

Plasma Exchange (PE)

Policy # 00249

Original Effective Date: 03/19/2010

Current Effective Date: 01/01/2026

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: Immune Globulin 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

- 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;

Plasma Exchange (PE)

Policy # 00249

Original Effective Date: 03/19/2010

Current Effective Date: 01/01/2026

- 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; acute, short-term treatment;
- 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, major ABO incompatible
- 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:

Plasma Exchange (PE)

Policy # 00249

Original Effective Date: 03/19/2010

Current Effective Date: 01/01/2026

- Acute disseminated encephalomyelitis;
- 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 after kidney transplant);
- Heart transplant rejection treatment (other than desensitization/rejection prophylaxis);
- Hemolytic uremic syndrome (HUS), typical (diarrheal-related);
- Idiopathic thrombocytopenic purpura, refractory or nonrefractory (other than in emergency situations);
- Inclusion body myositis;
- Lambert-Eaton myasthenic syndrome (LEMS);
- Multiple sclerosis (MS) with chronic progressive or relapsing remitting course;
- Neuromyelitis optica spectrum disorders (NMOSD), except for acute attack/relapse when refractory to glucocorticoids;
- Mushroom poisoning;
- Myasthenia gravis;
- Overdose and 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);

Plasma Exchange (PE)

Policy # 00249

Original Effective Date: 03/19/2010

Current Effective Date: 01/01/2026

- 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

Plasma Exchange (PE)

Policy # 00249

Original Effective Date: 03/19/2010

Current Effective Date: 01/01/2026

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

Plasma Exchange (PE)

Policy # 00249

Original Effective Date: 03/19/2010

Current Effective Date: 01/01/2026

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

Plasma Exchange (PE)

Policy # 00249

Original Effective Date: 03/19/2010

Current Effective Date: 01/01/2026

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.3.2026) 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:

Plasma Exchange (PE)

Policy # 00249

Original Effective Date: 03/19/2010

Current Effective Date: 01/01/2026

- 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

Plasma Exchange (PE)

Policy # 00249

Original Effective Date: 03/19/2010

Current Effective Date: 01/01/2026

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	TPE	III	2C

Plasma Exchange (PE)

Policy # 00249

Original Effective Date: 03/19/2010

Current Effective Date: 01/01/2026

antibodies syndrome (CANDA)			
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

Plasma Exchange (PE)

Policy # 00249

Original Effective Date: 03/19/2010

Current Effective Date: 01/01/2026

▪ 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

Plasma Exchange (PE)

Policy # 00249

Original Effective Date: 03/19/2010

Current Effective Date: 01/01/2026

▪ 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 cytaphe- resis	II	1B
▪ Crohn disease	Adsorptive cytaphe- resis/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

Plasma Exchange (PE)

Policy # 00249

Original Effective Date: 03/19/2010

Current Effective Date: 01/01/2026

▪ 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
<i>N</i> -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	TPE	II	1B

Plasma Exchange (PE)

Policy # 00249

Original Effective Date: 03/19/2010

Current Effective Date: 01/01/2026

syndrome (PANS), exacerbation			
▪ 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

Plasma Exchange (PE)

Policy # 00249

Original Effective Date: 03/19/2010

Current Effective Date: 01/01/2026

▪ 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 <i>THBD</i> , <i>DGKE</i> , or <i>PLG</i>	TPE	III	2C
▪ Complement-mediated, due to factor H autoantibodies	TPE	I	2C

Plasma Exchange (PE)

Policy # 00249

Original Effective Date: 03/19/2010

Current Effective Date: 01/01/2026

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 <i>Escherichia coli</i> (STEC-HUS), severe	TPE/IA	III	2C
Infection-associated, from <i>Streptococcus pneumoniae</i> (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

Plasma Exchange (PE)

Policy # 00249

Original Effective Date: 03/19/2010

Current Effective Date: 01/01/2026

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

Plasma Exchange (PE)

Policy # 00249

Original Effective Date: 03/19/2010

Current Effective Date: 01/01/2026

▪ 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

Plasma Exchange (PE)

Policy # 00249

Original Effective Date: 03/19/2010

Current Effective Date: 01/01/2026

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.

