PREMERA | BLUE CROSS

MEDICAL POLICY – 8.02.02
Plasma Exchange

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RELATED MEDICAL POLICIES:

7.03.04	Intestinal and Multivisceral Organ Transplant Surgery
8.01.36	Extracorporeal Photopheresis
8.02.04	Lipid Apheresis

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EVIDENCE REVIEW | REFERENCES | APPENDIX | HISTORY

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Introduction

Blood is made up of solids and liquids. The solid parts include red and white blood cells and platelets. Plasma is the liquid portion of blood. Plasma makes up about half of all blood and contains water, salts, enzymes, antibodies, and proteins. It is responsible for many important functions, including helping to maintain blood pressure and providing particular proteins for clotting. Plasma exchange is the process of replacing plasma in the body. Whole blood is withdrawn and a specialized machine separates the solids from the liquid. The plasma is then discarded, and the blood cells, platelets, and other solids are mixed with a protein fluid. This mixture is then returned to the patient with a special pump. Plasma exchange is a proven technique for a number of autoimmune, blood, nervous system, and kidney conditions as well as in certain transplant situations. This policy describes when plasma exchange may be considered medically necessary.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria

Condition	Medical Necessity
Autoimmune	**Plasma exchange is considered medically necessary for the following 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	**Plasma exchange is considered medically necessary for the following hematologic conditions:** • ABO-incompatible hematopoietic progenitor cell transplantation • Hyperviscosity syndromes associated with multiple myeloma or Waldenström macroglobulinemia • Idiopathic thrombocytopenic purpura 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	**Plasma exchange is considered medically necessary for the following neurologic conditions:** • Acute inflammatory demyelinating polyneuropathy (Guillain-Barré syndrome [GBS]; 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 GBS) • 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

Condition	Medical Necessity
	• Paraproteinemia polyneuropathy; immunoglobulin A and G • N-methyl-D-aspartate receptor antibody encephalitis; • Progressive multifocal leukoencephalopathy associated with natalizumab
Renal diseases	**Plasma exchange is considered medically necessary for the following renal diseases:** • Antiglomerular basement membrane disease (Goodpasture syndrome) • Antineutrophil cytoplasmic antibody-associated vasculitis (eg, Wegener granulomatosis [also known as granulomatosis with polyangitis] with associated renal failure • Dense deposit disease with factor H deficiency and/or elevated C3 nephritic factor

Transplantation	**Plasma exchange is considered medically necessary in the following transplant situations:**
	• ABO-incompatible solid organ transplantation:
	  ○ Kidney
	  ○ Heart (infants)
	• Renal transplantation: antibody mediated rejection; human leukocyte antigen desensitization
	• Focal segmental glomerulosclerosis after renal transplant

Condition	Investigational
All other conditions	**Plasma exchange is considered investigational in all other conditions not listed above, including, but not limited, to the following:** • ABO-incompatible solid organ transplant; liver • Acute disseminated encephalomyelitis • Acute inflammatory demyelinating polyneuropathy (Guillain-Barré 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 without renal failure)

Condition	Investigational
	• 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 nonrefractory • Inclusion body myositis • Lambert-Eaton myasthenic syndrome • Multiple sclerosis with chronic progressive or relapsing remitting course • Neuromyelitis optica • 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

Condition	Investigational
	• Sydenham chorea • Systemic lupus erythematosus (including systemic lupus erythematosus nephritis) • Thyrotoxicosis • Hyperviscosity syndromes with renal failure (other than associated with multiple myeloma or Waldenström macroglobulinemia)

Note: This policy only addresses plasma exchange (PE) as a therapeutic apheresis procedure.

Additional Guidelines
Patients receiving PE as a treatment of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) should meet the diagnostic criteria for CIDP that are included in the **Appendix**. Patients receiving PE as a treatment of acute inflammatory demyelinating polyneuropathy, also known as Guillain-Barré syndrome (GBS), should meet the criteria of diagnostic severity that are included in the **Appendix**. The use of PE in patients with acute, life-threatening complications of chronic autoimmune diseases, such as rheumatoid arthritis (RA) 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, in which it is hoped that the use of PE can acutely lower the level of serum autoantibodies until an alternate long-term treatment strategy can be implemented. However, in these situations, the treatment goals and duration of treatment 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.

Coding

Code	Description
CPT	
36514	Therapeutic apheresis; for plasma pheresis

Note: CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

Related Information

Definition of Terms

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

Apheresis: An umbrella term for procedures in which blood of the patient or donor is passed through a medical device which separates out one or more components of the blood, takes that component away, and returns the rest of the blood to the person. This term includes plasmapheresis (in which plasma it taken away).

Plasmapheresis: A procedure in which the blood of a patient or donor is passed through a medical device which separates out plasma from the other components of blood and the plasma is removed, but not replaced.

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

Evidence Review

Description

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.

Background

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 two 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 (AMR) 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 AMR, plasmapheresis is often used in combination with intravenous immunoglobulin (IVIg) or anti-CD20 therapy (ie, Rituxan® (rituximab)).

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.

