathy, organomegaly, endocrinopathy, M protein, skin changes);
- Psoriasis;
- Red blood cell alloimmunization in pregnancy;
- Rheumatoid arthritis;
- Sepsis;
- Scleroderma (systemic sclerosis);
- Stiff person syndrome;
- Sydenham chorea (SC);
- Systemic lupus erythematosus (including systemic lupus erythematosus nephritis);
- Thyrotoxicosis; and
- Hyperviscosity syndromes with renal failure (other than associated with multiple myeloma or Waldenström macroglobulinemia).

Policy Guidelines

Patients receiving plasma exchange (PE) as a treatment of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) should meet the diagnostic criteria for CIDP, which were established by the American Academy of Neurology in 1991 and have not been updated since. The use of PE in patients with acute, life-threatening complications of chronic autoimmune diseases, such as rheumatoid arthritis and systemic lupus erythematosus, may need to be considered on an individual basis. An example of such a situation would be the development of a severe vasculitis, for which it is hypothesized that the use of PE can acutely lower the level of serum autoantibodies until an alternative long-term treatment strategy can be implemented. However, in these situations, the treatment goals and treatment duration with PE need to be clearly established before its initiation; without such treatment goals, the use of an acute short- term course of PE may insidiously evolve to a chronic use of PE with uncertain benefit.

Background/Overview

TERMINOLOGY

The terms therapeutic apheresis, plasmapheresis, and plasma exchange (PE) are often used interchangeably, but when properly used denote different procedures. The American Society for Apheresis definitions for these procedures are as follows:

Apheresis is a procedure in which blood of the patient or donor is passed through a medical device that separates out one or more components of blood and returns remainder with or without extracorporeal treatment or replacement of the separated component.

Plasmapheresis is a procedure in which blood of a patient or the donor is passed through a medical device that separates plasma from the other components of blood and the plasma is removed (ie, <15% of total plasma volume) without the use of replacement solution.

Plasma exchange is a therapeutic procedure in which blood of the patient is passed through a medical device that separates plasma from other components of blood, the plasma is removed, and it is replaced with a replacement solution such as colloid solution (eg, albumin and/ or plasma) or a combination of crystalloid/colloid solution.

This medical policy addresses only PE as a therapeutic apheresis procedure.

PLASMA EXCHANGE

The rationale for PE is based on the fact that circulating substances, such as toxins or autoantibodies, can accumulate in the plasma. Also, it is hypothesized that removal of these factors can be therapeutic in certain situations. PE is a symptomatic therapy, because it does not remove the source of the pathogenic factors. Therefore the success of PE depends on whether the pathogenic substances are accessible through the circulation and whether their rate of production and transfer to the plasma component can be adequately addressed by PE. For example, PE can rapidly reduce levels of serum autoantibodies; however, through a feedback mechanism, this rapid reduction may lead to a rebound overproduction of the same antibodies. This rebound production of antibodies is thought to render the replicating pathogenic clone of lymphocytes more vulnerable to cytotoxic drugs; therefore, PE is sometimes used in conjunction with cyclophosphamide.

Applications

Applications of PE can be broadly subdivided into 2 general categories: (1) acute self-limited diseases, in which PE is used to acutely lower the circulating pathogenic substance; and (2) chronic diseases, in which there is ongoing production of pathogenic autoantibodies. Because PE does not address underlying pathology, and, because of the phenomenon of rebound antibody production, its use in chronic diseases has been more controversial than in acute self-limited diseases.

Also, plasmapheresis has been used in the setting of solid organ transplantation. It has been used as a technique to desensitize high-risk patients before transplant and also as a treatment of antibody-mediated rejection reaction occurring after transplant. Before transplant, plasmapheresis has been most commonly used to desensitize patients receiving an ABO mismatched kidney, often in combination with a splenectomy. As a treatment of antibody-mediated rejection, plasmapheresis is often used in combination with intravenous immunoglobulin or anti-CD20 therapy (ie, rituximab).

