Reference number(s)
5317-A

Jurisdiction Specific Medicare Part B Intravenous Immune Globulin (IVIG)

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name
Alyglo
Asceniv
Bivigam
Flebogamma DIF
Gammagard liquid
Gammagard S/D
Gammaked
Gammaplex
Gamunex
Gamunex-C
Octagam
Panzyga
Privigen
Yimmugo

Covered Uses

The indications below are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

- Primary Humoral Immunodeficiency Syndromes including but not limited to:
  - Common Variable Immunodeficiency (CVID)
  - Congenital Agammaglobulinemia (X-Linked Agammaglobulinemia)
  - Severe Combined Immunodeficiency (SCID)

    - X-Linked Immunodeficiency with Hyperimmunoglobulin M (IgM)
    - Wiskott-Aldrich Syndrome
- Human Immunodeficiency Virus (HIV) Disease
- Guillain-Barre Syndrome
- Relapsing-Remitting Multiple Sclerosis (RRMS)
- Chronic Inflammatory Demyelinating Polyneuropathy (and variant syndromes such as multifocal motor neuropathy)
- Myasthenia Gravis
- Refractory Polymyositis
- Refractory Dermatomyositis
- Chronic Lymphocytic Leukemia (CLL)
- Hematopoietic Stem Cell Transplantation (HSCT)
- Kawasaki Disease (Mucocutaneous Lymph Node Syndrome)
- Autoimmune Hemolytic Anemia
- Autoimmune Neutropenia
- Pemphigus Vulgaris
- Pemphigus Foliaceus
- Bullous Pemphigoid
- Mucous Membrane Pemphigoid (Cicatricial Pemphigoid)
- Epidermolysis Bullosa Acquisita
- Multiple Myeloma
- Stiff-Man Syndrome/Stiff-Person Syndrome
- Hypogammaglobulinemia with NNI (Non-Neutropenic Infection)
- Chronic Graft versus Host Disease (GVHD)
- Primary Immune Thrombocytopenia/Immune Thrombocytopenic Purpura (ITP)

All other indications will be assessed on an individual basis. Submissions for indications other than those listed in this criteria should be accompanied by supporting evidence from Medicare approved compendia.

Coverage Criteria

Common Variable Immunodeficiency (CVID)

Authorization of 6 months may be granted for initial treatment of common variable immunodeficiency when either of the following criteria is met:

- The member must have a lack of response to immunization along one of the following conditions:
    - IgG level of less than 400mg/dl
    - IgG level greater than or equal to 400 mg/dl with evidence of recurrent severe infections with documented antibiotic therapy and recurrent infections are not viral upper respiratory infections, including simple viral rhinosinusitis

- Documentation that member has been receiving long term IVIG therapy for the condition when diagnostic testing information is unavailable

Authorization of 6 months may be granted for continued treatment of common variable immunodeficiency when all of the following criteria is met:

- The member must have one of the following:
  - IgG level of less than 400mg/dl and a lack of response to immunization
  - IgG level greater than or equal to 400 mg/dl with evidence of recurrent severe infections with documented antibiotic therapy and a lack of response to immunization and recurrent infections are not viral upper respiratory infections, including simple viral rhinosinusitis
  - Documentation on receiving long term IVIG therapy for the condition when diagnostic testing information is unavailable
- Documentation of serum trough levels below 400mg/dl when dose was 400-600 mg/kg and maintenance dose is now greater than 600mg/kg

Primary Humoral Immunodeficiency Syndromes

Authorization of 6 months may be granted for treatment of primary humoral immunodeficiency syndromes [congenital agammaglobulinemia (X-linked agammaglobulinemia), severe combined immunodeficiency, X-linked immunodeficiency with hyperimmunoglobulin M (IgM), Wiskott-Aldrich syndrome) when either of the following criteria is met:

- The member must have the following:
  - Lack of response to immunization
  - Low IgG level
- Documentation that member has been receiving long term IVIG therapy for the condition when diagnostic testing information is unavailable

Authorization of 6 months may be granted for continued treatment of primary humoral immunodeficiency syndromes when all of the following criteria is met:

- The member must have one of the following:
  - Low IgG level and lack of response to immunization
  - Documentation on receiving long term IVIG therapy for the condition when diagnostic testing information is unavailable
- Documentation of serum trough levels below 400mg/dl when dose was 400-600 mg/kg and maintenance dose is now greater than 600mg/kg and the member has one of the following conditions:
  - Congenital Agammaglobulinemia (X-Linked Agammaglobulinemia)
  - Severe Combined Immunodeficiency (SCID),
  - X-Linked Immunodeficiency with Hyperimmunoglobulin M (IgM),
  - Wiskott-Aldrich Syndrome