Plasma Exchange (PE)

Policy # 00249

Original Effective Date: 03/19/2010

Current Effective Date: 01/01/2026

- 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

Plasma Exchange (PE)

Policy # 00249

Original Effective Date: 03/19/2010

Current Effective Date: 01/01/2026

- Treatment of last resort for life threatening systemic lupus erythematosus (SLE) when conventional therapy has failed to prevent clinical deterioration.”

References

1. Therapeutic apheresis (plasma exchange or cytapheresis): Indications and technology. UpToDate. Updated through Mar 2024. https://www.uptodate.com/contents/therapeutic-apheresis-plasma-exchange-or-cytapheresis-indications-and-technology?search=plasma%20pheresis&source=search_result&selectedTitle=1%7E150&usage_type=default&display_rank=1:
2. PANDAS: Pediatric autoimmune neuropsychiatric disorder associated with group A streptococci. UpToDate. Updated through Apr 2024. Accessed 12/05/2024. https://www.uptodate.com/contents/pandas-pediatric-autoimmune-neuropsychiatric-disorder-associated-with-group-a-streptococci?search=PANDAS&source=search_result&selectedTitle=1%7E10&usage_type=default&display_rank=1#H3621472933
3. (2023), Issue Information. J Clin Apher, 38: 75-76. <https://doi.org/10.1002/jca.21987>
4. Connelly-Smith L, Alquist CR, Aquil NA, et al. Guidelines on the use of therapeutic apheresis in clinical practice - Evidence-based approach from the Writing Committee of the American Society for Apheresis: The Ninth Special Issue. J Clin Apher 2023; 38:77. <https://www.uptodate.com/contents/image?csi=c5b9cb23-1256-4c63-94cc-ca6ade4c2c7c&source=contentShare&imageKey=HEME%2F86468>
5. Food and Drug Administration (FDA). Compliance Program Guidance Manual; Chapter 42- Blood and Blood Products. 2011; <https://www.fda.gov/downloads/Enforcement/UCM247371.pdf>.
6. Shumak KH, Rock GA. Therapeutic plasma exchange. N Engl J Med. Mar 22 1984;310(12):762-771. PMID 6199669
7. Kronbichler A, Brezina B, Quintana LF, et al. Efficacy of plasma exchange and immunoadsorption in systemic lupus erythematosus and antiphospholipid syndrome: A systematic review. Autoimmun Rev. Jan 2016;15(1):38- 49. PMID 26318215
8. Lewis EJ, Hunsicker LG, Lan SP, et al. A controlled trial of plasmapheresis therapy in severe lupus nephritis. The Lupus Nephritis Collaborative Study Group. N Engl J Med. May 21 1992;326(21):1373-1379. PMID 1569973
9. Danieli MG, Palmieri C, Salvi A, et al. Synchronised therapy and high-dose cyclophosphamide in proliferative lupus nephritis. J Clin Apher. 2002;17(2):72-77. PMID 12210709
10. Khatri BO, McQuillen MP, Harrington GJ, et al. Chronic progressive multiple sclerosis: double-blind controlled study of plasmapheresis in patients taking immunosuppressive drugs. Neurology. Mar 1985;35(3):312-319. PMID 3974889
11. Weiner HL, Dau PC, Khatri BO, et al. Double-blind study of true vs. sham plasma exchange in patients treated with immunosuppression for acute attacks of multiple sclerosis. Neurology. Sep 1989;39(9):1143-1149. PMID 2549450
12. Canadian Cooperative Multiple Sclerosis Study Group. The Canadian cooperative trial of cyclophosphamide and plasma exchange in progressive multiple sclerosis. The Canadian

Plasma Exchange (PE)

