Pharmacy Prior Authorization
Clinical Guidelines – Immune Globulins

Formulary Immune Globulins: Gamunex-C, Gammagard, Gammagard SD, Gammaked and Flebogamma DIF

Bivigam, Carimune NF, Cuvitru, Gamastan, Gammaplex, Hizentra, Hyqvia, Octagam, Privigen

Authorization Guidelines:

Documentation of ALL of the following:

I. The dose prescribed, frequency of use and duration of therapy is within the Food and Drug Administration (FDA)-approved range for the indication or is supported by compendia/peer-reviewed literature

II. Request is not for experimental/investigational use or for a clinical trial

III. Products are not interchangeable, selection of product should be based on member factors including diagnosis, past history and individual comorbidities

IV. The use of parenteral immune globulin therapy is approved for members with any of the following conditions:

1. Primary immunodeficiencies
   - 1.1 Common Variable Immunodeficiency (CVID)
   - 1.2 Congenital agammaglobulinemia
   - 1.3 Hyper Immunoglobulin M (IgM) syndromes
   - 1.4 Hypogammaglobulinemia
   - 1.5 X-linked Immunodeficiency with hyperimmunoglobulin (elevated or normal Immunoglobulin M (IgM))
   - 1.6 Immunodeficiency with thymoma (Good syndrome)
   - 1.7 Severe Combined Immunodeficiency (SCID)
   - 1.8 Selective Immunoglobulin G (IgG) subclass deficiencies (with evidence of recurrent infections)
   - 1.9 Wiscott-Aldrich Syndrome
   - 1.10 X-linked agammaglobulinemia

   - Medical records and clinical notes showing the following will be required for approval:
     - Laboratory confirmation of immune globulin deficiency
     - Persistent infections despite antibiotic prophylaxis
     - Documented lack of ability to mount immunologic response to antigenic challenge

2. B-cell chronic lymphocytic leukemia (prevention of recurrent bacterial infections)
   - Immunoglobulin G (IgG) level less than 400 mg/dl; and
   - One (1) severe bacterial infection within preceding 6 months or 2 or more bacterial infections in 1 year or evidence of specific antibody deficiency

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3. Multiple myeloma
    - Immunoglobulin G (IgG) less than 500 mg/dl and recurrent bacterial infections should be documented for immune globulin treatment

4. Bone marrow transplantation (prevention of infections)
    - Bone marrow transplant within last 100 days
    - Documented severe hypogammaglobulinemia (Immunoglobulin G (IgG) less than 400 mg/dl)

5. Idiopathic Thrombocytopenic Purpura (ITP) (immune thrombocytopenia)
    - Other causes of thrombocytopenia have been ruled out
    - Idiopathic Thrombocytopenic Purpura (ITP) (Adults)
        - Unresponsive to corticosteroid therapy; and
        - Documentation of one of the following:
            - Management of acute bleeding due to severe thrombocytopenia (platelet counts less than 30,000/µl); or
            - To increase platelet counts prior to invasive major surgical procedures (e.g., splenectomy), or
            - To defer or avoid splenectomy; or
            - In members with severe thrombocytopenia (platelet counts less than 20,000/µl) considered to be at risk for intra-cerebral hemorrhage.
    - Idiopathic Thrombocytopenic Purpura (ITP) (Chronic Refractory)
        - Duration of illness of greater than 6 months; and
        - No concurrent illness/disease explaining thrombocytopenia; and
        - Prior treatment with corticosteroids and splenectomy has failed or member is at high-risk for post-splenectomy sepsis
    - Idiopathic Thrombocytopenic Purpura (ITP) (Pediatrics)
        - Acute Idiopathic Thrombocytopenic Purpura (ITP):
            - IVIG as initial therapy if platelet count less than 20,000/µl, especially when member has emergency bleeding or is at risk for severe life-threatening bleeding; or
            - Severe thrombocytopenia (platelet counts less than 20,000/µl) considered to be at risk for intra-cerebral hemorrhage.
        - Chronic Idiopathic Thrombocytopenic Purpura (ITP):
            - Member has low platelet count or is symptomatic; and
            - Failure of other therapies, or
            - Member is a high risk for post-splenectomy sepsis
    - Idiopathic Thrombocytopenic Purpura (ITP) (Pregnancy)