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

The U.S. Food and Drug Administration has a compliance program to ensure that source plasma, source leukocytes, and therapeutic exchange plasma for further manufacture into products for human use are safe, pure, potent, and appropriately labeled. The compliance program covers products intended for use both in injectable drug products (eg, immune globulin, albumin) and non-injectable products (eg, in vitro devices such as blood bank reagents).

Product code for therapeutic exchange plasma: 57DI-65.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Plasma exchange (PE) is a procedure in which the plasma is isolated, then discarded and replaced with a fluid such as albumin. PE is a nonspecific therapy, because the entire plasma is discarded. PE has been used in a wide variety of acute and chronic conditions, as well as in the setting of solid organ transplantation.

Data from published studies clinical input and/or guidelines from the American Society for Apheresis support the use of PE for selected autoimmune, hematologic, neurologic, renal, and transplantation conditions.

For individuals who were diagnosed with pediatric autoimmune neuropsychiatric disorder associated with group A streptococci (PANDAS) who receive plasma exchange, the evidence includes one randomized controlled trial (RCT). The potential benefits of treatment with plasma exchange (five single-volume exchanges over 2 weeks, 10 children) or IVIG (9 children) compared with placebo (10 children) were evaluated in a randomized controlled trial in 29 children who met PANDAS criteria and were severely affected (i.e., obsessive-compulsive disorder or tic disorders, including Tourette syndrome) Symptom severity was rated at baseline and at 1 and 12 months after treatment. Substantial improvement in symptoms from baseline was noted in the treatment groups at one month; improvements were maintained at one year, although psychotropic medications were decreased or discontinued in only 7 of 13 patients who required them at baseline. Adverse effects occurred in approximately two-thirds of patients in the treatment groups and included nausea, vomiting, headache, and dizziness. Limitations of the trial included the lack of a control for plasma exchange, open treatment of controls after the one-month follow-up (making it impossible to exclude the possibility of spontaneous improvement in the control group at the 12-month follow-up), lack of correlation between therapeutic response and rate of antibody removal, and poorly understood mechanism of therapeutic benefit. Authors concluded that further studies are needed to determine the active mechanism of these interventions, and to determine which children with OCD and tic disorders will benefit from immunomodulatory therapies. A subsequent randomized trial of IVIG in 35 children who met criteria for PANDAS and moderate to severe OCD failed to demonstrate a benefit of IVIG over placebo. A subsequent open trial of plasma exchange in children with OCD who did not meet PANDAS criteria failed to demonstrate a benefit. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Supplemental Information

CLINICAL INPUT FROM PHYSICIAN SPECIALTY SOCIETIES AND ACADEMIC MEDICAL CENTERS

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, input was received through 2 physician specialty societies and 3 academic medical centers while this policy was under review in 2012. There was consensus or near-consensus that plasma exchange (PE) for dense deposit disease with factor H deficiency and/or elevated C3 nephritis factor, catastrophic antiphospholipid syndrome, focal segmental glomerulosclerosis after renal transplant, and myeloma with acute renal failure may be considered medically necessary. Input was mixed on the medical necessity of hyperviscosity syndromes with renal failure (other than associated with multiple myeloma or Waldenström macroglobulinemia). Also, there was no consensus about an optimal creatinine threshold for instituting PE in patients with renal failure associated with antineutrophil cytoplasmic antibody-associated vasculitis or other diagnoses.

PRACTICE GUIDELINES AND POSITION STATEMENTS

National Comprehensive Cancer Network

It is noted in the current National Comprehensive Cancer Network guidelines on multiple myeloma (v.1.2025) that plasmapheresis should also be used as adjunctive therapy for symptomatic hyperviscosity. Additionally, institutions differ in their use of plasmapheresis for adjunctive treatment of renal dysfunction. While the benefit of mechanical removal of serum free light chains (FLCs) has not been established, there is limited evidence for the use of plasmapheresis or high-cutoff dialysis to reduce pathogenic light chains.

American Academy of Neurology

In 2011, the American Academy of Neurology issued evidence-based guidelines on plasmapheresis for the treatment of neurologic disorders. The primary conclusions, based on the evidence review, are provided in Table 1.

