



Division: Pharmacy Policy	Subject: Prior Authorization Criteria IVIG and SCIG
Original Development Date: Original Effective Date: Revision Date:	June 6, 2013, June 19, 2014, November 18, 2014, April 21, 2016, July 20, 2017, September 10, 2020, October 2, 2020, January 13, 2021, September 28, 2021, December 8, 2021

Immune Globulins- IVIG and SCIG

Florida Medicaid Prescribed Drug Services requires prior authorization for all Immune Globulin (IVIG and SCIG) claims.

GENERAL NOTES ON COVERAGE:

Florida Medicaid covers immune globulin therapy that is medically necessary and proven effective for treatment of specific humoral immunodeficiencies and certain covered conditions (listed below).

- The use of immune globulin therapy (including dosage, frequency, site of administration, and duration of therapy) must be clinically appropriate and supported by evidence-based literature.
- Adjustment(s) of dosage, frequency, site of administration, and duration of therapy must be reasonable and appropriate based on condition and severity, alternative available treatments, and previous response to immune globulin therapy.
- The use of immune globulin therapy will not be approved for any use that is considered investigational, is unproven and/or is not supported by evidence-based literature.

GENERAL ELIGIBILITY CRITERIA:

Medically necessary immune globulin is authorized when General Eligibility Criteria (below) and relevant Condition-Specific Criteria are met:

1. Medical record documentation confirms the recipient has been definitively diagnosed (by an appropriate specialist) with one of the Covered Conditions listed below;
2. The diagnosis is confirmed by evidence-based diagnostic criteria (supported by peer-reviewed, published literature) and supportive testing, and clearly documented in clinical notes;
3. The recipient is closely followed by the prescribing specialist, and treatment response has clearly defined endpoints to measure effectiveness;
4. The use (including requested frequency and dosage) of immunoglobulin is supported by evidence-based literature.

LENGTH OF AUTHORIZATION:

Varies per indication, please refer to chart.

CLINICAL NOTES:

Immune globulin therapy is derived from the pooled plasma of thousands of donors and contains primarily ($\geq 98\%$) human immunoglobulin G (IgG) with trace amounts of IgA and IgM. The products differ by route of administration (intravenous (IV) or subcutaneous (SC)), specific titers of each IgG subclass, viral inactivation processes, and additives such as sucrose and sodium. While all immune globulins have comparable efficacy in the treatment of immune deficiencies, the products are not interchangeable. Selection of product should take into consideration various patient factors including diagnosis, past history and individual comorbidities.

Florida Medicaid will cover immune globulin therapy for the following conditions based on specified requirements:



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1. Alloimmune Conditions

- a. Fetal alloimmune thrombocytopenia (FAIT)
- b. Neonatal alloimmune thrombocytopenia (NAIT)
- c. Neonatal hemochromatosis
- d. Post-transfusion purpura

2. Autoimmune Disorders

- a. Acquired red cell aplasia
- b. Autoimmune Hemolytic Anemia
- c. Autoimmune mucocutaneous blistering diseases
 - i. Pemphigus vulgaris
 - ii. Pemphigus foliaceus
 - iii. Bullous pemphigoid
 - iv. Mucous membrane pemphigoid
 - v. Epidermolysis bullosa acquisita
- d. Autoimmune Neutropenia
- e. Immune or idiopathic thrombocytopenic purpura (ITP)
- f. Kawasaki Disease
- g. Lambert-Eaton myasthenic syndrome

3. Collagen-vascular diseases

- a. Dermatomyositis

4. Immunodeficiency Disorders or Diseases caused by Immunodeficiency Disorders

- a. HIV-associated thrombocytopenia, pediatric or adult
- b. Pediatric Human Immunodeficiency Virus (HIV) Infection
- c. Primary Humoral Immunodeficiency Syndromes
 - i. CVID (Common Variable Immunodeficiency)
 - ii. Congenital agammaglobulinemia
 - iii. Hyper IgM syndromes
 - iv. Hypogammaglobulinemia
 - v. IgM (X-linked Immunodeficiency with Hyperimmunoglobulin)
 - vi. Immunodeficiency with thymoma (Good syndrome)
 - vii. SCID (Severe Combined Immunodeficiency)
 - viii. Selective IgG subclass deficiencies
 - ix. Wiscott-Aldrich Syndrome
 - x. X-linked Agammaglobulinemia