Policy # 00249

Original Effective Date: 03/19/2010

Current Effective Date: 01/01/2026

- Cooperative Multiple Sclerosis Study Group. *Lancet*. Feb 23 1991;337(8739):441-446. PMID 1671468
13. Tim RW, Massey JM, Sanders DB. Lambert-Eaton myasthenic syndrome: electrodiagnostic findings and response to treatment. *Neurology*. Jun 13 2000;54(11):2176-2178. PMID 10851390
 14. Sanders DB, Massey JM, Sanders LL, et al. A randomized trial of 3,4-diaminopyridine in Lambert-Eaton myasthenic syndrome. *Neurology*. Feb 08 2000;54(3):603-607. PMID 10680790
 15. Anderson NE, Rosenblum MK, Posner JB. Paraneoplastic cerebellar degeneration: clinical-immunological correlations. *Ann Neurol*. Oct 1988;24(4):559-567. PMID 3239956
 16. Dwosh IL, Giles AR, Ford PM, et al. Plasmapheresis therapy in rheumatoid arthritis. A controlled, double-blind, crossover trial. *N Engl J Med*. May 12 1983;308(19):1124-1129. PMID 6339939
 17. Miller FW, Leitman SF, Cronin ME, et al. Controlled trial of plasma exchange and leukapheresis in polymyositis and dermatomyositis. *N Engl J Med*. May 21 1992;326(21):1380-1384. PMID 1472183
 18. Guillaume JC, Roujeau JC, Morel P, et al. Controlled study of plasma exchange in pemphigus. *Arch Dermatol*. Nov 1988;124(11):1659-1663. PMID 3178248
 19. Vicari AM, Folli F, Pozza G, et al. Plasmapheresis in the treatment of stiff-man syndrome. *N Engl J Med*. Jun 01 1989;320(22):1499. PMID 2716805
 20. Brashear HR, Phillips LH, 2nd. Autoantibodies to GABAergic neurons and response to plasmapheresis in stiff-man syndrome. *Neurology*. Oct 1991;41(10):1588-1592. PMID 1922799
 21. Harding AE, Thompson PD, Kocen RS, et al. Plasma exchange and immunosuppression in the stiff man syndrome. *Lancet*. Oct 14 1989;2(8668):915. PMID 2571826
 22. Pagano MB, Murinson BB, Tobian AA, et al. Efficacy of therapeutic plasma exchange for treatment of stiff-person syndrome. *Transfusion*. Jul 2014;54(7):1851-1856. PMID 24527774
 23. Pham HP, Williams LA, 3rd. Therapeutic plasma exchange in two patients with stiff-person syndrome. *J Clin Apher*. Oct 2016;31(5):493-494. PMID 26407506
 24. Rockx MA, Clark WF. Plasma exchange for treating cryoglobulinemia: a descriptive analysis. *Transfus Apher Sci*. Jun 2010;42(3):247-251. PMID 20382569
 25. Michael M, Elliott EJ, Craig JC, et al. Interventions for hemolytic uremic syndrome and thrombotic thrombocytopenic purpura: a systematic review of randomized controlled trials. *Am J Kidney Dis*. Feb 2009;53(2):259-272. PMID 18950913
 26. Noris M, Remuzzi G. Atypical hemolytic-uremic syndrome. *N Engl J Med*. Oct 22 2009;361(17):1676-1687. PMID 19846853
 27. Yu X, Gan L, Wang Z, et al. Chemotherapy with or without plasmapheresis in acute renal failure due to multiple myeloma: a meta-analysis. *Int J Clin Pharmacol Ther*. May 2015;53(5):391-397. PMID 25816886
 28. Chevret S, Hughes RA, Annane D. Plasma exchange for Guillain-Barre syndrome. *Cochrane Database Syst Rev*. Feb 27 2017;2:Cd001798. PMID 28241090
 29. El-Bayoumi MA, El-Refaey AM, Abdelkader AM, et al. Comparison of intravenous immunoglobulin and plasma exchange in treatment of mechanically ventilated children with Guillain Barre syndrome: a randomized study. *Crit Care*. Jul 11 2011;15(4):R164. PMID 21745374

Plasma Exchange (PE)

