

Intravenous Immune Globulins (Asceniv, Bivigam, Flebogamma DIF, Gammagard Liquid, Gammagard S/D, Gammaked, Gammaplex, Gamunex-C, Octagam, Panzyga, Privigen)

When requesting Intravenous Immune Globulins (Asceniv, Bivigam, Flebogamma DIF, Gammagard Liquid, Gammagard S/D, Gammaked, Gammaplex, Gamunex-C, Octagam, Panzyga, Privigen), the individual requiring treatment must be diagnosed with an FDA-approved indication or an approved off-label compendial use and meet the specific coverage guidelines and applicable safety criteria for the covered indication.

FDA-Approved Indications

Intravenous Immune globulin (IVIG) injection is indicated for the treatment of:

- Primary humoral immunodeficiency including but not limited to, congenital agammaglobulinemia, common variable immunodeficiency, x-linked agammaglobulinemia, Wiskott-Aldrich syndrome, and severe combined immunodeficiencies.
- Idiopathic thrombocytopenia purpura (ITP) to raise platelet counts to prevent bleeding or to allow a patient with ITP to undergo surgery
- Chronic inflammatory demyelinating polyneuropathy (CIDP) to improve neuromuscular disability and impairment and for maintenance therapy to prevent relapse
- Multifocal motor neuropathy (MMN) to improve muscle strength and disability
- Prevention of bacterial infections in hypogammaglobulinemia and/or recurrent bacterial infections associated with B-cell chronic lymphocytic leukemia
- Prevention of coronary artery aneurysms associated with Kawasaki syndrome

Approved Off-Label Compendial Uses

- Secondary humoral immunodeficiency
- Antibody-mediated rejection in solid organ transplant
- Autoimmune mucocutaneous blistering disease
- Cytomegalovirus (CMV) interstitial pneumonia
- Dermatomyositis or polymyositis
- Guillain-Barre syndrome
- Human immunodeficiency virus (HIV) associated thrombocytopenia
- Myasthenia gravis
- Lambert-Eaton myasthenic syndrome
- Multiple sclerosis

- Stiff-person syndrome
- Multiple myeloma
- Pure red blood cell aplasia (PRCA)
- Post-exposure prophylaxis of measles
- Post-exposure prophylaxis of varicella
- Feto-neonatal alloimmune thrombocytopenia
- For desensitization therapy prior to and immediately after solid organ transplantation
- Immunotherapy-related toxicities associated with checkpoint inhibitor therapy

Coverage Guidelines

Primary humoral immunodeficiency (PID)

Must have one of the following PID subtypes:

- Common variable immunodeficiency (CVID)
- X-linked agammaglobulinemia
- Congenital agammaglobulinemia
- Other agammaglobulinemia due to the absence of B-cells
- Severe combined immunodeficiency (SCID)
- Wiskott-Aldrich syndrome
- Hyper-Immunoglobulin M (IgM) syndromes
- IgG level lower than 250 mg/dL
- Ataxia telangiectasia
- DiGeorge syndrome
- Other combined immunodeficiencies with significant hypogammaglobulinemia
- Unspecified hypogammaglobulinemia (unspecified IgG deficiency)

For an initial authorization request:

- The requested product is prescribed by or in consultation with one of the following physician specialists: allergist, immunologist, otolaryngologist (ear, nose, and throat [ENT] physician), pulmonologist, or an infectious disease physician who treats patients with PID
- For CVID, unspecified hypogammaglobulinemia, or other combined immunodeficiencies with significant hypogammaglobulinemia indication:
 - The patient pretreatment IgG level is below the normal range (age-related and according to the normal reference range for the reporting laboratory) AND
 - The patient has an impaired antibody response (i.e., failure to produce antibodies to specific antigen) OR
 - The patient has recurrent infections OR
 - The patient has an IgG subclass deficiency or a diagnosis of selective antibody deficiency (SAD) and meets the following criteria:

- a. The patient has an impaired antibody response (i.e., failure to produce antibodies to specific antigen) AND
- b. The patient has recurrent infections

NOTE: An exception can be made for the impaired antibody response if, according to the prescriber, the delay caused by pre-vaccination and post-vaccination antibody measurement would be deleterious to the patient's health.