Table 1. Guidelines on Use Plasmapheresis to Treat Neurologic Disorders

Recommendation	Conclusion
Acute inflammatory demyelinating polyneuropathy/Guillain-Barré syndrome	Established effective
Chronic inflammatory demyelinating polyneuropathy, short-term treatment	Established effective
Relapses in multiple sclerosis	Probably effective
Fulminant demyelinating central nervous system disease	Possibly effective
Chronic or secondary progressive multiple sclerosis	Established ineffective
Myasthenia gravis	Insufficient evidence
Sydenham chorea	Insufficient evidence
Acute obsessive-compulsive disorder and tics in PANDAS	Insufficient evidence

PANDAS: pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections.

In 2003, the American Academy of Neurology published a practice parameter on Guillain-Barré syndrome (GBS). The following are the key findings: (1) treatment with plasma exchange (PE) or intravenous immunoglobulin hastens recovery from GBS; (2) combining the 2 treatments is not beneficial; and (3) steroid treatment given alone is not beneficial. The American Academy of Neurology's recommendations are:

- PE is recommended for adults with GBS who are non-ambulant and who seek treatment within 4 weeks of the onset of neuropathic symptoms;
- PE should be considered for ambulant patients examined within 2 weeks of the onset of neuropathic symptoms);
- PE is a treatment option for children with severe GBS.

American Society for Apheresis
A comprehensive review of conditions and indications based on detailed literature reviews is published approximately every two to three years by the American Society for Apheresis (ASFA).

Conditions and indications are assigned to one of four categories based on evidence of clinical efficacy as determined by evaluation of peer-reviewed literature.

The value of the ASFA guidelines lies in the comprehensive nature of the literature reviews and the concise format for each of the conditions and indications. Information is presented in Fact Sheets that include categories, evidence-based grades (1A-C and 2A-C), a succinct literature synopsis, a recommended treatment schedule, replacement fluids, exchange volumes, procedure frequency, and other practical information.

The ASFA categorizations are summarized in the 2023 guidelines (9th edition), see Table 2.

Table 2. American Society for Apheresis 2023 indications for therapeutic apheresis and cytapheresis procedures

Indication	Modality	Category	Evidence
Acute disseminated encephalomyelitis (ADEM): Steroid refractory	TPE	II	2C
Acute fatty liver of pregnancy	TPE	III	2B
Acute inflammatory demyelinating polyradiculoneuropathy (Guillain-Barré syndrome): Primary treatment	TPE	I	1A
	IA	I	1B

Acute liver failure	TPE	III	2B
	TPE-HV	I	1A
Age-related macular degeneration, dry, high-risk	DFPP	III	2B
Alzheimer disease, mild or moderate	TPE	III	2A
Amyloidosis, systemic, dialysis-related	Beta2 microglobulin adsorption	II	2B
Anti-glomerular basement membrane disease (Goodpasture syndrome)			
▪ Diffuse alveolar hemorrhage (DAH)	TPE	I	1C
▪ Dialysis-independence	TPE	I	1B
▪ Dialysis-dependence, no DAH	TPE	III	2B
Atopic dermatitis (atopic eczema), recalcitrant	ECP/IA/TPE/DFPP	III	2B
Autoimmune dysautonomia	TPE	III	2C
Autoimmune hemolytic anemia (AIHA), severe			
▪ Severe cold agglutinin disease	TPE	II	2C
▪ Severe warm AIHA	TPE	III	2C
Babesiosis, severe	RBC exchange	III	2C
Burn shock resuscitation	TPE	III	2B
Cardiac neonatal lupus	TPE	III	2C
Catastrophic antiphospholipid syndrome (CAPS)	TPE	I	2C
Chronic acquired demyelinating polyneuropathies			
▪ IgG/IgA/IgM related	TPE	I	1B