Ongoing And Unpublished Clinical Trials

Some currently unpublished trials that might influence this review are listed in **Table 1**.

Table 1. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT01442233	Plasma Exchanges in Multiple Sclerosis (MS) Relapses (PLASMASEP)	80	Dec 2017
NCT02622854	Plasma Exchange vs Conservative Management in Non-severe Acute Hypertriglyceridemic Pancreatitis	20	Dec 2018
NCT02647255	Trial of Plasma Exchange for Severe Crescentic IgA Nephropathy (RESCUE)	150	Dec 2019

NCT: national clinical trial.

Clinical Input Received from Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may provide appropriate reviewers who collaborate with and make recommendations during this process, 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 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 ANCA-associated vasculitis or other diagnoses.

Practice Guidelines and Position Statements

National Comprehensive Cancer Network (NCCN)

In the current NCCN guidelines on multiple myeloma (v.2.2018), use of plasmapheresis to improve renal function is a category 2B recommendation.[53] Plasmapheresis should also be used as adjunctive therapy for hyperviscosity.

American Academy of Neurology (AAN)

In 2011, the AAN (Therapeutics and Technology Assessment Subcommittee) issued evidence-based guidelines on plasmapheresis in the treatment of neurologic disorders.[54] The primary conclusions, based on their evidence review, are provided in **Table 2**:

Table 2. 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).[55] 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 nonambulant 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 (ASFA)

In 2016, the ASFA updated its guidelines on the use of therapeutic apheresis (Seventh Special Issue).[56] Previously, the guidelines had been updated in 2013 (Sixth Special Issue).[57] The following is a description of the Society categories (see **Table 3**) and 2013 recommendations (see **Table 4**) and new indications added in 2016 (see **Table 5**).

Table 3. American Society for Apheresis Categories

Category	Description
I	Diseases for which TA is accepted as first-line treatment, either as a primary standalone treatment or in conjunction with other treatments. Note that this designation need not imply that TA is mandatory in all cases.
II	Diseases for which TA is accepted as second-line treatment, either as a standalone treatment or in conjunction with other treatments.
III	Diseases for which the optimum role of TA is not established and treatment decisions on an individual basis are recommended.
IV	Disorders for which published evidence suggests or demonstrates that TA is ineffective or harmful.

TA: therapeutic apheresis.

Table 4. American Society for Apheresis 2013 Key Recommendations

Disease Group/Name/Condition	2013 Category
Autoimmune	
Catastrophic antiphospholipid syndrome	II
Cryoglobulinemia	I
Pemphigus vulgaris	III

Disease Group/Name/Condition	2013 Category
Systemic lupus erythematosus	
Manifestations other than nephritis	NC
Severe	II
Nephritis	IV
Hematologic	
ABO-incompatible hematopoietic progenitor cell transplantation	II
Aplastic anemia	III
Pure red blood cell aplasia	III
Idiopathic thrombocytopenic purpura	NC
Coagulation factor inhibitors	IV
Hyperviscosity in monoclonal gammopathies	I
Refractory immunoadsorption	NC
Refractory or nonrefractory	NC
Autoimmune hemolytic anemia	
Warm autoimmune hemolytic anemia	III
Cold agglutinin disease	II
Myeloma and acute renal failure (in 2010 and 2013 myeloma cast nephropathy)	
Post-transfusion purpura	III
Red blood cell alloimmunization in pregnancy	III
Thrombotic thrombocytopenic purpura	I
Metabolic	
Acute liver failure	III
Sepsis	III
Thyrotoxicosis	III
Neurologic	
Acute disseminated encephalomyelitis	II
AIDP (Guillain-Barré syndrome)	I
AIDP, post IVIg	III
Chronic inflammatory demyelinating polyradiculoneuropathy	I
Lambert-Eaton myasthenic syndrome	II
Multiple sclerosis	

Disease Group/Name/Condition	2013 Category
Acute CNS inflammatory demyelinating disease	II
Devic syndrome	NC
Chronic progressive	III
Myasthenia gravis	
In 2013, moderate-severe	I
In 2013, pre-thymectomy	I
Paraneoplastic neurologic syndromes	III
Paraproteinemic polyneuropathies	
IgG/IgA	I
IgM	I
Multiple myeloma	III
Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections; SC	
PANDAS (2007, severe)	I
SC (2007, severe)	I
Rasmussen encephalitis	III
Stiff person syndrome	III
Neuromyelitis optica spectrum disorders	
Acute	II
Maintenance	III
Renal	
ANCA-associated rapidly progressive glomerulonephritis (Wegener granulomatosis)	
Dialysis dependence	I
Dialysis independence	III
Antiglomerular basement membrane disease (Goodpasture syndrome)	
DAH	I
Dialysis dependence and no DAH	III
Dialysis independence	I
Focal segmental glomerulosclerosis	
Primary	NC