For re-authorization request:

- The patient has been diagnosed with a primary immunodeficiency and is continuing to receive benefit from the product (e.g., increased IgG levels, preventing or controlling infections)

Approval duration (initial and renewal): 12 months

Secondary humoral immunodeficiency:

Must have one of the following diseases/conditions:

- B-cell chronic lymphocytic leukemia
- Hematologic neoplasm-associated hypogammaglobulinemia
- Post hematopoietic stem cell transplantation
- Human immunodeficiency virus (HIV) infection in pediatrics

For B-cell chronic lymphocytic leukemia

For an initial authorization request:

- Has an immunoglobulin G (IgG) level less than 500 mg/dL OR has a history of recurrent bacterial infections AND
- The requested product is prescribed by or in consultation with an oncologist, hematologist, or infectious disease physician

For a re-authorization request:

- Is maintaining an IgG trough level of about 500 mg/dL and up to 700 mg/dL to prevent bacterial infections

Approval duration (initial): 4 months

Approval duration (renewal): 12 months

For hematologic neoplasm-associated hypogammaglobulinemia

For an initial authorization request:

- Has an immunoglobulin G (IgG) level less than 500 mg/dL AND
- Has recurrent or severe bacterial infections or has high risk of infection AND
- The requested product is prescribed by or in consultation with an oncologist, hematologist, infectious disease physician, or immunologist

For a re-authorization request:

- An individual is maintaining an IgG level of over 400 mg/dL and having a positive response to therapy (e.g., decrease in infections)

Approval duration (initial and renewal): 6 months

For post hematopoietic stem cell transplantation (HCT)

For an initial authorization request:

- Has had a HCT within the previous year AND
- Has an immunoglobulin G (IgG) level less than 500 mg/dL OR has multiple myeloma or malignant macroglobulinemia AND
- Has a significant risk of having frequent and/or severe bacterial infections AND
- The requested product is prescribed by or in consultation with a hematologist, oncologist, or infectious disease physician

For a re-authorization request:

- Needs IVIG to maintain trough IgG levels greater than 400 to 500 mg/dL AND
- Has significant risk of having frequent and/or severe bacterial infections

Approval duration (initial): 3 months

Approval duration (renewal): 6 months

HIV-Infection in pediatrics

For an initial authorization request:

- Has hypogammaglobulinemia (i.e., IgG less than 400 mg/dL) OR
- Functional antibody deficiency is demonstrated by poor specific antibody titers (i.e., does not develop specific antibody response against protein and polysaccharide antigens) OR
- Functional antibody deficiency is demonstrated by the patient having recurrent (2 or more per year) serious bacterial infections (e.g., bacteremia, meningitis, pneumonia) despite administration of combination antiretroviral therapy and appropriate antimicrobial prophylaxis AND
- Is receiving combination antiretroviral therapy AND
- Is less than 18 years of age AND
- The requested product is prescribed by or in consultation with an infectious disease specialist or an immunologist

For a re-authorization request:

- The frequency and/or severity of infections have decreased

Approval duration (initial): 6 months

Approval duration (renewal): 12 months

Chronic inflammatory demyelinating polyneuropathy (CIDP)

For an initial authorization request:

- The requested product is prescribed by or in consultation with a neurologist AND

- Electrodiagnostic studies support the diagnosis of CIDP

For a re-authorization request:

- Must have a clinically significant improvement in neurologic symptoms (e.g., improvement in disability, nerve conduction study results improved or stabilized, physical examination show improvement in neurological symptoms, strength, and sensation)

Approval duration (initial): 3 months

Approval duration (renewal): 12 months

Idiopathic (immune) thrombocytopenic purpura (ITP)

For an initial authorization request:

- The requested product is prescribed by or in consultation with a hematologist

For a pregnant patient:

- It will be given before normal vaginal delivery, cesarean section, or spinal or epidural anesthesia OR pregnant patient is in any trimester

Approval duration: 2 weeks (if given before delivery) OR 3 months (if given in any trimester)

For children and adolescents (less than or equal to 17 years of age):

- Has significant acute mucous membrane bleeding or other noncutaneous bleeding OR
- Has persistent or chronic ITP and requires IVIG to prevent bleeding OR
- Is at risk of bleeding and inaccessibility, activity level of the patient, or noncompliance is a concern OR
- Need to increase the platelet count before major surgery such as splenectomy, or before other surgery, dental extraction(s), or other procedures likely to cause blood loss

Approval duration: 12 months or 1 month (if given before surgery or for acute use)

For adults and adolescents (18 years of age or older):

Has one of the following reasons for requesting IVIG: acute bleeding, undergoing surgical/dental procedures, or persistent/chronic ITP

For acute bleeding:

- Has platelet count less than 30,000/mm³ AND
- Has tried a systemic corticosteroid (e.g., prednisone) OR
- Has an urgent need to increase the platelet count quickly and IVIG will be started with a systemic corticosteroid OR
- Has a contraindication to a systemic corticosteroid