Human Immunodeficiency Virus (HIV) Disease

Authorization of 6 months may be granted for treatment of HIV disease in pediatric members when all of the following criteria are met:

- All of the following apply to the member:
  - Does not have primary immune thrombocytopenia (ITP)
  - Age less than 13 years
  - IgG level less than 400 mg/dl
  - Entry CD4+ lymphocyte cell count is greater than or equal to 200/mm3
- At least one of the following criteria are met:
  - Member has had two or more bacterial infections in a 1-year period despite antibiotic chemoprophylaxis with TMP-SMZ or another active agent
  - Member has received two doses of measles vaccine and lives in a region with a high prevalence of measles
  - Member has chronic bronchiectasis whose immunological response is suboptimal to antimicrobial and pulmonary therapy
  - Member has immune abnormalities with symptomatic or asymptomatic HIV, as evidenced by a lack of ability to produce an antibody response to immunization with protein antigens (e.g., tetanus) or carbohydrate antigens (e.g., pneumococcal capsular polysaccharides. such as, Pneumovax)

Guillain-Barre Syndrome

Authorization of 1 month may be granted for treatment of Guillain-Barre syndrome when all of the following criteria are met:

- Member has experienced rapid disease progression or relapse, or other forms of treatment have failed.
- If the condition improves with IVIG therapy, the prescriber will attempt to reduce the IVIG dose or frequency of administration.
- If the condition does not improve with IVIG therapy, the prescriber will discontinue the treatment.

Relapsing-Remitting Multiple Sclerosis (RRMS)

Authorization of 3 months may be granted for initial treatment of relapsing-remitting multiple sclerosis when both of the following criteria are met:

- There is clear documentation of relapsing remitting disease
- The member has experienced one of the following:
  - Rapid progression of disease or relapse
  - Other forms of treatment have failed or are contraindicated

Authorization of 6 months may be granted for continued treatment of relapsing-remitting multiple sclerosis when all of the following criteria are met:

- The member has shown improvement within 3 months from start of IVIG treatment as documented by a quantitative assessment (e.g., activities of daily living (ADL) measurements)
- Attempt to wean the dosage is made when improvement has occurred by either a reduction in dose or frequency of administration
- Attempt to stop IVIG is made if improvement is sustained with dosage reduction
- If the condition does not improve with IVIG therapy, the prescriber will discontinue the treatment

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP), and Variant Syndromes such as Multifocal Motor Neuropathy

Authorization of 3 months may be granted for initial treatment of chronic inflammatory demyelinating polyneuropathy (and variant syndromes such as multifocal motor neuropathy) when all of the following criteria are met:

- Evidence of rapid progression of disease or relapse
- The member had one of the following:
    - No response or an inadequate response to corticosteroids
    - Unacceptable side effects to the use of corticosteroids and dosage reduction is not clinically feasible
    - Documented contraindication to corticosteroids

Authorization of 6 months may be granted for continued treatment of chronic inflammatory demyelinating polyneuropathy (and variant syndromes such as multifocal motor neuropathy) when all of the following criteria are met:

- The member has shown improvement within 3 months from start of IVIG treatment as documented by a quantitative assessment (e.g., activities of daily living (ADL) measurements)
- Attempt to wean the dosage is made when improvement has occurred by either a reduction in dose or frequency of administration
- Attempt to stop IVIG is made if improvement is sustained with dosage reduction
- If the condition does not improve with IVIG therapy, the prescriber will discontinue the treatment

Myasthenia Gravis

Authorization of 3 months may be granted for initial treatment of myasthenia gravis when either of the following criteria are met:

- The member has both of the following:
    - Evidence of rapid progression of disease or relapse
    - The member has experienced all of the following with previous therapies:

    - Inadequate response or intolerable side effects to acetylcholinesterase inhibitors
    - Refractory to corticosteroids over a 6 week period; or have been unable to successfully taper corticosteroids below moderately high doses; or develop severe side effects due to steroid therapy
    - Failed at least one immunosuppressive agent (e.g., azathioprine, methotrexate, cyclophosphamide, cyclosporine)
- For first line therapy, IVIG may be used when either of the following apply:
    - The member is experiencing a myasthenic crisis
    - Preoperatively for planned thymectomy

Authorization of 6 months may be granted for continued treatment of myasthenia gravis when all of the following criteria are met:

- The member has shown improvement within 3 months from start of IVIG treatment as documented by a quantitative assessment (e.g., activities of daily living (ADL) measurements)
- Attempt to wean the dosage is made when improvement has occurred by either a reduction in dose or frequency of administration
- Attempt to stop IVIG is made if improvement is sustained with dosage reduction
- If the condition does not improve with IVIG therapy, the prescriber will discontinue the treatment