Disease Group/Name/Condition	2013 Category
Secondary	NC
Recurrent	I
HUS; thrombotic microangiopathy; transplant-associated microangiopathy	
Idiopathic HUS	NC
Transplant-associated microangiopathy	NC
Diarrhea-associated pediatric	NC
Atypical HUS due to complement factor H	I
Diarrhea-associated HUS or typical HUS	
In 2013, Shiga toxin-associated	IV
Streptococcus pneumoniae associated	III
Renal transplantation: antibody-mediated rejection; HLA desensitization	
Antibody-mediated rejection	I
HLA desensitization	II
Desensitization, living-donor, positive cross-match due to donor-specific HLA antibody	I
High PRA: cadaveric donor	III
Rheumatic	
Scleroderma (progressive systemic sclerosis)	III
Transplantation	
ABO-incompatible solid organ transplantation	
Kidney	
In 2013, desensitization, living-donor	I
Humeral rejection	II
Heart (infants)	NC
Liver (2010 perioperative)	
In 2013, desensitization living-donor	I
Desensitization, deceased-donor	II
Humeral rejection	III
Heart transplant rejection	
Treatment	NC

ABO: A, B, and O blood types; AIDP: acute inflammatory demyelinating polyneuropathy; ANCA: antineutrophil cytoplasmic antibody; CNS: central nervous system; DAH: diffuse alveolar hemorrhage; HLA: human leukocyte antigen; HUS: hemolytic uremic syndrome; Ig: immunoglobulin; IVIg: intravenous immunoglobulin; NC: not categorized;

PANDAS: pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection; PRA: Panel Reactive Antibody; SC: Sydenham chorea.

Table 5. American Society for Apheresis New Indications in 2016

Disease Group/Name/Condition	2016 Category
Atopic (neuro-) dermatitis (atopic eczema), recalcitrant	III
Cardiac neonatal lupus	III
Complex regional pain syndrome	III
Erythropoietic porphyria, liver disease	III
Hashimoto encephalopathy: steroid-responsive encephalopathy associated with autoimmune thyroiditis	II
HELLP syndrome[a]	
Postpartum	III
Antepartum	IV
Hematopoietic cell transplantation, human leukocyte antigen desensitization	III
Hemophagocytic lymphohistiocytosis; hemophagocytic syndrome; macrophage activating syndrome	III
N-methyl-d-aspartate receptor antibody encephalitis	I
Prevention of Rhesus D alloimmunization after red blood cell exposure	III
Progressive multifocal leukoencephalopathy associated with natalizumab	I
Pruritus due to hepatobiliary diseases	III
Thrombotic microangiopathy, coagulation mediated	III
Vasculitis	
HBV-PAN	II
Idiopathic PAN	IV
EGPA	III
Behçet disease	III

EGPA: eosinophilic granulomatosis with polyangiitis; HBV: hepatitis B virus; PAN: polyarteritis nodosa.

[a] A severe form of preeclampsia, characterized by hemolysis, elevated liver enzymes, and low platelet counts.

Medicare National Coverage

The national coverage determination for apheresis (therapeutic pheresis)[58] 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.

Regulatory Status

The U.S. Food and Drug Administration (FDA) 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 noninjectable products (eg, in vitro devices such as blood bank reagents).[1]

Product code for therapeutic exchange plasma: 57DI-65

Appendix

Diagnostic Criteria for Diagnosis of Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

The following criteria are adapted from the Task Force Report of the Ad Hoc Subcommittee of the American Academy of Neurology AIDS Task Force (Neurology 1991; 41:617-18, PMID 2027473). The report included mandatory, supportive, and exclusionary diagnostic criteria. Only the mandatory criteria are excerpted here. The criteria are based on a combination of clinical observations, physiologic studies, pathologic features (ie, nerve biopsy), and studies of the cerebral spinal fluid (CSF).

- Clinical: Mandatory
    - Progressive or relapsing motor and sensory, rarely only motor or sensory, dysfunction of more than 1 limb or a peripheral nerve nature, developing over at least 2 months.
    - Hypo- or areflexia. This will usually involve all four limbs.
- Physiologic Studies: Mandatory

Nerve conduction studies including studies of proximal nerve segments in which the predominant process is demyelination.

Must have 3 out of 4 of the following criteria in the list of second-level bullets:

- Reduction in conduction velocity (CV) in 2 or more motor nerves
  - < 80% of lower limit of normal (LLN) is amplitude > 80% of LLN
  - < 70% of LLN is amplitude < 80% of LLN
- Partial conduction block or abnormal temporal dispersion in 1 or more motor nerves: either peroneal nerve between ankle and below fibular head, median nerve between wrist and elbow, or ulnar nerve between wrist and below elbow.
- Criteria suggestive of partial conduction block: < 15% change in duration between proximal and distal sites and > 20% drop in negative-peak (p) area or peak to peak (p-p) amplitude between proximal and distal sites.
- Criteria for abnormal temporal dispersion and possible conduction block: > 15% change in duration between proximal and distal sites and > 20% drop in p area or p-p amplitude between proximal and distal sites and > 20% drop in p or p-p amplitude between proximal and distal sites. These criteria are only suggestive of partial conduction block as they are derived from studies of normal individuals.
- Additional studies, such as stimulation across short segments or recording of individual motor unit potentials, are required for confirmation.
- Prolonged distal latencies in two or more nerves:
  - >125% of upper limit of normal (LEN) is amplitude > 80% of LLN
  - >150% of LEN if amplitude < 80% of LLN
- Absent F waves or prolonged minimum:
  - > 120% of ULN if amplitude > 80% of LLN
  - > 150% of ULN if amplitude < 80% of LLN

- Pathologic Features: Mandatory

Nerve biopsy showing unequivocal evidence of demyelination and remyelination.