Undergoing surgical procedures (e.g., splenectomy) or dental procedures:

- Platelet count is less than 50,000 per mm³ OR
- Platelet count is less than 75,000 per mm³ and undergoing major surgery (e.g., central nervous system or cardiac surgery)

Approval duration: 1 month

For persistent or chronic ITP

- Requires IVIG to prevent bleeding AND
- Has tried a systemic corticosteroid (e.g., prednisone) OR
- Has an urgent need to increase the platelet count quickly and IVIG will be started with a systemic corticosteroid OR
- Has a contraindication to a systemic corticosteroid

Approval duration: 12 months

For a re-authorization request:

- *For persistent or chronic ITP only:* must have responded to therapy with increased platelet count and/or absence of significant bleeding and requires additional therapy with IVIG to prevent bleeding

Approval duration: 12 months

Kawasaki disease

- The requested product is prescribed by or in consultation with a pediatric cardiologist or a pediatric infectious disease physician AND
- An individual has persistent or recurring fever or signs of inflammation at least 36 hours after completing the initial IVIG infusion(s)

Approval duration: one dose

Multifocal motor neuropathy (MMN)

For an initial authorization request:

- The requested product is prescribed by or in consultation with a neurologist

For a re-authorization request:

- An individual has improvement in neurologic symptoms

Approval duration (initial): 6 months

Approval duration (renewal): 12 months

Antibody-mediated rejection (ABMR) in solid organ transplant (e.g., kidney, heart, lung, liver)

- The requested product is prescribed by or in consultation with a physician affiliated with a transplant center

Approval duration: 12 months

Autoimmune mucocutaneous blistering diseases (pemphigus vulgaris, pemphigus foliaceus, bullous pemphigoid, mucous membrane pemphigoid, and epidermylysis bullosa acquisita)

For an initial authorization request:

- Has tried both a systemic corticosteroid and an immunosuppressive agent (e.g., azathioprine, cyclophosphamide, methotrexate, cyclosporine, mycophenolate, tacrolimus) unless contraindicated to both agents OR
- Has rapid, debilitating, progressive disease that cannot be controlled with a systemic corticosteroid and an immunosuppressive agent OR
- Has a serious disease that there is inadequate time for therapy with a systemic corticosteroid and an immunosuppressive agent to have a rapid enough effect AND
- The requested product is prescribed by or in consultation with a dermatologist

For a re-authorization request:

- An individual is responding to therapy (e.g., previous lesions are healing and there are fewer new lesions)

Approval duration (initial): 6 months

Approval duration (renewal): 12 months

Cytomegalovirus (CMV) interstitial pneumonia

- Has cancer or transplant-related infection AND
- The requested product is prescribed by or in consultation with an oncologist, hematologist, or an infectious disease physician

Approval duration: 2 months

Dermatomyositis or polymyositis

For an initial authorization request:

- Has tried a systemic corticosteroid unless contraindicated AND
- Has tried an immunosuppressive agent (e.g., azathioprine, methotrexate, cyclosporine, cyclophosphamide, mycophenolate) unless contraindicated AND
- The requested product is prescribed by or in consultation with a neurologist or a rheumatologist

For a re-authorization request:

- An individual is responding to therapy (e.g., improved muscle strength, neuromuscular symptoms, or functional ability)

Approval duration (initial): 6 months

Approval duration (renewal): 12 months

For desensitization therapy prior to and immediately after solid organ transplantation

For an initial authorization request:

- The request product is prescribed by or in consultation with physician affiliated with a transplant center

Approval duration (initial): 4 months

Approval duration (renewal): 12 months if given before transplantation OR 1 dose if given post-transplantation

Guillain Barre Syndrome (GBS)

For an initial authorization request:

- The requested product will be initiated within 2 weeks and no longer than 4 weeks of onset of neuropathic symptoms (weakness, inability to stand or walk without assistance, respiratory or bulbar weakness) OR had a relapse but had an initial response to IVIG AND
- The requested product is prescribed by or in consultation with a neurologist or a specialist with experience in diagnosing and treating patients with GBS

For a re-authorization request:

- The request is for second course of therapy (has not received more than 2 courses of therapy) AND
- Has been at least 3 weeks after the first course

Approval duration (initial and renewal): 1 month

Human Immunodeficiency Virus (HIV)-Associated Thrombocytopenia

- Is receiving combination antiretroviral therapy (cART) OR
- Has clinically significant bleeding complications AND
- The requested product is prescribed by or in consultation with an infectious disease specialist or a physician who specializes in the treatment of HIV infection