5. Infectious

- a. Enteroviral meningoencephalitis
- b. Parvovirus B19 infection, chronic, with severe anemia
- c. Staphylococcal toxic shock syndrome
- d. Toxic epidermal necrolysis/Stevens Johnson syndrome
- e. Toxic shock syndrome or toxic necrotizing fasciitis due to group A streptococcus



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6. Malignancies

- a. B-cell chronic lymphocytic leukemia (CLL)
- b. Hematological malignancy patients who are immunosuppressed
- c. Multiple Myeloma
- d. Bone marrow transplant
- e. Paraneoplastic opsoclonus-myoclonus-ataxia associated with neuroblastoma

7. Neurological Disorders

- a. Chronic Inflammatory Demyelinating Polyneuropathy
- b. Guillain-Barré Syndrome
- c. Multifocal motor neuropathy
- d. Myasthenia Gravis
- e. Opsoclonus Myoclonus Syndrome
- f. Polymyositis
- g. Rasmussen's encephalitis
- h. Relapsing-Remitting Multiple Sclerosis

8. Transplantation

- a. Renal transplantation from live donor with ABO incompatibility or positive crossmatch
- b. Solid organ transplant recipients who are iatrogenically immunosuppressed to reduce risk of recurrent bacterial or viral infections
- c. Solid organ transplantation recipients prior to transplant to suppress anti-human leukocyte antigens (HLA) antibodies
- d. Solid organ transplant recipients for treatment of antibody mediated rejection of solid organ transplants
- e. Stem cell or bone marrow transplant recipients receiving an allogeneic or syngeneic transplant.

Condition	Indications
Autoimmune hemolytic anemia, refractory	Warm-type autoimmune hemolytic anemia that does not respond to corticosteroids or splenectomy, or those with contraindications to these treatments Initial Approval : 5 weeks
Autoimmune Mucocutaneous Blistering Diseases –pemphigus vulgaris, pemphigus foliaceus, bullous pemphigoid, mucous membrane pemphigoid, epidermolysis bullosa acquisita	<ol style="list-style-type: none"> 1. The diagnosis has been proven by biopsy and confirmed by pathology report; AND 2. The condition is rapidly progressing, extensive or debilitating; AND 3. Corticosteroids, immuno-suppressive agents have failed or the patient has experienced significant complications from standard treatment, such as diabetes or steroid-induced osteoporosis. Initial Approval: 6 months
Bacterial infection in HIV-infected children	Consistent with recommendations of the Working Group on Antiretroviral Therapy of the National Pediatric HIV Resource Center immune globulin is considered medically necessary in children with HIV-infection who meet any of the following criteria: <ol style="list-style-type: none"> 1. Those with hypogammaglobulinemia, i.e., serum IgG concentration less than 250 mg/dL; 2. Those with recurrent serious bacterial infections, i.e., defined as two or more infections such as bacteremia, meningitis, or pneumonia in a 1-year period;