- Refractory to steroids with platelet counts less than 10,000/µl in the 3rd trimester; or
- Platelet counts less than 30,000/µl associated with bleeding before vaginal delivery or C-section; or
- Pregnant member with prior history of delivery with autoimmune thrombocytopenia; or
- Pregnant member who have platelet counts less than 50,000/µl during the current pregnancy; or
- Pregnant member with past history of splenectomy

6. Chronic inflammatory demyelinating polyneuropathy
    - Documentation of symmetric or focal neurologic deficits with slowly progressive or relapsing course over 2 months or longer (with neurophysiological abnormalities)

7. Multifocal motor neuropathy

8. Kawasaki disease (prevention of coronary artery aneurisms)

9. Human Immunodeficiency infection (reduction of serious opportunistic infections in pediatric members)
    - Member is less than 13 years of age;
    - Immunoglobulin G (IgG) level is less than 400 mg/dl

10. Guillain-Barre Syndrome (GBS) and Guillain-Barre Syndrome (GBS) variants (infective polyneuritis (includes Guillain-Barre Syndrome (GBS) variants: Miller-Fisher syndrome (MFS), pan autonomic polyneuropathy, acute pandysautonomia, acute motor axonal neuropathy (AMAN), and acute motor and sensory axonal neuropathy (AMSAN)))
    - Severe Guillain-Barre syndrome with significant weakness such as inability to stand or walk without aid, respiratory or bulbar weakness, or Miller-Fisher syndrome (MFS); and
    - The disorder has been diagnosed during the first 2 weeks of the illness; and
    - Immune globulin therapy is initiated within one month of symptom onset

11. Relapsing-remitting multiple sclerosis (RRMS)
    - Documentation of the following severe manifestations of relapsing-remitting multiple sclerosis (RRMS) (not primary or secondary progressive multiple sclerosis (MS)); and
    - Documentation of trial and failure of standard approaches (for example, interferons (Betaseron, Avonex, Rebif), glatiramer (Copaxone)), or they are contraindicated.

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12. Graves ophthalmopathy

13. Autoimmune neutropenia, refractory
    - Documentation that treatment with Granulocyte-Colony Stimulating Factors (G-CSF) is not appropriate.

14. Autoimmune hemolytic anemia, refractory
    - Documentation of an inadequate response or contraindication to corticosteroids or splenectomy

15. Polymyositis, dermatomyositis
    - Documentation of trial and failure of corticosteroids (for example, prednisone); and trial of an immunosuppressant (e.g., methotrexate, azathioprine)

16. Streptococcal and staphylococcal toxic shock syndrome or toxic necrotizing fascitis due to group A streptococcus

17. Moersch-Woltmann (Stiff-man) syndrome
    - Documentation of trial and failure with benzodiazepines, baclofen, gabapentin, valproate, tiagabine, or levetiracetam

18. Myasthenia Gravis
    - Documentation of treatment of acute myasthenic crisis with decompensation (respiratory failure, or disabling weakness requiring hospital admission)).
    - Documentation of trial and failure of other therapies such as azathioprine, cyclosporine and cyclophosphamide

19. Birdshot (vitiligenous) retinochoroidopathy
    - Documentation of trial and failure to immunosuppressive agents (for example, corticosteroids, cyclosporine)

20. Enteroviral meningoencephalitis

21. Neonatal alloimmune thrombocytopenia (NAIT)

22. Neonatal hemochromatosis prophylaxis

- Documentation that member is pregnant with a history of pregnancy that ended in neonatal hemochromatosis

23. Autoimmune mucocutaneous blistering diseases
    i. Pemphigus vulgaris
    ii. Pemphigus foliaceus
    iii. Bullous pemphigoid
    iv. Mucous membrane pemphigoid
    v. Epidermolysis bullosa acquisita
    - The condition is rapidly progressing, extensive or debilitating; and
    - Corticosteroids or immuno-suppressive agents have failed or the member has experienced significant complications from standard treatment, such as diabetes or steroid-induced osteoporosis.

