MEDICAL POLICY

POLICY TITLE	PLASMA EXCHANGE (PE)
POLICY NUMBER	MP 4.031

CLINICAL BENEFIT	☐ MINIMIZE SAFETY RISK OR CONCERN. ☐ MINIMIZE HARMFUL OR INEFFECTIVE INTERVENTIONS. ☐ ASSURE APPROPRIATE LEVEL OF CARE. ☐ ASSURE APPROPRIATE DURATION OF SERVICE FOR INTERVENTIONS. ☒ ASSURE THAT RECOMMENDED MEDICAL PREREQUISITES HAVE BEEN MET. ☐ ASSURE APPROPRIATE SITE OF TREATMENT OR SERVICE.
Effective Date:	**4/1/2026**

POLICY

Plasma Exchange (PE)

Plasma exchange (PE) may be considered **medically necessary** for any of the conditions listed below:

AUTOIMMUNE DISEASES

- Severe multiple manifestations of mixed cryoglobulinemia (MC) such as cryoglobulinemic nephropathy, skin ulcers, sensory motor neuropathy, and widespread vasculitis in combination with immunosuppressive treatment;
- Catastrophic antiphospholipid syndrome.

HEMATOLOGIC CONDITIONS

- ABO incompatible hematopoietic progenitor cell transplantation;
- Hyperviscosity syndromes associated with multiple myeloma or Waldenström macroglobulinemia;
- Idiopathic thrombocytopenic purpura (ITP) in emergency situations;
- Thrombotic thrombocytopenic purpura (TTP);
- Atypical hemolytic-uremic syndrome;
- 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-Barre syndrome; severity grade 1–2 within 2 weeks of onset; severity grade 3–5 within 4 weeks of onset; and children younger than 10 years old with severe Guillain-Barre syndrome);
- Chronic inflammatory demyelinating polyradiculoneuropathy;
- Multiple sclerosis, with acute fulminant central nervous system demyelination;

- Neuromyelitis optica;
- Myasthenia gravis in crisis or as part of preoperative preparation;
- Paraproteinemia polyneuropathy; immunoglobulin A and G;
- *N*-methyl-d-aspartate receptor antibody encephalitis;
- Progressive multifocal leukoencephalopathy associated with natalizumab.

RENAL DISEASES

- Anti-glomerular basement membrane disease (Goodpasture syndrome);
- Antineutrophil cytoplasmic antibody-associated vasculitis (e.g., Wegener granulomatosis) (also known as granulomatosis with polyangiitis [GPA]) with associated renal failure;
- Dense deposit disease with factor H deficiency and/or elevated C3 nephritic factor.

TRANSPLANTATION

- ABO incompatible solid organ transplantation:
  - o Kidney;
  - o Heart (infants);
- Renal transplantation: antibody mediated rejection; human leukocyte antigen desensitization;
- Focal segmental glomerulosclerosis after renal transplant.

Plasma exchange (PE) is considered **investigational** in all other conditions, including, but not limited, to the following:

- ABO- incompatible solid organ transplant: liver;
- Acute disseminated encephalomyelitis;
- Acute inflammatory demyelinating polyneuropathy (Guillain-Barre syndrome) in children younger than 10 years old with mild or moderate forms;
- Acute liver failure;
- Amyotrophic lateral sclerosis;
- Antineutrophil cytoplasmic antibody-associated rapidly progressive glomerulonephritis (Wegener granulomatosis or granulomatosis with polyangiitis (GPA) without renal failure);
- Aplastic anemia;
- Asthma;
- Autoimmune hemolytic anemia; warm autoimmune hemolytic anemia; cold agglutinin disease;
- Chronic fatigue syndrome;
- Coagulation factor inhibitors;
- Cryoglobulinemia; except for severe mixed cryoglobulinemia, as noted above;

- Dermatomyositis and polymyositis;
- Focal segmental glomerulosclerosis (other than after renal transplant);
- Heart transplant rejection treatment;
- Hemolytic uremic syndrome typical (diarrheal-related);
- Idiopathic thrombocytopenic purpura, refractory or non-refractory;
- Inclusion body myositis;
- Lambert-Eaton myasthenic syndrome;
- Multiple sclerosis with chronic progressive or relapsing remitting course;
- Mushroom poisoning;
- Myasthenia gravis with anti-MuSK antibodies;
- Overdose and poisoning (other than mushroom poisoning);
- Paraneoplastic syndromes;
- Paraproteinemia polyneuropathy IgM;
- Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections;
- 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’s chorea;
- Systemic lupus erythematosus (including systemic lupus erythematosus nephritis);
- Thyrotoxicosis; AND
- Hyperviscosity syndromes with renal failure (other than associated with multiple myeloma or Waldenström macroglobulinemia).

There is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure for the above listed indications.

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. 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.