Policy # 00249

Original Effective Date: 03/19/2010

Current Effective Date: 01/01/2026

30. Mehndiratta MM, Hughes RA, Pritchard J. Plasma exchange for chronic inflammatory demyelinating polyradiculoneuropathy. *Cochrane Database Syst Rev*. Aug 25 2015;8(8):CD003906. PMID 26305459
31. Weinshenker BG, O'Brien PC, Petterson TM, et al. A randomized trial of plasma exchange in acute central nervous system inflammatory demyelinating disease. *Ann Neurol*. Dec 1999;46(6):878-886. PMID 10589540
32. Kohler W, Bucka C, Klingel R. A randomized and controlled study comparing immunoadsorption and plasma exchange in myasthenic crisis. *J Clin Apher*. Dec 2011;26(6):347-355. PMID 22095647
33. Alipour-Faz A, Shojaei M, Peyvandi H. A comparison between IVIG and plasma exchange as preparations before thymectomy in myasthenia gravis patients. *Mar 2017*;117(1):245-249. PMID 27530310
34. Dyck PJ, Low PA, Windebank AJ, et al. Plasma exchange in polyneuropathy associated with monoclonal gammopathy of undetermined significance. *N Engl J Med*. Nov 21 1991;325(21):1482-1486. PMID 1658648
35. Abboud H, Petrak A, Mealy M, et al. Treatment of acute relapses in neuromyelitis optica: Steroids alone versus steroids plus plasma exchange. *Mult Scler*. Feb 2016;22(2):185-192. PMID 25921047
36. Bonnan M, Valentino R, Olindo S, et al. Plasma exchange in severe spinal attacks associated with neuromyelitis optica spectrum disorder. *Mult Scler*. Apr 2009;15(4):487-492. PMID 19324982
37. Merle H, Olindo S, Jeannin S, et al. Treatment of optic neuritis by plasma exchange (add-on) in neuromyelitis optica. *Arch Ophthalmol*. Jul 2012;130(7):858-862. PMID 22776923
38. Kleiter I, Gahlen A, Borisow N, et al. Neuromyelitis optica: Evaluation of 871 attacks and 1,153 treatment courses. *Ann Neurol*. Feb 2016;79(2):206-216. PMID 26537743
39. Ipe TS, Pham HP, Williams LA, 3rd. Critical updates in the 7th edition of the American Society for Apheresis guidelines. *J Clin Apher*. Jun 27 2017. PMID 28653762
40. DeSena AD, Noland DK, Matevosyan K, et al. Intravenous methylprednisolone versus therapeutic plasma exchange for treatment of anti-N-methyl-D-aspartate receptor antibody encephalitis: A retrospective review. *J Clin Apher*. Aug 2015;30(4):212-216. PMID 25664728
41. Khatri BO, Man S, Giovannoni G, et al. Effect of plasma exchange in accelerating natalizumab clearance and restoring leukocyte function. *Neurology*. Feb 03 2009;72(5):402-409. PMID 19188571
42. Couser WG. Rapidly progressive glomerulonephritis: classification, pathogenetic mechanisms, and therapy. *Am J Kidney Dis*. Jun 1988;11(6):449-464. PMID 3287904
43. Cole E, Cattran D, Magil A, et al. A prospective randomized trial of plasma exchange as additive therapy in idiopathic crescentic glomerulonephritis. The Canadian Apheresis Study Group. *Am J Kidney Dis*. Sep 1992;20(3):261-269. PMID 1519607
44. Walsh M, Catapano F, Szpirt W, et al. Plasma exchange for renal vasculitis and idiopathic rapidly progressive glomerulonephritis: a meta-analysis. *Am J Kidney Dis*. Apr 2011;57(4):566-574. PMID 21194817

Plasma Exchange (PE)