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	<ol style="list-style-type: none"> 3. Those who fail to form antibodies to common antigens, such as measles, pneumococcal, and/or Haemophilus influenzae type b vaccine; 4. Those living in areas where measles is highly prevalent and who have not developed an antibody response after two doses of measles, mumps, and rubella virus vaccine live; 5. Single dose for HIV-infected children who are exposed to measles; 6. HIV-infected children with chronic bronchiectasis that is suboptimally responsive to antimicrobial and pulmonary therapy. <p>Initial Approval: 1 year</p>
Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)	<p>Symmetric or focal neurologic deficits with slowly progressive or relapsing course over 2 months or longer (with neurophysiological abnormalities).</p> <p><u>Note:</u> A meta-analysis comparing the efficacy of immune globulin, plasma exchange, and oral glucocorticoids found equivalence between all three, at least within the first 6 weeks of therapy (Van Schaik et al, 2002). Immune globulin is considered under accepted guidelines as the preferred treatment, particularly in children, when there is difficulty with venous access for plasmapheresis, and those susceptible to the complications of long-term corticosteroid therapy (Orange et al, 2006). Persons typically respond to immune globulin or plasma exchange within the first several weeks of treatment and may demonstrate sustained improvement for many weeks or months. Relapses may require periodic isolated treatments with a single dose of immune globulin or single plasma exchange. If a person responds successfully to infrequent booster treatments of either immune globulin or plasma exchange, it is considered medically necessary to prescribe maintenance therapy with immune globulin to prevent relapse, rather than adding corticosteroids or other immunosuppressants.</p> <p>Initial Approval: 3 months</p>
Chronic Lymphocytic Leukemia (CLL)	<p>CLL patients with IgG level less than 600 mg/dL; AND</p> <ol style="list-style-type: none"> 1. One severe bacterial infection within preceding 6 months or 2 or more bacterial infections in 1 year; OR 2. Evidence of specific antibody deficiency. <p>Initial Approval: 1 year</p>
Dermatomyositis, Polymyositis (includes juvenile)	<p>Patients presenting at least one item from the 1st criterion (skin lesions) and four items from the 2nd through 9th criteria are said to have dermatomyositis. Patients presenting no items from the 1st criterion and at least four items from the 2nd through 9th criteria are said to have polymyositis.</p> <ol style="list-style-type: none"> 1. Skin lesions <ol style="list-style-type: none"> a. Heliotrope rash (red purple edematous erythema on the upper eyelid) b. Gottron's sign (red purple keratotic, atrophic erythema, or macules on the extensor surface of finger joints) c. Erythema on the extensor surface of extremity joints: slightly raised red purple erythema over elbows or knees 2. Proximal muscle weakness (upper or lower extremity and trunk) 3. Elevated serum CK (creatin kinase) or aldolase level 4. Muscle pain on grasping or spontaneous pain 5. Myogenic changes on EMG (short duration, polyphasic motor unit potentials with spontaneous fibrillation potentials) 6. Positive anti-Jo-1 (histidyl tRNA synthetase) antibody 7. Non-destructive arthritis or arthralgias



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	<ol style="list-style-type: none"> 8. Systemic inflammatory signs (fever: more than 37°C at axilla, elevated serum CRP level or accelerated erythrocyte sedimentation rate (ESR) of more than 20 mm/h by the Westergren method) 9. Pathological findings compatible with inflammatory myositis (inflammatory infiltration of skeletal evidence of active regeneration may be seen) AND patient has severe active illness AND patient is intolerant or refractory to 1st and 2nd line therapies: 1st line therapy - Corticosteroids (e.g., prednisone); 2nd line therapy - Immunosuppressants (e.g., methotrexate, azathioprine, cyclophosphamide, and cyclosporine). <p>Initial Approval: 1 year</p>
Enteroviral meningoencephalitis	In severe cases lacking other therapeutic options Initial Approval: 6 months
Fetal Alloimmune Thrombocytopenia (FAIT)	At 20 weeks or later of pregnancy, cordocentesis reveals fetal platelets less than $20 \times 10^3/\mu\text{L}$ OR Mother has had previous pregnancy affected by FAIT Initial Approval: approval should cover the pregnancy term
Guillain Barré syndrome (GBS)	<ol style="list-style-type: none"> 1. Severe GBS with significant weakness such as inability to stand or walk without aid, respiratory or bulbar weakness, or Miller-Fisher syndrome (MFS); AND 2. The disorder has been diagnosed during the first 2 weeks of the illness; AND 3. Immune globulin is initiated within one month of symptom onset. <u>Note:</u> Based on the 2003 American Academy of Neurology (AAN) guidelines, immune globulin should usually be initiated within 2 weeks and no longer than 4 weeks of onset of neuropathic symptoms. <p>Initial Approval: 5 days</p>
Hematopoietic Stem Cell Transplant (HSCT) or Bone Marrow Transplant (BMT)	Prophylaxis in allogeneic (related donor) or syngeneic (twin donor) transplant recipients within the first 100 days post-transplant After 100 days post-transplant, for patients who are markedly hypogammaglobulinemic (IgG less than 400 mg/dL), who have a primary immunodeficiency disease, or who have Epstein-Barr virus (EBV) or Respiratory Syncytial Virus (RSV) infection Corticosteroid-resistant graft versus host disease (GVHD) in patients 20 years of age or older in the first 100 days post-transplant and who are hypogammaglobulinemic (IgG level less than 400 mg/dL) Initial Approval: 1 year
HIV-associated thrombocytopenia- Adults	<ol style="list-style-type: none"> 1. Significant bleeding in thrombocytopenic patients or platelet count less than $20,000/\mu\text{L}$; AND 2. Failure of RhIG in Rh-positive patients. <p>Initial Approval: 6 months</p>
HIV-associated thrombocytopenia- Pediatric	Infants and children less than 13 years of age whose IgG level is less than 400 mg/dL; and <ol style="list-style-type: none"> 1. Two or more bacterial infections in a 1-year period despite antibiotic chemoprophylaxis with TMP-SMZ or another active agent; OR 2. Child has received 2 doses of measles vaccine and lives in a region with a high prevalence of measles; OR 3. Child has HIV-associated thrombocytopenia despite anti-retroviral therapy; OR 4. Child has chronic bronchiectasis that is suboptimally responsive to antimicrobial and pulmonary therapy; OR



