Plasma Exchange (PE)

Policy #  00249
Original Effective Date:  03/19/2010
Current Effective Date:  11/13/2019

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: Immunoglobulin Therapy is addressed separately in medical policy 00170.

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

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 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’s macroglobulinemia;
- Idiopathic thrombocytopenic purpura (ITP) in emergency situations;
- Thrombotic thrombocytopenic purpura (TTP);
- Atypical hemolytic uremic syndrome (HUS);
- Post-transfusion purpura;
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- 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; severity grade 1-2 within 2 weeks of onset; severity grade 3-5 within 4 weeks of onset; and children <10 years old with severe Guillain-Barré syndrome);
- 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;
- 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 (GBM) disease (Goodpasture syndrome);
- Anti-neutrophil cytoplasmic antibody (ANCA)–associated vasculitis (eg, Wegener granulomatosis [also known as granulomatosis with polyangiitis]) with associated renal failure;
- Dense deposit disease with factor H deficiency and/or elevated C3 nephritic factor.

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

- ABO-incompatible solid organ transplant: liver;
- Acute disseminated encephalomyelitis;
- Acute inflammatory demyelinating polyneuropathy (Guillain-Barré syndrome) in children <10 years old with mild or moderate forms;
- Acute liver failure;
- Amyotrophic lateral sclerosis;
- Anti-neutrophil cytoplasmic antibody (ANCA)–associated rapidly progressive glomerulonephritis (Wegener granulomatosis or granulomatosis with polyangiitis 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 (MC) as noted above;
- Dermatomyositis and polymyositis;
- Focal segmental glomerulosclerosis (other than after renal transplant);
- Heart transplant rejection treatment;
- Hemolytic uremic syndrome (HUS), typical (diarrheal-related);
- Idiopathic thrombocytopenic purpura, refractory or nonrefractory;
- Inclusion body myositis;
- Lambert-Eaton myasthenic syndrome (LEMS);
- Multiple sclerosis (MS) with chronic progressive or relapsing remitting course;
- Mushroom poisoning;
- Myasthenia gravis with anti-MuSK antibodies;
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- Neuromyelitis optica;
- Overdose and poisoning (other than mushroom poisoning);
- Paraneoplastic syndromes;
- Paraproteinemia polyneuropathy IgM;
- Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS);
- Pemphigus vulgaris;
- Phytanic acid storage disease (Refsum disease);
- POEMS (polyneuropathy, organomegaly, endocrinopathy, M protein, skin changes);
- Psoriasis;
- Red blood cell alloimmunization in pregnancy;
- Rheumatoid arthritis;
- Sepsis;
- Scleroderma (systemic sclerosis);
- Stiff person syndrome;
- Sydenham chorea (SC);
- Systemic lupus erythematous (including systemic lupus erythematous 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 erythematous, 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;
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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 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
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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).


Rationale/Source
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
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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.

**Supplemental Information**

**CLINICAL INPUT FROM PHYSICIAN SPECIALTY SOCIETIES AND ACADEMIC MEDICAL CENTERS**

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

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

**PRACTICE GUIDELINES AND POSITION STATEMENTS**

**National Comprehensive Cancer Network**

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

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

PANDAS: pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections.

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

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

American Society for Apheresis
In 2016, the American Society for Apheresis updated its guidelines on the use of therapeutic apheresis (Seventh Special Issue). Previously, the guidelines had been updated in 2013 (Sixth
Special Issue). The following is a description of the Society categories (see Table 2), 2013 recommendations (see Table 3), and new indications added in 2016 (see Table 4).

Table 2. American Society for Apheresis Categories

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>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.</td>
</tr>
<tr>
<td>II</td>
<td>Diseases for which TA is accepted as second-line treatment, either as a standalone treatment or in conjunction with other treatments.</td>
</tr>
<tr>
<td>III</td>
<td>Diseases for which the optimum role of TA is not established and treatment decisions on an individual basis are recommended. Disorders for which published evidence suggests or demonstrates that TA is ineffective or harmful.</td>
</tr>
</tbody>
</table>

TA: therapeutic apheresis.