Demyelination by either electron microscopy (> 5 fibers) or teased fiber studies >12% of 50 fibers, minimum of 4 internodes each, demonstrating demyelination/ remyelination.

- CSF Studies: Mandatory
  - Cell count <10/mm-3 if HIV-seronegative or <50/mm-3 if HIV seropositive

- Negative VDRL

Guillain-Barré Syndrome Disability Scale

The scale appears below as it did in the Hughes et al. 2007 systematic review published in Brain 2007; 130[9]:2245-2257.[22]

0. Healthy

1. Minor symptoms or signs of neuropathy but capable of manual work/capable of running

2. Able to walk without support of a stick (5 m across an open space) but incapable of manual work/running

3. Able to walk with a stick, appliance or support (5m across an open space)

4. Confined to bed or chair bound

5. Requiring assisted ventilation (for any part of the day or night)

6. Death

References

1. Food and Drug Administration (FDA). Compliance Program Guidance Manual; Chapter 42- Blood and Blood Products. 2011; **https://www.fda.gov/downloads/Enforcement/UCM247371.pdf** . Accessed November 2017.
2. Shumak KH, Rock GA. Therapeutic plasma exchange. N Engl J Med. Mar 22 1984;310(12):762-771. PMID 6199669
3. 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
4. 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
5. 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
6. 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
7. 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

8. Canadian Cooperative Multiple Sclerosis Study Group. The Canadian cooperative trial of cyclophosphamide and plasma exchange in progressive multiple sclerosis. The Canadian Cooperative Multiple Sclerosis Study Group. Lancet. Feb 23 1991;337(8739):441-446. PMID 1671468

9. 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

10. 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

11. Anderson NE, Rosenblum MK, Posner JB. Paraneoplastic cerebellar degeneration: clinical-immunological correlations. Ann Neurol. Oct 1988;24(4):559-567. PMID 3239956

12. 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

13. 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

14. 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

15. 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

16. 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

17. 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

18. 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

19. 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

20. Rockx MA, Clark WF. Plasma exchange for treating cryoglobulinemia: a descriptive analysis. Transfus Apher Sci. Jun 2010;42(3):247-251. PMID 20382569

21. 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

22. Noris M, Remuzzi G. Atypical hemolytic-uremic syndrome. N Engl J Med. Oct 22 2009;361(17):1676-1687. PMID 19846853

23. 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

24. Chevret S, Hughes RA, Annane D. Plasma exchange for Guillain-Barre syndrome. Cochrane Database Syst Rev. Feb 27 2017;2:Cd001798. PMID 28241090

25. 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

26. 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

27. 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

28. 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

29. 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

30. 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

31. 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

32. 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

33. 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

34. 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

35. 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

36. 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

37. 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

38. Couser WG. Rapidly progressive glomerulonephritis: classification, pathogenetic mechanisms, and therapy. Am J Kidney Dis. Jun 1988;11(6):449-464. PMID 3287904

39. 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

40. 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

41. 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

42. 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

43. 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

44. 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

45. 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

46. Ibernon 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

47. 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

48. 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

49. 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

50. 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 20 2014;18(6):699. PMID 25527094

51. 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

52. 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

53. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Multiple Myeloma. Version 2.2018. https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed September 29, 2017.

54. 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

55. 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

56. 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

57. 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

58. 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** Accessed November 2017.

History

Date	Comments
11/13/01	Replace Policy - Revised Policy replaces P8.02.100
08/13/02	Replace Policy - Policy reviewed; new indications added.
05/13/03	Replace Policy - Update CPT codes only.
05/11/04	Replace Policy - Policy reviewed with literature search; references added. No change in policy statement.
06/14/05	Replace Policy - Policy updated with literature search; no change in policy statement. Reference 22 updated, and comparison between ASA recommendations and policy statement included in the Rationale Section.
02/06/06	Codes updated - No other changes.
05/16/06	Update Scope and Disclaimer - No other changes.