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	5. CD4 cell count is greater than or equal to 200/mm ³ Initial Approval: 1 year
Idiopathic (or Immune) Thrombocytopenic Purpura (ITP)- Adults	1. Other causes of thrombocytopenia have been ruled out by history and peripheral smear; AND Patient is unresponsive to corticosteroid therapy; AND Requires management of acute bleeding due to severe thrombocytopenia (platelet counts less than 30,000/μL); OR 2. To increase platelet counts prior to invasive major surgical procedures (e.g., splenectomy), OR 3. To defer or avoid splenectomy; OR 4. In members with severe thrombocytopenia (platelet counts less than 20,000/μL) considered to be at risk for intra-cerebral hemorrhage. Initial Approval: 5 days
Idiopathic (or Immune) Thrombocytopenic Purpura (ITP)- Pediatric	<u>Acute ITP:</u> 1. Immune globulin as initial therapy if platelet count less than 20,000/μL, especially when the patient has emergency bleeding or is at risk for severe life-threatening bleeding; OR 2. Patients with severe thrombocytopenia (platelet counts less than 20,000/μL) considered to be at risk for intracranial hemorrhage (Note: immune globulin is not indicated if patient has only mild manifestations of bleeding) <u>Chronic ITP:</u> In high-risk patients when the platelet count is low or patient is symptomatic; AND 1. Failure of other therapies, OR 2. Patient is a high risk for post-splenectomy sepsis. Initial Approval: 5 days
Idiopathic (or Immune) Thrombocytopenic Purpura, Chronic Refractory	1. Age of 10 years or older; AND 2. Duration of illness of greater than 6 months; AND 3. No concurrent illness/disease explaining thrombocytopenia; AND 4. Prior treatment with corticosteroids and splenectomy has failed OR patient is at high-risk for post-splenectomy sepsis. Initial Approval: 6 months
Immune Thrombocytopenic Purpura (ITP) in Pregnancy	1. Refractory to steroids with platelet counts less than 10,000/μL in the 3rd trimester; OR 2. Platelet counts less than 30,000/μL associated with bleeding before vaginal delivery or C-section; OR 3. Pregnant women who have previously delivered infants with autoimmune thrombocytopenia; OR 4. Pregnant women who have platelet counts less than 50,000/μL during the current pregnancy; OR 5. Pregnant women with past history of splenectomy Initial Approval: Should correspond to pregnancy term
Immunosuppressed Patients	To prevent or modify recurrent bacterial or viral infections in patients with iatrogenically induced, or disease associated immunosuppression (IgG less than 400 mg/dL) with one of the following: 1. Solid organ transplants or extensive surgery with immunosuppression (<u>Note:</u> In particular, immune globulin may be medically necessary in persons undergoing