Refractory Polymyositis/Refractory Dermatomyositis

Authorization of 3 months may be granted for initial treatment of refractory polymyositis/refractory dermatomyositis when all of the following criteria are met:

- Evidence of rapid progression of disease or relapse
- The member meets all of the following:
    - Member is refractory to corticosteroids over a 6 week period; or has been unable to successfully taper corticosteroids below moderately high doses even with addition of other immunosuppressive agents; or develops severe side effects due to steroid therapy;
    - Member has failed at least one immunosuppressive agent (e.g., azathioprine, methotrexate, cyclophosphamide, cyclosporine)
    - Documentation clearly indicates the member is unable to tolerate or has contraindications to corticosteroid or immunosuppressive therapy

Authorization of 6 months may be granted for continued treatment of refractory polymyositis/refractory dermatomyositis when all of the following criteria are met:

- The member has continued decreased muscle strength, elevated creatine phosphokinase (CPK), and/or electromyography (EMG) abnormalities
- The member has shown improvement within 3 months from start of IVIG treatment as documented by a quantitative assessment (e.g., activities of daily living (ADL) measurements)
- Attempt to wean the dosage is made when improvement has occurred by either a reduction in dose or frequency of administration

- Attempt to stop IVIG is made if improvement is sustained with dosage reduction
- If the condition does not improve with IVIG therapy, the prescriber will discontinue the treatment

Chronic Lymphocytic Leukemia (CLL)

Authorization of 6 months may be granted for treatment of hypogammaglobulinemia associated with chronic lymphocytic leukemia when all of the following criteria are met:

- Therapy is used for prevention of recurrent bacterial infections
- IgG level is less than 600 mg/dl.

Hematopoietic Stem Cell Transplantation (HSCT)

Authorization of 6 months may be granted for treatment of hematopoietic stem cell transplantation when all of the following criteria are met:

- Therapy will be used to prevent the risk of acute graft-versus-host disease, associated interstitial pneumonia (infectious or idiopathic) and infections (e.g., cytomegalovirus infections [CMV], varicella-zoster virus infection, and recurrent bacterial infection)
- The member is 20 years of age or older
- Member is not undergoing an autologous BMT (i.e., using the member's own stem cells)
- Therapy will be used during the first 100 days after transplantation

Kawasaki Disease (Mucocutaneous Lymph Node Syndrome)

Authorization of 1 month may be granted for treatment of Kawasaki disease when used in conjunction with aspirin

Autoimmune Hemolytic Anemia

Authorization of 6 months may be granted for treatment of autoimmune hemolytic anemia when either of the following criteria are met:

- The member has failed to respond to other forms of therapy such as corticosteroids, immunosuppressive and cytotoxic agents and monoclonal antibodies
- The member requires rapid cessation of hemolysis due to severe or life-threatening manifestations of the condition

Autoimmune Neutropenia

Authorization of 6 months may be granted for treatment of autoimmune neutropenia when both of the following criteria are met:

- Absolute neutrophil count is less than 800mm

- The member has recurrent bacterial infections

Autoimmune Mucocutaneous Blistering Diseases

Authorization of 6 months may be granted for treatment of autoimmune mucocutaneous blistering disease when all of the following criteria are met:

- The member has one of the following biopsy proven diagnoses:
  - Pemphigus vulgaris
  - Pemphigus foliaceus
  - Bullous pemphigoid
  - Mucous membrane pemphigoid (cicatricial pemphigoid)
  - Epidermolysis bullosa acquisita
- At least one of the following is met regarding prior treatment with conventional therapy:
  - The member has failed conventional therapy
  - The member has a contraindication to conventional therapy
  - The member has rapidly progressive disease and a clinical response could not be affected quickly enough using conventional agents, and IVIG will be given along with conventional treatment(s).
- IVIG will be used for short-term control of the member's condition and will not be used as maintenance therapy

Multiple Myeloma

Authorization of 6 months may be granted for treatment of multiple myeloma when one of the following criteria are met:

- The member meets all of the following criteria:
  - IVIG is being used to reduce the incidence of recurrent bacterial infections while in plateau phase of disease
  - IgG level is less than 600mg/dl
  - History of one documented, serious bacterial infection requiring IV antibiotic therapy in previous six months or two or more such infections in previous one year
  - Therapy will not be used during primary induction of chemotherapy or during relapse of the disease
- The member has failed to mount an appropriate IgG humoral response to pneumococcal vaccine

Stiff-Man Syndrome/Stiff-Person Syndrome

Authorization of 6 months may be granted for initial treatment of stiff-man syndrome when all of the following criteria are met:

- The member must meet the current defined criteria for the diagnosis
- The member must have failed conservative treatment, such as benzodiazepines

Authorization of 6 months may be granted for continued treatment of stiff-man syndrome if the member has documented positive, objective response to therapy.