Policy # 00249

Original Effective Date: 03/19/2010

Current Effective Date: 01/01/2026

45. Jayne DR, Gaskin G, Rasmussen N, et al. Randomized trial of plasma exchange or high-dosage methylprednisolone as adjunctive therapy for severe renal vasculitis. *J Am Soc Nephrol.* Jul 2007;18(7):2180-2188. PMID 17582159
46. Walsh M, Casian A, Flossmann O, et al. Long-term follow-up of patients with severe ANCA-associated vasculitis comparing plasma exchange to intravenous methylprednisolone treatment is unclear. *Kidney Int.* Aug 2013;84(2):397-402. PMID 23615499
47. Montgomery RA, Zachary AA. Transplanting patients with a positive donor-specific crossmatch: a single center's perspective. *Pediatr Transplant.* Dec 2004;8(6):535-542. PMID 15598320
48. Jordan SC, Vo AA, Tyan D, et al. Current approaches to treatment of antibody-mediated rejection. *Pediatr Transplant.* Jun 2005;9(3):408-415. PMID 15910400
49. Lehrich RW, Rocha PN, Reinsmoen N, et al. Intravenous immunoglobulin and plasmapheresis in acute humoral rejection: experience in renal allograft transplantation. *Hum Immunol.* Apr 2005;66(4):350-358. PMID 15866697
50. Ibern M, Gil-Vernet S, Carrera M, et al. Therapy with plasmapheresis and intravenous immunoglobulin for acute humoral rejection in kidney transplantation. *Transplant Proc.* Nov 2005;37(9):3743-3745. PMID 16386524
51. Gubensek J, Buturovic-Ponikvar J, Kandus A, et al. Plasma exchange and intravenous immunoglobulin in the treatment of antibody-mediated rejection after kidney transplantation: a single-center historic cohort study. *Transplant Proc.* May 2013;45(4):1524-1527. PMID 23726611
52. Larsen FS, Schmidt LE, Bernsmeier C, et al. High-volume plasma exchange in patients with acute liver failure: An open randomised controlled trial. *J Hepatol.* Jan 2016;64(1):69-78. PMID 26325537
53. Ellingsen I, Florvaag E, Andreassen AH, et al. Plasmapheresis in the treatment of steroid-dependent bronchial asthma. *Allergy.* Dec 2001;56(12):1202-1205. PMID 11736751
54. Rimmer E, Houston BL, Kumar A, et al. The efficacy and safety of plasma exchange in patients with sepsis and septic shock: a systematic review and meta-analysis. *Crit Care.* Dec 2014;18(6):699. PMID 25527094
55. Perlmutter SJ, Leitman SF, Garvey MA, et al. Therapeutic plasma exchange and intravenous immunoglobulin for obsessive-compulsive disorder and tic disorders in childhood. *Lancet.* Oct 02 1999;354(9185):1153-1158. PMID 10513708
56. Garvey MA, Snider LA, Leitman SF, et al. Treatment of Sydenham's chorea with intravenous immunoglobulin, plasma exchange, or prednisone. *J Child Neurol.* May 2005;20(5):424-429. PMID 15968928
57. Perlmutter SJ, Leitman SF, et al. PANDAS: Pediatric autoimmune neuropsychiatric disorder associated with group A streptococci. Therapeutic plasma exchange and intravenous immunoglobulin for obsessive-compulsive disorder and tic disorders in childhood. *Lancet.* 1999;354(9183):1153. PMID 10513708
58. Williams KA, Swedo SE, et al. PANDAS: Pediatric autoimmune neuropsychiatric disorder associated with group A Randomized, Controlled Trial of Intravenous Immunoglobulin for Pediatric Autoimmune Neuropsychiatric Disorders Associated With Streptococcal Infections. streptococci. *J Am Acad Child Adolesc Psychiatry.* 2016 Oct;55(10):860-867. PMID 27663941

Plasma Exchange (PE)