▪ Anti-myelin-associated glycoprotein	TPE	III	1C
▪ Chronic ataxic neuropathy, ophthalmoplegia, IgM paraprotein, cold agglutinins, and disialosyl antibodies (CANOMAD)/Chronic ataxic neuropathy with disialosyl antibodies syndrome (CANDA)	TPE	III	2C
Chronic focal encephalitis (Rasmussen encephalitis)	TPE/IA	III	2C
Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)	TPE/IA	I	1B
Coagulation factor deficiency and inhibitors	IA	III	2B
	TPE	III	2C
Complex regional pain syndrome, chronic	TPE	III	2C
Cryoglobulinemia, severe/symptomatic	TPE/DFPP	II	2A
	IA	II	2B
Cutaneous T cell lymphoma (CTCL)			
▪ Erythrodermic mycosis fungoides/Sézary syndrome	ECP	I	1B
▪ Non-erythrodermic mycoses fungoides	ECP	III	2B
Dilated cardiomyopathy, idiopathic, NYHA II-IV	IA	II	1B
	TPE	III	2C
Erythrocytosis			
▪ Polycythemia vera	Erythrocytapheresis	I	1B

▪ Secondary erythrocytosis	Erythrocytapheresis	III	1C
Erythropoietic protoporphyria, liver disease	TPE/RBC exchange	II	2C
Familial hypercholesterolemia			
▪ Homozygous individuals	LA	I	1A
▪ Heterozygous individuals	LA	II	1A
▪ All patients	TPE	II	1B
Focal segmental glomerulosclerosis (FSGS)			
▪ Recurrent in kidney transplant	TPE/IA	I	1B
▪ All types	LA	II	2C
▪ Steroid resistant in native kidney	TPE	III	2C
Graft-versus-host disease (GVHD)			
▪ Acute	ECP	II	1B
▪ Chronic	ECP	II	1B
Hemophagocytic lymphocytosis (HLH)	TPE	III	2C
Heparin-induced thrombocytopenia and thrombosis			
▪ Pre-procedure	TPE/IA	III	2C
▪ Refractory or with thrombosis	TPE	III	2C
Hereditary hemochromatosis	Erythrocytapheresis	I	1B
Hyperleukocytosis	Leukocytapheresis	III	2B
Hypertriglyceridemic pancreatitis			

▪ Severe	TPE/LA	III	1C
▪ Prevention of relapse	TPE/LA	III	2C
Hyperviscosity in hypergammaglobulinemia			
▪ Symptomatic	TPE	I	1B
▪ Prophylaxis for rituximab	TPE	I	1C
Idiopathic inflammatory myopathies			
▪ Anti-synthetase-syndrome	TPE	III	2B
▪ Clinically amyopathic dermatomyositis	TPE	III	2B
▪ Immune-mediated necrotizing myopathies	TPE	III	2B
IgA nephropathy (Berger's disease)			
▪ Chronic progressive	TPE	III	2C
▪ Crescentic	TPE	III	2B
Immune checkpoint inhibitors, immune-related adverse events	TPE	III	2C
Immune thrombocytopenia (ITP), refractory	TPE/IA	III	2C
Inflammatory bowel disease			
▪ Ulcerative colitis	Adsorptive cytapheresis	II	1B
▪ Crohn disease	Adsorptive cytapheresis/ECP	III	1B/2C
Lambert-Eaton myasthenic syndrome	TPE	II	2C

Lipoprotein(a) hyperlipoproteinemia, progressive atherosclerotic cardiovascular disease	LA	II	1B
Malaria, severe*	RBC exchange	III	2B
Multiple sclerosis			
▪ Acute attack/relapse	TPE/IA	II	1A/1B
▪ Chronic	TPE/IA	III	2B
Myasthenia gravis			
▪ Acute, short-term treatment	TPE/DFPP/IA	I	1B
▪ Long-term treatment	TPE/DFPP/IA	II	2B
Myeloma cast nephropathy	TPE	II	2B
Nephrogenic systemic fibrosis	ECP/TPE	III	2C
Neuromyelitis optical spectrum disorders (NMOSD)			
▪ Acute attack/relapse	TPE/IA	II	1B/1C
▪ Maintenance	TPE	III	2C
N-methyl-D-aspartate receptor antibody encephalitis	TPE/IA	I	1C
Overdose, envenomation, and/or poisoning			
▪ Mushroom poisoning	TPE	II	2C
▪ Envenomation	TPE	III	2C
▪ Other	TPE/RBC exchange	III	2C
Paraneoplastic autoimmune retinopathies	TPE	III	2C
Paraneoplastic neurologic syndromes	TPE/IA	III	2C
Pediatric autoimmune neuropsychiatric disorders			