Cross-Reference:

MP 9.053 Hematopoietic Cell Transplantation for Autoimmune Diseases

PRODUCT VARIATIONS

This policy is only applicable to certain programs and products administered by Capital Blue Cross and subject to benefit variations. Please see additional information below.

FEP PPO - Refer to FEP Medical Policy Manual. The FEP Medical Policy manual can be found at: https://www.fepblue.org/benefit-plans/medical-policies-and-utilization-management-guidelines/medical-policies

DESCRIPTION/BACKGROUND

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 (i.e., <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 (e.g., albumin and/ or plasma) or a combination of crystalloid/colloid solution.

This evidence review 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 (i.e., rituximab).

Regulatory Status

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 (e.g., immune globulin, albumin) and noninjectable products (e.g., in vitro devices such as blood bank reagents).

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

RATIONALE

Summary of Evidence

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.

In 2023, the American Society for Apheresis published an updated Ninth Special Issue of Guidelines on the Use of Therapeutic Apheresis in Clinical Practice. The update included new fact sheets, new indications, and changes in category recommendations for existing fact sheets. However, after review of this literature, there were no significant changes to alter the conclusions reached above.

DEFINITIONS

PATHOGENIC means capable of causing or producing a disease.

PLASMA refers to the watery straw-colored fluid part of the lymph and the blood in which the leukocytes, erythrocytes, and platelets are suspended. Plasma is made up of water, electrolytes, proteins, glucose, fats, bilirubin, and gases and is essential for carrying the cellular elements of the blood through circulation, transporting nutrients, maintaining the acid-base balance of the body, and transporting wastes from the tissue.

PROGENITOR CELL refers to a parent cell that gives rise to a distinct cell lineage by a series of cell divisions.

PLATELET refers to the smallest cells in the blood, essential for coagulation and for hemostasis.

DISCLAIMER

Capital Blue Cross' medical policies are used to determine coverage for specific medical technologies, procedures, equipment, and services. These medical policies do not constitute medical advice and are subject to change as permitted by law or applicable clinical evidence from independent treatment guidelines. Treating providers are solely responsible for medical advice and treatment of members. These polices are not a guarantee of coverage or payment. Payment of claims is subject to a determination regarding the member's benefit program and eligibility on the date of service, and a determination that the services are medically necessary and appropriate. Final processing of a claim is based upon the terms of contract that applies to the members' benefit program, including benefit limitations and exclusions. If a provider or a member has a question concerning this medical policy, please contact Capital Blue Cross' Provider Services or Member Services.

CODING INFORMATION

Note: This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

Covered when medically necessary:

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Procedure Codes								
36514								

ICD-10-CM Diagnosis Codes	Description
C88.00	Waldenstrom macroglobulinemia not having achieved remission
C88.01	Waldenstrom macroglobulinemia, in remission
C90.00	Multiple myeloma not having achieved remission
C90.02	Multiple myeloma in relapse
D59.30	Hemolytic-uremic syndrome, unspecified
D59.31	Infection-associated hemolytic-uremic syndrome
D59.32	Hereditary hemolytic-uremic syndrome
D59.39	Other hemolytic-uremic syndrome
D68.61	Antiphospholipid syndrome
D69.3	Immune thrombocytopenic purpura
D69.51	Posttransfusion purpura
D89.1	Cryoglobulinemia
E88.09	Other disorders of plasma-protein metabolism, not elsewhere classified
G35	Multiple sclerosis
G35.A	Relapsing-remitting multiple sclerosis
G35.B	Primary progressive multiple sclerosis
G35.B0	Primary progressive multiple sclerosis, unspecified
G35.B1	Active primary progressive multiple sclerosis
G35.B2	Non-active primary progressive multiple sclerosis
G35.C	Secondary progressive multiple sclerosis
G35.C0	Secondary progressive multiple sclerosis, unspecified
G35.C1	Active secondary progressive multiple sclerosis
G35.C2	Non-active secondary progressive multiple sclerosis
G35.D	Multiple sclerosis, unspecified
G36.0	Neuromyelitis optica (Devic)
G61.0	Guillan Barre disease
G61.81	Chronic inflammatory demyelinating polyneuritis
G70.00	Myasthenia gravis without (acute) exacerbation
G70.01	Myasthenia gravis with (acute) exacerbation
G72.49	Other inflammatory and immune myopathies, not elsewhere classified