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	<p>multiple courses of plasmapheresis as a treatment for allograft rejection or for other indications; these persons may receive immune globulin at the completion of therapy if their IgG level is less than 400 mg/dL); OR</p> <ol style="list-style-type: none"> 2. Hematological malignancy; OR 3. Collagen-vascular disease. <p>Initial Approval: 1 year</p>
Kawasaki Disease (Mucocutaneous Lymph Node Syndrome [MCLS])	<p>Diagnosis must be established -- no specific lab test -- diagnosis is established by meeting the following criteria:</p> <ol style="list-style-type: none"> 1. Fever present for at least 5 days; AND 2. Four of the following 5 conditions are met: <ol style="list-style-type: none"> a. Mucous membrane changes such as a red tongue and dry fissured lips; b. Swelling of the hands and feet; c. Enlarged lymph nodes in the neck; d. Diffuse red rash covering most of the body; e. Redness of the eyes. <p>Initial Approval: 1 year</p>
Lambert-Eaton Myasthenic Syndrome (LEMS)	<p>No response to anti-cholinesterases and dalfampridine (Ampyra); AND</p> <ol style="list-style-type: none"> 1. Used as an alternative to plasma exchange if weakness is severe; OR 2. When there is difficulty with venous access for plasmapheresis. <p>Initial Approval: 3 months</p>
Myasthenia Gravis	<p>Treatment of acute myasthenic crisis with decompensation (respiratory failure, or disabling weakness requiring hospital admission); AND other treatments have been unsuccessful or are contraindicated (e.g., azathioprine, cyclosporine, and cyclophosphamide).</p> <p><u>Note:</u> For management of acute myasthenic crises, immune globulin is administered over 2 to 5 days. Use of immune globulin as maintenance therapy is considered experimental and investigational.</p> <p>Initial Approval: 1 year</p>
Multifocal Motor Neuropathy with Conduction Block	<p>Progressive, symptomatic multifocal motor neuropathy that has been diagnosed on the basis of electrophysiologic findings that rule out other possible conditions that may not respond to immune globulin treatment</p> <p>Initial Approval: 1 year</p>
Multiple Myeloma	<ol style="list-style-type: none"> 1. "Plateau Phase" multiple myeloma (greater than 3 months since diagnosis); AND 2. IgG level less than 600 mg/dL; AND 3. Two or more significant infections in last year or a single life-threatening infection; <p>OR</p> <p>Evidence of specific antibody deficiency</p> <p>Initial Approval: 1 year</p>
Multiple Sclerosis (MS)-Relapsing-Remitting (not primary or secondary progressive MS)	<ol style="list-style-type: none"> 1. Severe manifestations of relapsing-remitting MS (not primary or secondary progressive MS); AND 2. Standard FDA approved therapies (i.e., interferons, glatiramer, etc) have failed, become intolerable, or are contraindicated <p>Initial Approval: 1 year</p>
Neonatal Hemochromatosis	<p>Pregnant women who have a history of pregnancy ending with documented neonatal hemochromatosis (Note: Dosage should be 1 mg/kg weekly from the 18th week until the end of pregnancy)</p> <p>Initial Approval: 6 months</p>



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Neonatal Alloimmune Thrombocytopenia (NAIT)	Thrombocytopenia (< 30,000/ μ L) AND Failure, intolerance, or contraindication to platelet transfusion Initial Approval: 1 month
Neuroblastoma associated paraneoplastic opsoclonus-myoclonus-ataxia syndrome	Opsoclonus-myoclonus-ataxia syndrome in patients diagnosed with neuroblastoma Initial Approval: 6 months
Opsoclonus-myoclonus	Last resort treatment for refractory opsoclonus-myoclonus Initial Approval: 6 months
Parvovirus B19 infection (Erythrovirus), Chronic with severe anemia (pure red cell aplasia)	Severe, refractory anemia with documented Parvo B19 (erythrovirus) viremia Initial Approval: 3 months
Post-transfusion purpura (PTP)	1. Decreased platelets (usually less than 10,000/ μ L); AND 2. Two to 14 days post-transfusion with bleeding. Initial Approval: 5 days
Primary Humoral Immunodeficiencies: 1. Selective IgM Immunodeficiency 2. Congenital hypogammaglobulinemia 3. Immunodeficiency with near/normal IgM (absent IgG, IgA) – a.k.a. Hyper IgM syndrome 4. Other deficiency of humoral immunity 5. Combined immunodeficiency disorders (e.g., X-SCID, jak3, ZAP70, ADA, PNP, RAG defects, Ataxia Telangiectasia, DiGeorge syndrome, common variable immunodeficiency)	1. Agammaglobulinemia (total IgG less than 200 mg/dL or infants with BTK gene and/or absence of B lymphocytes); OR 2. Persistent hypogammaglobulinemia (total IgG less than 400 mg/dL or two standard deviations below the mean for age) with recurrent bacterial infections and/or lack of response to protein or polysaccharide antigens (inability to make IgG antibody against diphtheria and tetanus toxoids, pneumococcal polysaccharide vaccine, or both- see notes below): a. Serum antibody titers to tetanus and/or diphtheria should be obtained prior to immunization with diphtheria and/or tetanus vaccine and 3 to 4 weeks after immunization. The protective level for diphtheria is 0.01 to 0.1 international units/mL and for tetanus greater than 0.1 international units/mL. If post vaccination titers are above these levels, the patients response to protein antigens is normal b. Serum antibody titers to pneumococcus should be measured prior to immunization and 4 to 6 weeks after immunization with polyvalent pneumococcal polysaccharide vaccine (e.g., Pneumovax). A normal response to pneumococcus for children from 24 months to 5 years of age is a conversion of 50% or more of the serotypes tested. For persons aged 6 years of age and older, a normal response is defined as conversion of 70% of the serotypes tested. A normal response for a single serotype present in a pneumococcal vaccine is defined as the conversion from a non-protective to a protective titer. A protective (normal or adequate) response to each pneumococcal serotype is defined as a titer equal to or greater than 1.3 mcg/mL antibody. (Note: When reported, the conversion factor for nanograms of antibody nitrogen per milliliter (ng N/mL) to antibody micrograms per milliliter is as follows: 160 ng N/mL - 1.0 mcg/mL); or 3. Selective IgG subclass deficiencies (see criteria in section of selective IgG subclass deficiency below); OR 4. Normal total IgG levels with severe polysaccharide non-responsiveness and evidence of recurrent severe difficult-to-treat infections (e.g., recurrent otitis media, bronchiectasis, recurrent infections requiring IV antibiotics, multiple antibiotic