Hypogammaglobulinemia with NNI (Non-Neutropenic Infection)

Authorization of 6 months may be granted for treatment of hypogammaglobulinemia with NNI when all of the following criteria are met:

- Recent treatment with rituximab in combination with cytotoxic chemotherapy
- Laboratory proven hypogammaglobulinemia and an absolute neutrophil count over 1,000
- Acute infection requiring hospitalization or an infection lasting over 2 weeks in spite of antibiotics or an infection relapsing immediately after discontinuation of antibiotics

Chronic Graft versus Host Disease (GVHD)

Authorization of 6 months may be granted for treatment of chronic graft versus host disease when all of the following criteria are met:

- IgG levels less than 400 mg/dl.
- At least one acute infection requiring hospitalization and/or parenteral antibiotics
- Confirmed diagnosis of chronic GVHD
- At least 100 days post-transplant.

Primary Immune Thrombocytopenia/Immune Thrombocytopenic Purpura (ITP)

Authorization of 6 months may be granted for treatment of ITP when all of the following criteria are met:

- The member has one of the following conditions:
  - Severe ITP (bleeding)
  - Adult with platelet count less than or equal to 30 x109/L especially if risk factors for bleeding are present
  - In preparation for procedures or surgery with risk of bleeding
  - Professional or lifestyle risk factors for trauma
- The member has one of the following conditions:
  - Need for rapid response (needed in less than 48 hours)
  - Contraindication or inability to tolerate corticosteroids
  - Lack of response to corticosteroids defined as platelet count less than 30 x109/L or less than 2-fold increase in baseline platelets

Dosage and Administration

Human Immunodeficiency Virus (HIV) Disease

Dosing guideline for pediatric (HIV) Infection is 400-mg/kg body weight given every 28 days to prevent serious bacterial infection. Claims reimbursed with dosages in larger or decreased frequency of administration are subject to medical review.

Neurologic Disorders

Where it is necessary to administer larger doses than noted in the dosage guidelines, the medical record must document that such higher doses are required to maintain response. Such documentation must include evidence that lower doses are not efficacious in producing the needed functional response for any individual member.

- Guillain-Barre' Syndrome
  - 1,000 mg/kg body weight daily for two days; or 400 mg/kg body weight daily for five days.
- Relapsing-Remitting Multiple Sclerosis
  - Usual dosing is 200-400 mg/kg every 4 weeks.
- Chronic Inflammatory Demyelinating Polyneuropathy (and variant syndromes such as multifocal motor neuropathy)
  - Initial therapy - 400 mg/kg body weight per day for five days.
  - Maintenance therapy - 250-400 mg/kg body weight no more frequently than every two weeks.
- Refractory Polymyositis/ Refractory Dermatomyositis
  - 1,000 mg/kg body weight daily for two days every four weeks or 400mg/kg body weight for five days every four weeks in members intolerant of high-dose therapy.

Stiff-Man Syndrome/Stiff-Person Syndrome

Initial coverage is limited to up to 2g of immune globulin per kilogram of body weight per month

All Other Indications

Where no dosage guidelines are provided and realizing dosage may vary based on a member's individual situation, the dosage must be in keeping with the recommended dosage in current literature and the standard of practice. Initial and/or maintenance doses of IVIG may be administered as a single infusion or may be divided and administered over several days. Any time there is a departure from the standard dosing (either dose or frequency of administration), the rationale for this must be documented in the medical record.

References

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2. Billing and Coding: Intravenous Immune Globulin (A56779) Version R10. Available at: https://www.cms.gov/medicare-coverage-database/indexes/national-and-local-indexes.aspx. May 14, 2024.
3. Immune Thrombocytopenia (ITP) Therapy (L38268) Version R6. Available at: https://www.cms.gov/medicare-coverage-database/indexes/national-and-local-indexes.aspx. May 14, 2024.
4. Billing and Coding: Immune Thrombocytopenia (ITP) Therapy (A57160) Version R5. Available at: https://www.cms.gov/medicare-coverage-database/indexes/national-and-local-indexes.aspx. May 14, 2024.
5. National Coverage Determination (NCD) for Intravenous Immune Globulin for the Treatment of Autoimmune Mucocutaneous Blistering Diseases (250.3- Version1). Accessed at: https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=158&ncdver=1&SearchType=Advanced&CoverageSelection. May 14, 2024.