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ICD-10-CM Diagnosis Codes	Description
M31.0	Hypersensitivity angiitis
M31.10	Thrombotic microangiopathy, unspecified
M31.11	Hematopoietic stem cell transplantation-associated thrombotic microangiopathy [HSCT-TMA]
M31.19	Other thrombotic microangiopathy
M31.31	Wegener's granulomatosis with renal involvement
N00.A	Acute nephritic syndrome with C3 glomerulonephritis
N00.B1	Acute nephritic syndrome with idiopathic immune membranoproliferative glomerulonephritis (ic-mpgn)
N00.B2	Acute nephritic syndrome with secondary immune complex membranoproliferative glomerulonephritis (ic-mpgn)
N00.6	Acute nephritic syndrome with dense deposit disease
N01.A	Rapidly progressive nephritic syndrome with C3 glomerulonephritis
N01.6	Rapidly progressive nephritic syndrome with dense deposit disease
N02.A	Recurrent and persistent hematuria with C3 glomerulonephritis
N02.B1	Recurrent and persistent immunoglobulin A nephropathy with glomerular lesion
N02.B2	Recurrent and persistent immunoglobulin A nephropathy with focal and segmental glomerular lesion
N02.B3	Recurrent and persistent immunoglobulin A nephropathy with diffuse membranoproliferative glomerulonephritis
N02.B4	Recurrent and persistent immunoglobulin A nephropathy with diffuse membranous glomerulonephritis
N02.B5	Recurrent and persistent immunoglobulin A nephropathy with diffuse mesangial proliferative glomerulonephritis
N02.B6	Recurrent and persistent immunoglobulin A nephropathy with diffuse mesangiocapillary glomerulonephritis
N02.B9	Other recurrent and persistent immunoglobulin A nephropathy
N02.6	Recurrent and persistent hematuria with dense deposit disease
N03.A	Chronic nephritic syndrome C3 glomerulonephritis
N03.6	Chronic nephritic syndrome with dense deposit disease
N04.A	Nephrotic syndrome with C3 glomerulonephritis
N04.B1	Nephrotic syndrome with idiopathic immune complex membranoproliferative glomerulonephritis (ic-mpgn)
N04.B2	Nephrotic syndrome with secondary immune complex membranoproliferative glomerulonephritis (ic-mpgn)
N04.1	Nephrotic syndrome with focal and segmental glomerular lesions
N04.20	Nephrotic syndrome with diffuse membranous glomerulonephritis, unspecified

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ICD-10-CM Diagnosis Codes	Description
N04.21	Primary membranous nephropathy with nephrotic syndrome
N04.22	Secondary membranous nephropathy with nephrotic syndrome
N04.29	Other nephrotic syndrome with diffuse membranous glomerulonephritis
N04.6	Nephrotic syndrome with dense deposit disease
N05.A	Unspecified nephritic syndrome with C3 glomerulonephritis
N05.5	Unspecified nephritic syndrome with diffuse mesangiocapillary glomerulonephritis
N05.6	Unspecified nephritic syndrome with dense deposit disease
N26.9	Renal sclerosis, unspecified
O14.20	HELLP syndrome (HELLP), unspecified trimester
O14.22	HELLP syndrome (HELLP), second trimester
O14.23	HELLP syndrome (HELLP), third trimester
O14.24	HELLP syndrome, complicating childbirth
O14.25	HELLP syndrome, complicating the puerperium
T86.11	Kidney transplant rejection
T86.19	Other complication of kidney transplant
T86.21	Heart transplant rejection
T86.298	Other complications of heart transplant

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IX. POLICY HISTORY

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MP 4.031	**04/07/2020 Consensus Review**. No change to policy statement. Rationale, references and coding reviewed. FEP clarification added.
	09/01/2020 Administrative Update. New ICD-10 codes added (N00A, N01A, N02A, N03A, N04A, N05A).
	08/09/2021 Consensus Review. No change to policy statement. References and coding reviewed.

POLICY TITLE	PLASMA EXCHANGE (PE)
POLICY NUMBER	MP 4.031

	09/07/2021 Administrative Update. Addition of new ICD-10 codes. 10/01/2021 effective date.
	07/26/2022 Administrative Update. Addition of new ICD-10 codes, D59.30, 59.31, D59.32, and D59.39. Deleted D59.3. Effective 10/01/2022.
	11/30/2022 Minor Review. Moved neuromyelitis optica from INV to MN. Added ICD-10 code G36.0. Updated references.
	09/07/2023 Administrative Update. Addition of 11 new ICD-10 codes. Effective 10/01/2023.
	12/04/2023 Consensus Review. Policy statement unchanged. Updated rationale, references. Coding reviewed, no changes. Removed M31.1.
	09/03/2024 Administrative Update. Addition of 2 new ICD-10 codes, C88.00 and C88.01. Deleted C88.0. Effective 10/01/2024.
	01/10/2025 Consensus Review. Policy statement unchanged. Updated references. Coding reviewed, no changes.
	09/02/2025 Administrative Update. Addition of new ICD-10 codes Effective 10/01/2025
	10/23/2025 Consensus Review. No change to policy statement. Updated policy guidelines and references. Removed codes N00.B and N04.B.