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hypersensitivities, chronic or recurrent sinusitis) with a documented requirement for antibiotic therapy:

- a. Patient has unexplained recurrent or persistent severe bacterial infections despite adequate treatment, including all of the following:
 1. Aggressive management of other conditions predisposing to recurrent sinopulmonary infections (e.g., asthma, allergic rhinitis);
 2. Prophylactic antibiotics;
 3. Increased vigilance and appropriate antibiotic therapy for infections; and
 4. Immunization with conjugate vaccines in patients who have not responded to polysaccharide vaccines.
- b. Serum antibody titers to pneumococcus should be measured prior to immunization and 4 to 6 weeks after immunization with polyvalent pneumococcal polysaccharide vaccine (e.g., Pneumovax); at least 14 polysaccharide antigens should be tested.
- c. Polysaccharide non-responsiveness is defined as lack of protective antibody titer (specific IgG antibody titer less than 1.3 mcg/ml) in greater than 70 % of antigens tested (more than 50 % in children aged 2 to 5 years).
- d. Further evidence of infection, including sinus and lung imaging, complete blood counts, C-reactive protein measurement, and erythrocyte sedimentation rate (ESR) determination, may be required to support the need for immune globulin supplementation.
- e. For children 12 years of age or younger with normal total IgG levels and severe polysaccharide nonresponsiveness, immune globulin should be discontinued, and the medical necessity of immune globulin should be re-evaluated 1 year after initiating therapy and every 2 years thereafter by reassessing immune response to protein and polysaccharide antigens. Immune response should be re-evaluated at least 3 months after discontinuation of immune globulin. Immune globulin should also be discontinued at that time if the number and/or severity of infections have not been reduced, as not all persons with polysaccharide nonresponsiveness benefit from immune globulin.

The use of immune globulin may not be beneficial in certain secondary immunodeficiency states; correction of the underlying condition is the preferred approach.

Initial Approval: 1 year

Rasmussen Encephalitis

For children whose symptoms do not improve with anti-epileptic drugs and corticosteroids

Initial Approval: 1 month

Selective IgG Subclass Deficiency

1. Deficiency of one or more IgG subclasses to levels less than 2 standard deviations below the age-specific mean (see table below). These levels should be assessed on at least two occasions while the patient is free of infections; **AND**
2. Member has unexplained recurrent or persistent severe bacterial infections despite adequate treatment, including **ALL** the following:
 - a. Aggressive management of other conditions predisposing to recurrent sinopulmonary infections (e.g., asthma, allergic rhinitis);