Date	Comments
08/08/06	Replace Policy - Policy revised with addition of policy statements and discussion of plasmapheresis in the setting of solid organ transplantation, considered medically necessary; references added.
06/09/09	Replace Policy - Policy updated with literature search. Policy statement updated to include Wegener's Granulomatosis as a medically necessary indication.
04/13/10	Replace Policy - Policy reviewed with literature search The policy statement has been modified to include: Guillain-Barré syndrome severity grades 1-2 as medically necessary; use in the pediatric population is investigational for mild and moderate forms of GBS and medically necessary for the severe form of GBS; the policy statement has been modified to include severe manifestations of mixed cryoglobulinemia (MC) as medically necessary when used in combination with immunosuppressive therapy; typical- hemolytic uremic syndrome is investigational (considered medically necessary in previous updates) and investigational for treatment of PANDAS, Sydenham Chorea, Refsum's disease, cryoglobulinemia (except severe MC), myasthenia gravis with anti-MuSk antibodies; additional conditions were added as investigational based on American Society for Apheresis (ASFA) review. Title changed from "Plasma Exchange (Plasmapheresis) to "Plasma Exchange." References added.
06/08/10	Cross Reference Update - No other changes.
06/13/11	Replace Policy - Policy reviewed with literature search from May 2009 through January 2011. No changes to policy statements. Rationale rewritten. References 16, 24, 31 and 41 added; other references renumbered or removed. ICD-10 codes added to policy.
06/20/12	Minor update: Related Policies updated; 8.01.17 replaced 8.01.507 effective June 12, 2012.
07/10/12	Replace policy. Policy statement revised with additional conditions that may be medically necessary myeloma with acute renal failure, catastrophic antiphospholipid syndrome; dense deposit disease with Factor H deficiency and/or elevated C3 nephritis factor and focal segmental glomerulosclerosis after renal transplant. The investigational statement on focal segmental glomerulosclerosis was modified to indicate that it applied to situations other than after renal transplant. Hyperviscoscity syndromes with renal failure (other than associated with multiple myeloma or Waldenstrom's macroglobulinermia) added as investigational. In addition, the serum creatinine threshold was removed from the medically necessary policy statement on ANCA-associated vasculitis. Rationale rewritten. Updated literature review with references 22, 26 and 29 added, other references renumbered or removed.
09/28/12	Update Related Policies – Add 7.03.509; ICD-10 codes are now effective 10/01/2014.
02/11/13	Replace policy. Minor clarification regarding medical necessity of MS for acute and chronic forms. The intent of the policy statement is unchanged.
04/18/13	Update Related Policies. Change title to 8.01.36.
07/24/13	Replace policy. Policy reviewed with literature search through March 21, 2013. Policy statements unchanged. References 19, 23 and 40 added.

Date	Comments
08/15/13	Update Related Policies. Change title to 7.03.05.
10/18/13	Update Related Policies. Change title to 8.01.17.
07/31/14	Annual Review. Policy updated with literature review through April 3, 2014. Minor changes to bullet points on multiple sclerosis for clarity only. References 16, 25, 29, 30, 40, 44 and 46 added.
10/22/14	Update Related Policies. Change title to 8.02.04.
07/14/15	Annual Review. Neuromyelitis optica (NMO) added to the list of investigational conditions. CAPS, abbreviation for catastrophic antiphospholipid syndrome, removed from medically necessary policy statement. Policy updated with literature review through April, 2015. References 32-35, 47 added. Retained the criteria for CIDP and Guillain-Barré syndrome in the Appendix. Investigational policy statement updated as noted. ICD-9 diagnosis codes removed; these were listed for informational purposes only. Related Policies updated, the following were removed: 7.03.05, 7.03.509, 7.03.510, 8.01.17, 8.01.25 and 8.01.503.
09/01/15	Update Related Policies. Add 7.03.04.
06/01/16	Annual Review, approved May 10, 2016. No change to policy statements. No new literature added.
12/01/17	Annual Review, approved November 9, 2017. Policy updated with literature review through July 21, 2017. References 3, 19, 24, 30, 35-37, and 56 added. N-methyl-D-aspartate receptor antibody encephalitis and progressive multifocal leukoencephalopathy associated with natalizumab added to medically necessary statement.

Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.

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200 Independence Avenue SW, Room 509F, HHH Building
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Getting Help in Other Languages

This Notice has Important Information. This notice may have important information about your application or coverage through Premera Blue Cross. There may be key dates in this notice. You may need to take action by certain deadlines to keep your health coverage or help with costs. You have the right to get this information and help in your language at no cost. Call 800-722-1471 (TTY: 800-842-5357).

አማሪኛ (Amharic):
ይህ ማስታወቂያ አስፈላጊ መረጃ ይዟል። ይህ ማስታወቂያ ስለ ማመልከቻዎ ወይም የ Premera Blue Cross ሽፋን አስፈላጊ መረጃ ሊኖረው ይችላል። በዚህ ማስታወቂያ ውስጥ ቁልፍ ቀኖች ሊኖሩ ይችላሉ። የጤናን ሽፋንዎን ለመጠበቅና በእከፋፈል እርዳታ ለማግኘት በተውሰኑ የጊዜ ገደቦች እርምጃ መውሰድ ይገባዎት ይሆናል። ይህን መረጃ እንዲያገኙ እና ያለምንም ክፍያ በቋንቋዎ እርዳታ እንዲያገኙ መብት አለዎት።በስልክ ቁጥር 800-722-1471 (TTY: 800-842-5357) ይደውሉ።