Table 3. American Society for Apheresis 2013 Key Recommendations

<table>
<thead>
<tr>
<th>Disease Group/Name/Condition</th>
<th>2013 Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autoimmune</td>
<td></td>
</tr>
<tr>
<td>Catastrophic antiphospholipid syndrome</td>
<td>II</td>
</tr>
<tr>
<td>Cryoglobulinemia</td>
<td>I</td>
</tr>
<tr>
<td>Pemphigus vulgaris</td>
<td>III</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
<td></td>
</tr>
<tr>
<td>Manifestations other than nephritis</td>
<td>NC</td>
</tr>
<tr>
<td>Severe</td>
<td>II</td>
</tr>
<tr>
<td>Nephritis</td>
<td>IV</td>
</tr>
<tr>
<td>Hematologic</td>
<td></td>
</tr>
<tr>
<td>ABO-incompatible hematopoietic progenitor cell transplantation</td>
<td>II</td>
</tr>
<tr>
<td>Aplastic anemia</td>
<td>III</td>
</tr>
<tr>
<td>Pure red blood cell aplasia</td>
<td>III</td>
</tr>
<tr>
<td>Autoimmune hemolytic anemia:</td>
<td></td>
</tr>
<tr>
<td>Warm autoimmune hemolytic anemia</td>
<td>III</td>
</tr>
<tr>
<td>Cold agglutinin disease</td>
<td>II</td>
</tr>
<tr>
<td>Coagulation factor inhibitors</td>
<td>IV</td>
</tr>
<tr>
<td>Hyperviscosity in monoclonal gammopathies</td>
<td>I</td>
</tr>
</tbody>
</table>

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 4. American Society for Apheresis New Indications in 2016

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

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

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

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:
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“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;
- Leukopheresis 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.”

ONGOING AND UNPUBLISHED CLINICAL TRIALS
Some currently unpublished trials that might influence this review are listed in Table 5.

Table 5. Summary of Key Trials

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

NCT: national clinical trial.

References
Cooperative Multiple Sclerosis Study Group. Lancet. Feb 23 1991;337(8739):441-446. PMID 1671468
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**Policy History**

<table>
<thead>
<tr>
<th>Date</th>
<th>Event</th>
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<tr>
<td>03/05/2010</td>
<td>Medical Policy Committee approval</td>
</tr>
<tr>
<td>03/19/2010</td>
<td>Medical Policy Implementation Committee approval. New policy.</td>
</tr>
<tr>
<td>03/03/2011</td>
<td>Medical Policy Committee review</td>
</tr>
<tr>
<td>03/16/2011</td>
<td>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 systemic lupus erythematosus bullet in the investigational statement.</td>
</tr>
<tr>
<td>03/01/2012</td>
<td>Medical Policy Committee review</td>
</tr>
<tr>
<td>03/21/2012</td>
<td>Medical Policy Implementation Committee approval. Added a new investigational indication. SLE 03/07/2013  Medical Policy Committee review</td>
</tr>
<tr>
<td>03/20/2013</td>
<td>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.</td>
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<tr>
<td>03/06/2014</td>
<td>Medical Policy Committee review</td>
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<tr>
<td>03/19/2014</td>
<td>Medical Policy Implementation Committee approval. No change to coverage.</td>
</tr>
<tr>
<td>08/03/2015</td>
<td>Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.</td>
</tr>
<tr>
<td>09/03/2015</td>
<td>Medical Policy Committee review</td>
</tr>
<tr>
<td>09/23/2015</td>
<td>Medical Policy Implementation Committee approval. Added neuromyelitis optica to list of INV conditions.</td>
</tr>
<tr>
<td>09/08/2016</td>
<td>Medical Policy Committee review</td>
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</table>
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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
11/07/2019 Medical Policy Committee review
12/10/2019 Coding update
Next Scheduled Review Date: 11/2020

Coding

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

<table>
<thead>
<tr>
<th>Code Type</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>36456, 36514</td>
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<tr>
<td>HCPCS</td>
<td>No codes</td>
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<tr>
<td>ICD-10 Diagnosis</td>
<td>A41.0-A41.9, A81.1-A81.2, A83.1-A83.5, C88.0, C90.0, D59.0-D59.9, D61.0-D61.9, D68.0-D68.9, D68.61, D69.0-D69.9, D89.1-D89.2, D89.89, E05.0-E05.9, E88.0-E88.9, G12.21, G13.0-G13.1, G25.4-G25.5, G36.0, G60.1, G61.81-G61.82, G62, G70.0-G70.9, G72.41, J45.2-J45.9, K72.00-K72.01, L10.0, L10.8, L94.0-L94.3, M05.1-M05.4, M31.0, M31.30-M31.31, M32.0-M32.9, M33.0-M33.9, N05.6, N08, O14.20-O14.24, P55.1, Q87.80-Q87.89, R53.82, T40.7-T40.9, T62.0, T80.30-T80.39, T86.1, Z94.1, Z94.3</td>
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<td>Codes added eff 1/1/2020: D81.31-D81.39</td>
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*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

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Plasma Exchange (PE)

Policy #  00249
Original Effective Date:  03/19/2010
Current Effective Date:  11/13/2019

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 the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated 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.

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