▪ Pediatric autoimmune neuropsychiatric disorder associated with group A streptococci (PANDAS)/Pediatric acute-onset neuropsychiatric syndrome (PANS), exacerbation	TPE	II	1B
▪ Sydenham chorea, severe	TPE	III	2B
Pemphigus vulgaris, severe	TPE	III	2B
	IA/ECP/DFPP	III	2C
Peripheral vascular diseases	LA	II	1B
Phytanic acid storage disease (Refsum disease)	TPE/LA	II	2C
Post-transfusion purpura (PTP)	TPE	III	2C
Progressive multifocal leukoencephalopathy (PML) associated with natalizumab	TPE	III	1C
Pruritus due to hepatobiliary disease, treatment resistant	TPE	III	1C
Psoriasis, disseminated pustular	ECP	III	2B
	Adsorptive cytapheresis	III	2C
	TPE	IV	2C
Red blood cell alloimmunization, pregnancy complications			
▪ Hemolytic disease of the fetus and newborn	TPE	III	2C
▪ RhD alloimmunization prophylaxis after transfusion	RBC exchange	IV	2C
Sepsis with multiorgan failure	TPE	III	2A

Sickle cell disease			
▪ Acute stroke	RBC exchange	I	1C
▪ Acute chest syndrome, severe	RBC exchange	II	1C
▪ Other acute complications	RBC exchange/TPE	III	2C
▪ Stroke prophylaxis	RBC exchange	I	1A
▪ Pregnancy	RBC exchange	II	2B
▪ Recurrent vaso-occlusive pain	RBC exchange	II	2B
▪ Preoperative management	RBC exchange	III	2A
Steroid-responsive encephalopathy associated with autoimmune thyroiditis (Hashimoto encephalopathy)	TPE	II	2C
Stiff-person syndrome	TPE	III	2C
Sudden sensorineural hearing loss	LA/DFPP/TPE	III	2A
Systemic lupus erythematosus (SLE): Severe complications	TPE	II	2C
Systemic sclerosis	ECP	III	2A
	TPE	III	2C
Thrombocytosis			
▪ Symptomatic	Thrombocytapheresis	II	2C
▪ Prophylactic or secondary	Thrombocytapheresis	III	2C
Thrombotic microangiopathy			
▪ Coagulation-mediated, due to pathogenic variants in *THBD*, *DGKE*, or *PLG*	TPE	III	2C

▪ Complement-mediated, due to factor H autoantibodies	TPE	I	2C
▪ Complement-mediated, due to pathogenic variants in complement regulatory genes	TPE	III	2C
▪ Drug-associated: Ticlopidine¶	TPE	I	2B
▪ Drug-associated: Clopidogrel	TPE	III	2B
▪ Drug-associated: Gemcitabine	TPE	IV	2C
▪ Drug-associated: Quinine	TPE	IV	2C
▪ Infection-associated, from Shiga toxin-producing *Escherichia coli* (STEC-HUS), severe	TPE/IA	III	2C
▪ Infection-associated, from *Streptococcus pneumoniae* (pHUS)	TPE	III	2C
▪ Pregnancy associated, severe	TPE	III	2C
▪ Pregnancy associated, extremely preterm preeclampsia, severe	TPE/LA	III	2C
▪ Thrombotic thrombocytopenic purpura (TTP; immune, with ADAMTS13 deficiency)	TPE	I	1A
▪ Transplantation-associated	TPE	III	2C
Thyroid storm	TPE	II	2C