العربية (Arabic):
يحوي هذا الإشعار معلومات هامة. قد يحوي هذا الإشعار معلومات مهمة بخصوص طلبك أو التغطية التي تريد الحصول عليها من خلال Premera Blue Cross. قد تكون هناك تواريخ مهمة في هذا الإشعار. وقد تحتاج لاتخاذ إجراء في تواريخ معينة للحفاظ على تغطيتك الصحية أو للمساعدة في دفع التكاليف. يحق لك الحصول على هذه المعلومات والمساعدة بلغتك دون تكبد أية تكلفة. اتصل بـ800-722-1471 (TTY: 800-842-5357)

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本通知有重要的訊息。本通知可能有關於您透過 Premera Blue Cross 提交的申請或保險的重要訊息。本通知內可能有重要日期。您可能需要在截止日期之前採取行動，以保留您的健康保險或者費用補貼。您有權利免費以您的母語得到本訊息和幫助。請撥電話 800-722-1471 (TTY: 800-842-5357)。

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Cet avis a d'importantes informations. Cet avis peut avoir d'importantes informations sur votre demande ou la couverture par l'intermédiaire de Premera Blue Cross. Le présent avis peut contenir des dates clés. Vous devrez peut-être prendre des mesures par certains délais pour maintenir votre couverture de santé ou d'aide avec les coûts. Vous avez le droit d'obtenir cette information et de l'aide dans votre langue à aucun coût. Appelez le 800-722-1471 (TTY: 800-842-5357).

Kreyòl ayisyen (Creole):
Avi sila a gen Enfòmasyon Enpòtan ladann. Avi sila a kapab genyen enfòmasyon enpòtan konsènan aplikasyon w lan oswa konsènan kouvèti asirans lan atravè Premera Blue Cross. Kapab genyen dat ki enpòtan nan avi sila a. Ou ka gen pou pran kèk aksyon avan sèten dat limit pou ka kenbe kouvèti asirans sante w la oswa pou yo ka ede w avèk depans yo. Se dwa w pou resevwa enfòmasyon sa a ak asistans nan lang ou pale a, san ou pa gen pou peye pou sa. Rele nan 800-722-1471 (TTY: 800-842-5357).

Deutsche (German):
Diese Benachrichtigung enthält wichtige Informationen. Diese Benachrichtigung enthält unter Umständen wichtige Informationen bezüglich Ihres Antrags auf Krankenversicherungsschutz durch Premera Blue Cross. Suchen Sie nach eventuellen wichtigen Terminen in dieser Benachrichtigung. Sie könnten bis zu bestimmten Stichtagen handeln müssen, um Ihren Krankenversicherungsschutz oder Hilfe mit den Kosten zu behalten. Sie haben das Recht, kostenlose Hilfe und Informationen in Ihrer Sprache zu erhalten. Rufen Sie an unter 800-722-1471 (TTY: 800-842-5357).

Hmoob (Hmong):
Tsab ntawv tshaj xo no muaj cov ntshiab lus tseem ceeb. Tej zaum tsab ntawv tshaj xo no muaj cov ntsiab lus tseem ceeb txog koj daim ntawv thov kev pab los yog koj qhov kev pab cuam los ntawm Premera Blue Cross. Tej zaum muaj cov hnub tseem ceeb uas sau rau hauv daim ntawv no. Tej zaum koj kuj yuav tau ua qee yam uas peb kom koj ua tsis pub dhau cov caij nyoog uas teev tseg rau hauv daim ntawv no mas koj thiaj yuav tau txais kev pab cuam kho mob los yog kev pab them tej nqi kho mob ntawd. Koj muaj cai kom lawv muab cov ntshiab lus no uas tau muab sau ua koj hom lus pub dawb rau koj. Hu rau 800-722-1471 (TTY: 800-842-5357).

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ແຈ້ງການນີ້ມີຂໍ້ມູນສຳຄັນ. ແຈ້ງການນີ້ອາດຈະມີຂໍ້ມູນສຳຄັນກ່ຽວກັບຄຳຮ້ອງສະໝັກ ຫຼື ຄວາມຄຸ້ມຄອງປະກັນໄພຂອງທ່ານຜ່ານ Premera Blue Cross. ອາດຈະມີວັນທີສຳຄັນໃນແຈ້ງການນີ້. ທ່ານອາດຈະຈຳເປັນຕ້ອງດຳເນີນການຕາມກຳນົດເວລາສະເພາະເພື່ອຮັກສາຄວາມຄຸ້ມຄອງປະກັນສຸຂະພາບ ຫຼື ຄວາມຊ່ວຍເຫຼືອເລື່ອງຄ່າໃຊ້ຈ່າຍຂອງທ່ານໄວ້. ທ່ານມີສິດໄດ້ຮັບຂໍ້ມູນນີ້ ແລະ ຄວາມຊ່ວຍເຫຼືອເປັນພາສາຂອງທ່ານໂດຍບໍ່ເສຍຄ່າ. ໃຫ້ໂທຫາ 800-722-1471 (TTY: 800-842-5357).