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	<ul style="list-style-type: none"> b. Prophylactic antibiotics; c. Increased vigilance and appropriate antibiotic therapy for infections; and d. Immunization with conjugate vaccines in patients who have not responded to polysaccharide vaccines; AND <p>3. Member has demonstrated an inability to mount an adequate response to protein and polysaccharide antigens, as determined by the following criteria:</p> <ul style="list-style-type: none"> a. Member has documented inability to mount an antibody response to protein antigens: Serum antibody titers to tetanus and/or diphtheria should be obtained prior to immunization with diphtheria and/or tetanus vaccine and 3 to 4 weeks after immunization. An inadequate response is defined as a post vaccination titer less than 0.1 international units/mL for diphtheria, and 0.1 international units/mL or less for tetanus; and b. Member has documented inability to mount an adequate antibody response to polysaccharide antigens. Serum antibody titers to at least 14 pneumococcus serotypes should be measured prior to immunization and 4 to 6 weeks after immunization with polyvalent pneumococcal polysaccharide vaccine (e.g., Pneumovax). An inadequate response is defined as lack of protective antibody titer (i.e., specific IgG concentration less than 1.3 mcg/mL) in at least 70 % of serotypes tested (in at least 50 % of serotypes tested in children aged 2 to 5 years) <p><u>Note:</u> Response to polysaccharide antigens is not reliable in children less than 2 years of age.</p> <p>4. In children 12 years of age or younger only, 1 year after initiating therapy, immune globulin should be discontinued and the medical necessity of immune globulin should be re-evaluated and every 2 years thereafter by re-assessing immune response to protein and polysaccharide antigens. Immune response should be re-evaluated at least 3 months after discontinuation of immune globulin. Immune globulin should also be discontinued at that time if the number and/or severity of infections have not been reduced, as not all persons with selective IgG subclass deficiencies benefit from immune globulin.</p> <p>Initial Approval: 1 year</p>
Staphylococcal Toxic Shock Syndrome	Severe cases of toxic shock syndrome that have not responded to fluids and vasopressors Initial Approval: 1 month
Toxic epidermal necrolysis and Stevens-Johnson syndrome	Severe cases of toxic epidermal necrolysis and Stevens-Johnson syndrome Initial Approval: 3 months
Toxic shock syndrome or toxic necrotizing fasciitis due to group A streptococcus	Patients who are sufficiently ill to require critical care unit support and have documented presence of fasciitis and microbiological data consistent with invasive streptococcal infection (culture or Gram stain) Initial Approval: 1 month



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The laboratory's own reference ranges should be used, where available. If the laboratory's reference ranges are not submitted with the immunoglobulin level results, the following standard reference ranges may be applied:

Normal Immunoglobulin Levels (mg/dl)				Normal IgG Subclass Levels (mg/dl)				
AGE	IgA	IgG	IgM	AGE	IgG1	IgG2	IgG3	IgG4
1 - 2 mo	1 - 53	251 - 906	20 - 87	cord	435 - 1084	143 - 453	27 - 146	1 - 47
2 - 3 mo	3 - 47	206 - 601	17 - 105	0 - 3 mo	218 - 496	40 - 167	4 - 23	1 - 33
3 - 4 mo	4 - 73	176 - 581	24 - 101	3 - 6 mo	143 - 394	23 - 147	4 - 100	1 - 14
4 - 5 mo	8 - 84	172 - 814	33 - 108	6 - 9 mo	190 - 388	37 - 60	12 - 62	1 - 1
5 - 6 mo	8 - 68	215 - 704	35 - 102	9 mo - 3 yr	286 - 680	30 - 327	13 - 82	1 - 65
6 - 8 mo	11 - 90	217 - 904	34 - 125	3 - 5 yr	381 - 884	70 - 443	17 - 90	1 - 116
8 mo - 1 yr	16 - 84	294 - 1069	41 - 149	5 - 7 yr	292 - 816	83 - 513	8 - 111	1 - 121
1 - 2 yr	14 - 106	345 - 1213	43 - 173	7 - 9 yr	442 - 802	113 - 480	15 - 133	1 - 84
2 - 3 yr	14 - 123	424 - 1051	48 - 168	9 - 11 yr	456 - 938	163 - 513	26 - 113	1 - 121
3 - 4 yr	22 - 159	441 - 1135	47 - 200	11 - 13 yr	456 - 952	147 - 493	12 - 179	1 - 168
4 - 6 yr	25 - 154	463 - 1236	43 - 196	13 - 15 yr	347 - 993	140 - 440	23 - 117	1 - 183
6 - 9 yr	33 - 202	633 - 1280	48 - 207	15 yr & up	422 - 1292	117 - 747	41 - 129	1 - 291
9 - 11 yr	45 - 236	608 - 1572	52 - 242					
11 yr & up	70 - 312	639 - 1349	56 - 352					