Toxic epidermal necrolysis (TEN), refractory	TPE	III	2B
Transplantation, heart			
▪ Cellular/recurrent rejection	ECP	II	1B
▪ Rejection prophylaxis	ECP/TPE	II	2A/IC
▪ Desensitization	TPE	II	1C
▪ Antibody-mediated rejection	TPE	III	2C
Transplantation, hematopoietic stem cell, ABO incompatible			
▪ Major ABO incompatible, hematopoietic cells obtained from bone marrow	TPE	II	1B
▪ Major ABO incompatible, hematopoietic cells obtained by apheresis	TPE	II	2B
▪ Minor ABO incompatible, hematopoietic cells obtained by apheresis	RBC exchange	III	2C
▪ Pure RBC aplasia	TPE	III	2C
Transplantation, hematopoietic stem cell, HLA desensitization	TPE	III	2C
Transplantation, intestine			
▪ Antibody mediated rejection	TPE	III	2C
▪ Desensitization	TPE	III	2C
Transplantation, kidney, ABO compatible			
▪ Antibody mediated rejection	TPE/IA	I	1B

▪ Desensitization/prophylaxis, living donor	TPE/IA	I	1B
Transplantation, kidney, ABO incompatible			
▪ Desensitization, living donor	TPE/IA	I	1B
▪ Antibody-mediated rejection	TPE/IA	II	1B
Transplantation, liver			
▪ Desensitization, ABO incompatible, living donor	TPE	I	1C
▪ Desensitization, ABO incompatible, deceased donor	TPE	III	2C
▪ Antibody-mediated rejection	ECP/TPE	III	2B/2C
▪ Immune suppression withdrawal	ECP	III	2B
▪ Desensitization, ABO incompatible	ECP	III	2C
Transplantation, lung			
▪ Chronic allograft dysfunction	ECP	II	1C
▪ Bronchiolitis obliterans syndrome	ECP	II	1C
▪ Antibody-mediated rejection/desensitization	TPE	III	2C
▪ Desensitization	TPE	III	2C
Vaccine-induced thrombotic thrombocytopenia, refractory	TPE	III	2C

Vasculitis, ANCA-associated			
▪ Microscopic polyangiitis	TPE	III	1B
▪ Granulomatosis with polyangiitis	TPE	III	1B
▪ Eosinophilic granulomatosis with polyangiitis (EGPA; Churg-Strauss)	TPE	III	2C
Vasculitis, IgA (Henoch-Schönlein purpura)			
▪ Crescentic rapidly progressive glomerulonephritis (RPGN)	TPE	III	2C
▪ Severe extrarenal manifestations	TPE	III	2C
Vasculitis, other			
▪ Hepatitis B polyarteritis nodosa	TPE	II	2C
▪ Kawasaki disease	TPE	III	2C
▪ Multisystem inflammatory syndrome in children (MIS-C)	TPE	III	2C
Voltage-gated potassium channel (VGKC) antibody-related disease	TPE/IA	II	1B
Wilson disease, fulminant	TPE	I	1C

TPE: therapeutic plasma exchange; IA: immunoadsorption; TPE-HV: high-volume therapeutic plasma exchange; ECP: extracorporeal photopheresis; DFPP: double filtration plasmapheresis; NYHA: New York Heart Association; RBC: red blood cell; LA: lipoprotein apheresis; Ig: immunoglobulin; HLA: human leukocyte antigen.

Category

- Category I: Disorders for which apheresis is accepted as first-line therapy, either as a standalone treatment or in conjunction with other therapies.

- Category II: Disorders for which apheresis is accepted as second-line therapy, either as a standalone treatment or in conjunction with other therapies.
- Category III: Disorders for which the optimal role of apheresis therapy is not established.
- Category IV: Disorders for which published evidence demonstrates or suggests apheresis to be ineffective or harmful.

Evidence

- Evidence grade 1: Strong recommendation.
- Evidence grade 2: Weak recommendation.
- Evidence quality A: High-quality evidence.
- Evidence quality B: Moderate-quality evidence.
- Evidence quality C: Low-quality or very low-quality evidence.

U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATIONS

Not applicable.