ភាសាខ្មែរ (Khmer):
សេចក្តីជូនដំណឹងនេះមានព័ត៌មានយ៉ាងសំខាន់។ សេចក្តីជូនដំណឹងនេះប្រហែលជាមានព័ត៌មានយ៉ាងសំខាន់អំពីទម្រង់បែបបទ ឬការរ៉ាប់រងរបស់អ្នកតាមរយៈ Premera Blue Cross ។ ប្រហែលជាមាន កាលបរិច្ឆេទសំខាន់នៅក្នុងសេចក្តីជូនដំណឹងនេះ។ អ្នកប្រហែលជាត្រូវការបញ្ចេញសមត្ថភាព ដល់កំណត់ថ្ងៃជាក់ច្បាស់នានា ដើម្បីនឹងរក្សាទុកការជានាវ៉ាប់រងសុខភាពរបស់អ្នក ឬប្រាក់ជំនួយចេញផ្លែ។ អ្នកមានសិទ្ធិទទួលព័ត៌មាននេះ និងជំនួយនៅក្នុងភាសារបស់អ្នកដោយមិនអស់លុយឡើយ។ សូមទូរស័ព្ទ 800-722-1471 (TTY: 800-842-5357)។

ਪੰਜਾਬੀ (Punjabi):
ਇਸ ਨੋਟਿਸ ਵਿਚ ਖਾਸ ਜਾਣਕਾਰੀ ਹੈ. ਇਸ ਨੋਟਿਸ ਵਿਚ Premera Blue Cross ਵਲੋਂ ਤੁਹਾਡੀ ਕਵਰੇਜ ਅਤੇ ਅਰਜੀ ਬਾਰੇ ਮਹੱਤਵਪੂਰਨ ਜਾਣਕਾਰੀ ਹੋ ਸਕਦੀ ਹੈ . ਇਸ ਨੋਜਿਸ ਜਵਚ ਖਾਸ ਤਾਰੀਖਾ ਹੋ ਸਕਦੀਆਂ ਹਨ. ਜੇਕਰ ਤੁਸੀ ਜਸਹਤ ਕਵਰੇਜ ਰਿੱਖਣੀ ਹੋਵੇ ਜਾ ਓਸ ਦੀ ਲਾਗਤ ਜਵਿੱਚ ਮਦਦ ਦੇ ਇਛੁੱਕ ਹੋ ਤਾਂ ਤੁਹਾਨੂੰ ਅੰਤਮ ਤਾਰੀਖ਼ ਤੋਂ ਪਹਿਲਾਂ ਕੁੱਝ ਖਾਸ ਕਦਮ ਚੁੱਕਣ ਦੀ ਲੋੜ ਹੋ ਸਕਦੀ ਹੈ ,ਤੁਹਾਨੂੰ ਮੁਫ਼ਤ ਵਿੱਚ ਤੇ ਆਪਣੀ ਭਾਸ਼ਾ ਵਿੱਚ ਜਾਣਕਾਰੀ ਅਤੇ ਮਦਦ ਪ੍ਰਾਪਤ ਕਰਨ ਦਾ ਅਧਿਕਾਰ ਹੈ ,ਕਾਲ 800-722-1471 (TTY: 800-842-5357).

فارسی (Farsi):
این اعلامیه حاوی اطلاعات مهم میباشد .این اعلامیه ممکن است حاوی اطلاعات مهم درباره فرم تقاضا و یا پوشش بیمه ای شما از طریق Premera Blue Cross باشد. به تاریخ های مهم در این اعلامیه توجه نمایید .شما ممکن است برای حفظ پوشش بیمه تان یا کمک در پرداخت هزینه های درمانی تان، به تاریخ های مشخصی برای انجام کارهای خاصی احتیاج داشته باشید .شما حق این را دارید که این اطلاعات و کمک را به زبان خود به طور رایگان دریافت نمایید. برای کسب اطلاعات با شماره 800-722-1471 (کاربران TTY تماس باشماره 800-842-5357) تماس برقرار نمایید.

Polskie (Polish):
To ogłoszenie może zawierać ważne informacje. To ogłoszenie może zawierać ważne informacje odnośnie Państwa wniosku lub zakresu świadczeń poprzez Premera Blue Cross. Prosimy zwrócic uwagę na kluczowe daty, które mogą być zawarte w tym ogłoszeniu aby nie przekroczyć terminów w przypadku utrzymania polisy ubezpieczeniowej lub pomocy związanej z kosztami. Macie Państwo prawo do bezpłatnej informacji we własnym języku. Zadzwońcie pod 800-722-1471 (TTY: 800-842-5357).

Português (Portuguese):
Este aviso contém informações importantes. Este aviso poderá conter informações importantes a respeito de sua aplicação ou cobertura por meio do Premera Blue Cross. Poderão existir datas importantes neste aviso. Talvez seja necessário que você tome providências dentro de determinados prazos para manter sua cobertura de saúde ou ajuda de custos. Você tem o direito de obter esta informação e ajuda em seu idioma e sem custos. Ligue para 800-722-1471 (TTY: 800-842-5357).