Policy # 00249

Original Effective Date: 03/19/2010

Current Effective Date: 01/01/2026

59. Nicolson R, Swedo SE, et al. PANDAS: Pediatric autoimmune neuropsychiatric disorder associated with group A streptococci. An open trial of plasma exchange in childhood-onset obsessive-compulsive disorder without poststreptococcal exacerbations. *J Am Acad Child Adolesc Psychiatry*. 2000;39(10):1313. PMID 11026187
60. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Multiple Myeloma. Version 3.2026.
https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf.
61. Lindsley H, Teller D, et al. Hyperviscosity syndrome in multiple myeloma. A reversible, concentration-dependent aggregation of the myeloma protein. *Amer J Med*. May 1973;54(5):682-688. [https://www.amjmed.com/article/0002-9343\(73\)90127-7/abstract](https://www.amjmed.com/article/0002-9343(73)90127-7/abstract).
62. Cortese I, Chaudhry V, So YT, et al. Evidence-based guideline update: Plasmapheresis in neurologic disorders: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology*. Jan 18 2011;76(3):294-300. PMID 21242498
63. Hughes RA, Wijdicks EF, Barohn R, et al. Practice parameter: immunotherapy for Guillain-Barre syndrome: report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. Sep 23 2003;61(6):736-740. PMID 14504313
64. Schwartz J, Padmanabhan A, Aqui N, et al. Guidelines on the use of therapeutic apheresis in clinical practice- evidence-based approach from the Writing Committee of the American Society for Apheresis: The Seventh Special Issue. *J Clin Apher*. Jun 2016;31(3):149-162. PMID 27322218
65. Schwartz J, Winters JL, Padmanabhan A, et al. Guidelines on the use of therapeutic apheresis in clinical practice-evidence-based approach from the Writing Committee of the American Society for Apheresis: the sixth special issue. *J Clin Apher*. Jul 2013;28(3):145-284. PMID 23868759
66. Centers for Medicare & Medicaid Services (CMS). National Coverage Determination (NCD) for Apheresis (therapeutic pheresis) (110.14). 1992; <https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?ncdid=82&ver=1>.

Policy History

Original Effective Date: 03/19/2010

Current Effective Date: 01/01/2026

- | | |
|------------|---|
| 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 |

Plasma Exchange (PE)

Policy # 00249

Original Effective Date: 03/19/2010

Current Effective Date: 01/01/2026

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

Plasma Exchange (PE)

Policy # 00249

Original Effective Date: 03/19/2010

Current Effective Date: 01/01/2026

- 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 (desensitization/rejection prophylaxis), and added criteria for Hematopoietic stem cell transplantation, ABO incompatible. Under Miscellaneous/Other, Revised the criteria for Familial hypercholesterolemia. 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.
- 12/04/2025 Medical Policy Committee review
- 12/10/2025 Medical Policy Implementation Committee approval.
- When Services May Be Eligible for Coverage section revisions:
- HEMATOLIGIC CONDITIONS
 - Removed “ABO-incompatible (ABOi) hematopoietic stem cell transplantation, major ABOi hematopoietic cells”. This is addressed under TRANSPLANTATION
 - NEUROLOGIC CONDITIONS
 - Added “acute, short-term treatment” to myasthenia gravis bullet
 - TRANSPLANTATION
 - For hematopoietic stem cell transplantation, added “major” to ABO incompatible
 - Removed sub-bullet for major ABO incompatible, second line therapy
 - Removed bullet for renal transplantation: antibody-mediated rejection; human leukocyte antigen (HLA) desensitization.
- When Services Are Investigational section revisions:
- Removed “acute inflammatory demyelinating polyneuropathy (Guillain-Barré syndrome) in children <10 years old with mild or moderate forms”
 - Revised bullet for focal segmental glomerulosclerosis
 - For heart transplant rejection treatment, added “(other than desensitization/rejection prophylaxis)”
 - For idiopathic thrombocytopenic purpura, refractory or nonrefractory, added “(other than in emergency situations)”

Plasma Exchange (PE)

Policy # 00249

Original Effective Date: 03/19/2010

Current Effective Date: 01/01/2026

- For neuromyelitis optica spectrum disorders (NMOSD), added the exception “for acute attack/relapse” when refractory to glucocorticoids
- Revised bullet for myasthenia gravis to include “long-term treatment”
- Removed “(other than mushroom poisoning)” from overdose and poisoning

Next Scheduled Review Date: 12/2026

Coding

The five character codes included in the Louisiana Blue Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)†, copyright 2024 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.

The responsibility for the content of Louisiana Blue Medical Policy Coverage Guidelines is with Louisiana Blue and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Louisiana Blue Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Louisiana Blue Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

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

Plasma Exchange (PE)

Policy # 00249

Original Effective Date: 03/19/2010

Current Effective Date: 01/01/2026

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.

‡ Indicated trademarks are the registered trademarks of their respective owners.

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.