DOSING AND ADMINISTRATION:

- Refer to product labeling at <https://www.accessdata.fda.gov/scripts/cder/daf/>



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Immune globulin therapy is considered experimental and investigational for any of the following conditions (alphabetical):

Hematologic/Oncologic Disorders	Immunologic Disorders	Infectious Disorders	Neurologic Disorders	Rheumatologic Disorders	Other Disorders
Acute lymphoblastic leukemia (ALL)	Cellular immunodeficiencies without IgG deficiencies	Chronic mucocutaneous candidiasis (CMCC)	Amyotrophic lateral sclerosis (ALS)	Behçet's syndrome	Adrenoleukodystrophy
Aplastic Anemia	Complement deficiencies	Chronic sinusitis	Demyelinating optic neuritis	Inclusion body myositis	Asthma
Diamond-Blackfan anemia	Selective IgA deficiency without IgG or IgG subclass deficiency, and impaired antibody response to vaccination	Lyme disease	Epilepsy	Rheumatoid arthritis	Atopic dermatitis
Red cell aplasia (except as noted above due to parvovirus in the setting of immunocompromise)		Post-infectious sequelae	Myasthenia gravis-chronic management	Scleroderma	Chronic fatigue syndrome
Thrombotic thrombocytopenic pupura		Recurrent otitis media	Primary progressive, secondary progressive or progressive relapsing Multiple Sclerosis	Systemic Lupus Erythematosus (SLE)	Cystic Fibrosis
Hemolytic uremia syndrome		Rheumatic fever	Pediatric autoimmune Neuropsychiatric Disorder associated with Streptococcal Infection (PANDAS), Pediatric Acute-Onset Neuropsychiatric Syndrome (PANS) Alzheimer's Disease Autism	Vasculitides other than Kawasaki Disease	Diabetes Mellitus Idiopathic environmental illness Organ transplant-cellular rejection Recent onset dilated cardiomyopathy Recurrent fetal loss Recurrent Spontaneous Abortion or recurrent spontaneous pregnancy loss



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Brand of Immune Globulin	FDA-Approved Indications
Asceniv (intravenous)	Primary humoral immunodeficiency
Bivigam (intravenous)	Primary humoral immunodeficiency
Carimune NF (intravenous)	Primary immunodeficiencies, immune thrombocytopenic purpura
Cutaquig (subcutaneous)	Primary humoral immunodeficiency
Cuvitru (subcutaneous)	Primary immunodeficiencies
Flebogamma (intravenous)	Primary immunodeficiencies, immune thrombocytopenic purpura (10%)
Gammagard liquid (intravenous or subcutaneous)	Primary immunodeficiencies, multifocal motor neuropathy
Gammagard S/D (intravenous)	Primary immunodeficiencies, B-cell Chronic Lymphocytic Leukemia, chronic idiopathic thrombocytopenic purpura, Kawasaki syndrome
Gammaked (intravenous or subcutaneous)	Primary immunodeficiencies, immune thrombocytopenic purpura, chronic inflammatory demyelinating polyneuropathy
Gammaplex (intravenous)	Primary immunodeficiencies, chronic immune thrombocytopenic purpura (10%)
Gammar-P I.V. (intravenous)	Primary immunodeficiencies
Gamunex-C (intravenous or subcutaneous)	Primary immunodeficiencies, immune thrombocytopenic purpura, chronic inflammatory demyelinating polyneuropathy
Hizentra (subcutaneous)	Primary immunodeficiencies
HyQvia (subcutaneous with recombinant human hyaluronidase)	Primary immunodeficiency in adults
Octagam (intravenous)	Primary immunodeficiencies, idiopathic thrombocytopenic purpura, dermatomyositis
Privigen (intravenous)	Primary immunodeficiencies, immune thrombocytopenic purpura
Xembify (subcutaneous)_	Primary immunodeficiencies

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