Română (Romanian):
Prezenta notificare conține informații importante. Această notificare poate conține informații importante privind cererea sau acoperirea asigurării dumneavoastre de sănătate prin Premera Blue Cross. Pot exista date cheie în această notificare. Este posibil să fie nevoie să acționați până la anumite termene limită pentru a vă menține acoperirea asigurării de sănătate sau asistența privitoare la costuri. Aveți dreptul de a obține gratuit aceste informații și ajutor în limba dumneavoastră. Sunați la 800-722-1471 (TTY: 800-842-5357).

Русский (Russian):
Настоящее уведомление содержит важную информацию. Это уведомление может содержать важную информацию о вашем заявлении или страховом покрытии через Premera Blue Cross. В настоящем уведомлении могут быть указаны ключевые даты. Вам, возможно, потребуется принять меры к определенным предельным срокам для сохранения страхового покрытия или помощи с расходами. Вы имеете право на бесплатное получение этой информации и помощь на вашем языке. Звоните по телефону 800-722-1471 (TTY: 800-842-5357).

Fa'asamoa (Samoan):
Atonu ua iai i lenei fa'asilasilaga ni fa'amatalaga e sili ona taua e tatau ona e malamalama i ai. O lenei fa'asilasilaga o se fesoasoani e fa'amatala atili i ai i le tulaga o le polokalame, Premera Blue Cross, ua e tau fia maua atu i ai. Fa'amolemole, ia e iloilo fa'alelei i aso fa'apitoa olo'o iai i lenei fa'asilasilaga taua. Masalo o le'a iai ni feau e tatau ona e faia ao le'i aulia le aso ua ta'ua i lenei fa'asilasilaga ina ia e iai pea ma maua fesoasoani mai ai i le polokalame a le Malo olo'o e iai i ai. Olo'o iai iate oe le aia tatau e maua atu i lenei fa'asilasilaga ma lenei fa'amatalaga i legagana e te malamalama i ai aunoa ma se togiga tupe. Vili atu i le telefoni 800-722-1471 (TTY: 800-842-5357).

Español (Spanish):
Este Aviso contiene información importante. Es posible que este aviso contenga información importante acerca de su solicitud o cobertura a través de Premera Blue Cross. Es posible que haya fechas clave en este aviso. Es posible que deba tomar alguna medida antes de determinadas fechas para mantener su cobertura médica o ayuda con los costos. Usted tiene derecho a recibir esta información y ayuda en su idioma sin costo alguno. Llame al 800-722-1471 (TTY: 800-842-5357).

Tagalog (Tagalog):
Ang Paunawa na ito ay naglalaman ng mahalagang impormasyon. Ang paunawa na ito ay maaaring naglalaman ng mahalagang impormasyon tungkol sa iyong aplikasyon o pagsakop sa pamamagitan ng Premera Blue Cross. Maaaring may mga mahalagang petsa dito sa paunawa. Maaring mangailangan ka na magsagawa ng hakbang sa ilang mga itinakdang panahon upang mapanatili ang iyong pagsakop sa kalusugan o tulong na walang gastos. May karapatan ka na makakuha ng ganitong impormasyon at tulong sa iyong wika ng walang gastos. Tumawag sa 800-722-1471 (TTY: 800-842-5357).

ไทย (Thai):
ประกาศนี้มีข้อมูลสำคัญ ประกาศนี้อาจมีข้อมูลที่สำคัญเกี่ยวกับการการสมัครหรือขอบเขตประกันสุขภาพของคุณผ่าน Premera Blue Cross และอาจมีกำหนดการในประกาศนี้ คุณอาจจะต้องดำเนินการภายในกำหนดระยะเวลาที่แน่นอนเพื่อจะรักษาการประกันสุขภาพของคุณหรือการช่วยเหลือที่มีค่าใช้จ่าย คุณมีสิทธิที่จะได้รับข้อมูลและความช่วยเหลือนี้ในภาษาของคุณโดยไม่มีค่าใช้จ่าย โทร 800-722-1471 (TTY: 800-842-5357)

Український (Ukrainian):
Це повідомлення містить важливу інформацію. Це повідомлення може містити важливу інформацію про Ваше звернення щодо страхувального покриття через Premera Blue Cross. Зверніть увагу на ключові дати, які можуть бути вказані у цьому повідомленні. Існує імовірність того, що Вам треба буде здійснити певні кроки у конкретні кінцеві строки для того, щоб зберегти Ваше медичне страхування або отримати фінансову допомогу. У Вас є право на отримання цієї інформації та допомоги безкоштовно на Вашій рідній мові. Дзвоніть за номером телефону 800-722-1471 (TTY: 800-842-5357).

Tiếng Việt (Vietnamese):
Thông báo này cung cấp thông tin quan trọng. Thông báo này có thông tin quan trọng về đơn xin tham gia hoặc hợp đồng bảo hiểm của quý vị qua chương trình Premera Blue Cross. Xin xem ngày quan trọng trong thông báo này. Quý vị có thể phải thực hiện theo thông báo đúng trong thời hạn để duy trì bảo hiểm sức khỏe hoặc được trợ giúp thêm về chi phí. Quý vị có quyền được biết thông tin này và được trợ giúp bằng ngôn ngữ của mình miễn phí. Xin gọi số 800-722-1471 (TTY: 800-842-5357).