Approval duration: 1 month

Lambert-Eaton Myasthenic Syndrome (LEMS)

For an initial authorization request:

- Has paraneoplastic LEMS OR
- Has non-paraneoplastic LEMS and has tried at least one of the following: a systemic corticosteroid, azathioprine, or another immunosuppressive agent (e.g., cyclosporine, mycophenolate) OR
- Has non-paraneoplastic LEMS and has contraindications to both a corticosteroid and azathioprine and/or other immunosuppressive agents AND
- The requested product is prescribed by or in consultation with a neurologist AND

- The patient is having refractory weakness after symptomatic treatment of LEMS with an amifampridine product (e.g., Firdapse, Ruzurgi), guanidine, or pyridostigmine

For a re-authorization request:

- Has shown a response to therapy (e.g., improved muscle strength, other clinical response) or continued effectiveness

Approval duration (initial): 1 month

Approval duration (renewal): 12 months

Multiple sclerosis (MS)

For acute severe exacerbation or relapses

- Has not responded to OR had a significant adverse reaction with systemic corticosteroids OR plasma exchange OR
- Is contraindicated to a systemic corticosteroid AND
- The requested product is prescribed by or in consultation with a neurologist or physician who specializes in the treatment of MS

Approval duration: 1 month

To prevent relapses in post-partum

- Is not currently taking a disease modifying therapy (DMT) for MS (e.g., interferon beta, fingolimod, glatiramer acetate, alemtuzumab, natalizumab, teriflunomide, cladribine, siponimod, dimethyl fumarate, mitoxantrone)
- For an initial request, the requested product is prescribed by or in consultation with a neurologist or physician who specializes in the treatment of MS

Approval duration (initial and renewal): 6 months

Multiple myeloma

For an initial authorization request:

- Has severe recurrent bacterial infections AND
- The requested product is prescribed by or in consultation with a hematologist, oncologist, or infectious disease specialist

Approval duration (initial): 6 months

Approval duration (renewal): 12 months

Myasthenia Gravis

For an initial authorization request for short-term (acute) use:

- Has an exacerbation of myasthenia gravis OR
- Requires stabilization of myasthenia gravis before surgery OR
- Has started on an immunosuppressive drug (e.g., azathioprine, cyclosporine, cyclophosphamide, mycophenolate, methotrexate, tacrolimus) and is waiting for full effect OR

- Is starting therapy with a corticosteroid and IVIG is being given to prevent or minimize exacerbations AND
- The requested product is prescribed by or in consultation with a neurologist

Approval duration: 5 days

For an initial authorization request for maintenance use

- Has refractory myasthenia gravis AND
- Has tried pyridostigmine AND
- Has tried at least one of the following immunosuppressive agents and had an inadequate response: azathioprine, cyclosporine, cyclophosphamide, mycophenolate, methotrexate, tacrolimus AND
- The requested product is prescribed by or in consultation with a neurologist

Approval duration: 12 months

For a re-authorization request for maintenance use:

- Is responding to IVIG therapy

Approval duration: 12 months

Stiff-person syndrome (Moersch-Woltman Syndrome)

For an initial authorization request:

- Has tried a benzodiazepine (e.g., diazepam) or baclofen OR has contraindication to both therapy AND
- The requested product is prescribed by or in consultation with a neurologist

For a re-authorization request:

- Is responding to therapy (e.g., reduced stiffness or frequency of spasms, ability to walk unassisted)

Approval duration (initial): 3 months

Approval duration (renewal): 12 months

Pure Red Blood Cell Aplasia (PRCA)

For an initial authorization request:

- Has tried a systemic corticosteroid (e.g., prednisone) AND
- Has tried either cyclophosphamide or cyclosporine AND
- The requested product is prescribed by or in consultation with one of the following specialist: an infectious disease specialist, immunologist, hematologist, or transplant specialist

For a re-authorization request:

- Is responding to therapy with an increase in hemoglobin and reticulocytosis

Approval duration (initial and renewal): 1 month

Pure Red Blood Cell Aplasia secondary to chronic parvovirus B19 infection

For an initial authorization request:

- Has a chronic immunodeficiency condition (e.g., patients with HIV infection, solid organ transplant, chemotherapy for hematologic malignancy) AND
- Has clinically significant anemia or is transfusion dependent AND
- The requested product is prescribed by or in consultation with one of the following specialist: an infectious disease specialist, immunologist, hematologist, or transplant specialist

For a re-authorization request:

- Had a response with an increase in hemoglobin to previous IVIG therapy but had relapse when IVIG was off OR
- Had a response with an increase in hemoglobin to previous IVIG therapy and requires maintenance therapy to prevent relapse

Approval duration (initial): 2 months

Approval duration (renewal): 3 months

Passive immunization for varicella (chickenpox), post-exposure prophylaxis

- An individual is HIV-infected, immune compromised, or pregnant AND
- VariZIG (varicella zoster immune globulin [human]) is not available AND
- Does not have evidence of immunity to varicella (i.e., does not have a history of the disease or age-appropriate vaccination) AND
- The requested product is prescribed by or in consultation with an infectious disease specialist or an immunologist

Approval duration: single dose

Passive immunization for measles, post-exposure prophylaxis

- An individual is either pregnant or severely immunocompromised AND
- Has been exposed to measles and IVIG will be given within 6 days of exposure AND
- If pregnant, must not have evidence of immunity to measles (i.e., does not have a history of the disease or age-appropriate vaccination)

Approval duration: single dose

Thrombocytopenia, Feto-neonatal alloimmune

- The requested product is prescribed by or in consultation with a hematologist or an obstetrician

Approval duration: 6 months

Immunotherapy-related toxicities associated with checkpoint inhibitor therapy

For an initial authorization request:

- The patient has tried a systemic corticosteroid (e.g., prednisone, methylprednisolone) and has not adequately responded to therapy OR
- IVIG is being started with a systemic corticosteroid OR
- A corticosteroid is contraindicated

For a re-authorization request:

- The patient is having a positive response to therapy and extended therapy is required

Approval duration (initial): 1 months

Approval duration (renewal): 6 months

Dosing Recommendations

Flebogamma/Octagam

Primary immunodeficiency (PI): the recommended dose is 300 to 600 mg/kg administered every 3 to 4 weeks

Idiopathic thrombocytopenic purpura (ITP): the recommended dose is 1 g/kg administered intravenously daily for 2 consecutive days

Gammagard Liquid

PI: the recommended dose is 300 to 600 mg/kg administered intravenously every 3 to 4 weeks. For subcutaneous administration, the recommended dose is 1.37 x previous intravenous dose

Multifocal motor neuropathy (MMN): The recommended dose is 0.5 to 2.4 g/kg per month based on clinical response

Gammagard S/D

PI: the recommended dose is 300 to 600 mg/kg administered every 3 to 4 weeks

B-cell chronic lymphocytic leukemia: The recommended dose is 400 mg/kg every 3 to 4 weeks

Kawasaki syndrome: The recommended dose is a single 1 g/kg or a dose of 400 mg/kg for 4 consecutive days beginning within seven days of the onset of fever

ITP: the recommended dose is 1 g/kg. The need for additional doses can be determined by clinical response and platelet count. Up to three separate doses may be given on alternate days if required.

Gammaked/Gamunex-C

PI: the recommended dose is 300 to 600 mg/kg administered intravenously every 3 to 4 weeks. For subcutaneous administration, the recommended dose is 1.37 x current IV dose in grams/IV dose intervals in weeks

ITP: the recommended dose is 2 g/kg, divided in two doses of 1 g/kg given intravenously on two consecutive days or into five doses of 0.4 g/kg given on five consecutive days.

Chronic inflammatory demyelinating polyneuropathy (CIDP): the recommended dose is loading dose 2 g/kg administered intravenously in divided doses over 2 to 4 consecutive days following with maintenance dose of 1 g/kg is administered over 1 day or divided into 2 doses of 0.5 g/kg given on 2 consecutive days, every 3 weeks.

Gammaplex

PI: The recommended dose is 300 to 800 mg/kg administered every 3-4 weeks

ITP: The recommended dose is 1 g/kg administered intravenously for 2 consecutive days

Privigen

PI: The recommended dose is 200 to 800 mg/kg administered intravenously every 3-4 weeks

ITP: The recommended dose is 1 g/kg administered intravenously for 2 consecutive days

CIPD: The recommended dose is loading dose 2 g/kg administered intravenously in divided doses over 2 to 5 consecutive days following with maintenance dose of 1 g/kg administered in 1 to 2 infusions on consecutive days, every 3 weeks.

Panzyga

PI: The recommended dose is 300 to 600 mg/kg administered intravenously every 3-4 weeks

ITP: The recommended dose is 1 g/kg administered intravenously daily for 2 consecutive days

Bivigam

PI: The recommended dose is 300 to 800 mg/kg administered every 3-4 weeks

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