MEDICARE NATIONAL COVERAGE

The national coverage determination for apheresis (therapeutic pheresis), last revised in 1992, states:

> "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).

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 pruritus 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."

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Policy History

Original Effective Date: 03/19/2010
Current Effective Date: 01/13/2025

03/05/2010	Medical Policy Committee approval
03/19/2010	Medical Policy Implementation Committee approval. New policy.
03/03/2011	Medical Policy Committee review
03/16/2011	Medical Policy Implementation Committee approval. Added “post-transfusion purpura” as eligible for coverage into the hematologic section. Deleted “ANCA-associated rapidly progressive glomerulonephritis (Wegener’s granulomatosis)” from investigational statement since it belongs in the eligible for coverage section only. Deleted unnecessary language (“manifestations other than nephritis; nephritis”) from systematic lupus erythematosus bullet in the investigational statement.
03/01/2012	Medical Policy Committee review

03/21/2012	Medical Policy Implementation Committee approval. Added a new investigational indication. SLE 03/07/2013 Medical Policy Committee review
03/20/2013	Medical Policy Implementation Committee approval. Two indications moved from investigational to eligible for coverage. New indication added to renal and transplantation sections. New investigational indication added.
03/06/2014	Medical Policy Committee review
03/19/2014	Medical Policy Implementation Committee approval. No change to coverage.
08/03/2015	Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.
09/03/2015	Medical Policy Committee review
09/23/2015	Medical Policy Implementation Committee approval. Added neuromyelitis optica to list of INV conditions.
09/08/2016	Medical Policy Committee review
09/21/2016	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/01/2017	Coding update: Removing ICD-9 Diagnosis Codes and CPT coding update
04/09/2017	Medical Policy Committee review
04/19/2017	Medical Policy Implementation Committee approval. Added neuromyelitis optica to coverage statement and removed it from investigational indications.
11/02/2017	Medical Policy Committee review
11/15/2017	Medical Policy Implementation Committee approval. N-methyl-D-aspartate receptor antibody encephalitis and progressive multifocal leukoencephalopathy associated with natalizumab added to the Neurological Conditions that are eligible for coverage.
11/08/2018	Medical Policy Committee review
11/21/2018	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
11/07/2019	Medical Policy Committee review
11/13/2019	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
12/10/2019	Coding update
09/14/2020	Coding update
11/05/2020	Medical Policy Committee review
11/11/2020	Medical Policy Implementation Committee approval. Revisions made in the coverage section for Autoimmune Diseases, Hematological Conditions, Neurological Conditions, Renal Diseases and Transplantation. Added “Miscellaneous/Other” category to the coverage section to include Wilson disease. Investigational indications revised according to the coverage changes.
11/04/2021	Medical Policy Committee review
11/10/2021	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
12/01/2022	Medical Policy Committee review

12/14/2022	Medical Policy Implementation Committee approval. Voltage-gated potassium channel (VGKC) antibody-related vasculitis/ disease and Familial hypercholesterolemia added as indications for eligible for coverage criteria.
12/07/2023	Medical Policy Committee review
12/13/2023	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
12/05/2024	Medical Policy Committee review
12/11/2024	Medical Policy Implementation Committee approval. Under Neurological Conditions, added criteria for Chronic acquired demyelinating polyneuropathy and revised the criteria for Neuromyelitis optica spectrum disorders. Under Transplantation, Changed the first criteria bullet to Solid organ transplantation, revised the Kidney sub criteria to include ABP compatible, revised the Heart sub criteria by removing (infants) and adding (desenitization/rejection prophylaxis), and added criteria for Hematopoietic stem cell transplantation, ABO incompatible. Under Miscellaneous/Other, Revised the criteria for Familial hypercholesteremia. Revised the investigational condition for Focal segmented glomerulosclerosis. Updated the Practice Guidelines and Position Statements in the Supplemental Information section with the 2023 American Society for Apheresis Guidelines.

Coding

The five character codes included in the Louisiana Blue Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2023 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	36456, 36514
HCPCS	No codes
ICD-10 Diagnosis	All related Diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: 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.