24. Acquired red cell aplasia

25. Parvovirus B19 infection, chronic, with severe anemia

26. Human Immunodeficiency Virus (HIV)-associated thrombocytopenia:
    - Significant bleeding in thrombocytopenic members or platelet count less than 20000/µl

27. Toxic epidermal necrolysis and Steven-Johnson syndrome

28. Preparation for thymoma surgery (to prevent myasthenia exacerbation)

29. Opsoclonus-myoclonus

30. Paraneoplastic opsoclonus-myoclonus-ataxia associated with neuroblastoma

31. Rasmussen encephalitis (Rasmussen's syndrome)
    - Documentation of inadequate response or inability to tolerate anti-epileptic drugs and corticosteroids

32. Lambert-Eaton myasthenic syndrome
    - No response to anticholinesterases (for example, pyridostigmine) and dalfampridine (Ampyra); and

- Used as an alternative to plasma exchange if weakness is severe or there is difficulty with venous access for plasmapheresis

33. Systemic lupus erythematosus (SLE), for members with severe active systemic lupus erythematosus (SLE) for whom other interventions have been unsuccessful, have become intolerable, or are contraindicated

34. Stem cell or bone marrow transplantation:
    - Prophylaxis in allogeneic or syngeneic transplant members within the first 100 days post-transplant;
    - After 100 days post-transplant, member has Immunoglobulin G (IgG) level less than 400 mg/dL and one of the following:
        - Member has primary immunodeficiency or
        - Member has cytomegalovirus infection, varicella-zoster virus infection, and recurrent bacterial infection
    - Steroid-resistant graft-versus-host disease in bone marrow transplant members 20 years of age or older, in the first 100 days post-transplant, and with Immunoglobulin G (IgG) level less than 400 mg/dl

35. Solid organ transplantation, for allosensitized members undergoing solid organ transplant

36. Severe hyperbilirubinemia in neonates

37. Post-transfusion purpura
    - Decreased platelets (less than 10,000/µl); and
    - 2 to 14 days post-transfusion with bleeding

38. Renal transplantation from live donor with ABO incompatibility or positive cross-match, where a suitable non-reactive live or cadaveric donor is unavailable (preparative regimen)

39. Acute disseminated encephalomyelitis

    - Documentation of trial and failure of intravenous corticosteroid treatment

40. Enteroviral meningoencephalitis

Criteria for Renewal:

- Supporting documentation showing clinical improvement or stabilization of the disease state.

General Approval Duration:

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- Initial approval: 6 months
- Renewal: 6 months

Initial Approval Duration for Specific Indications:

- Autoimmune hemolytic anemia: 5 days
- Guillain-Barre Syndrome: 5 days
- Idiopathic thrombocytopenic purpura (acute): 5 days
- Post-transfusion purpura: 5 days
- Chronic inflammatory demyelinating polyneuropathy: 3 months

Aetna considers parenteral immunoglobulins investigational and experimental for the following indications but not limited to:

- Isolated Immunoglobulin E (IgE) deficiency
- Isolated Immunoglobulin G_4 ($IgG_{4)}$ deficiency
- Selective Immunoglobulin A (IgA) deficiency
- Isolated Immunoglobulin M (IgM) deficiency
- Inclusion body myositis
- Autoimmune diabetes mellitus
- Atopic dermatitis
- Inflammatory bowel disease
- Chronic fatigue syndrome
- Acute rheumatic fever
- Viral load in Human Immunodeficiency Virus infection
- Demyelinating neuropathy associated with monoclonal Immunoglobulin M (IgM)
- Adrenoleukodystrophy
- Amyotrophic lateral sclerosis
- Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal protein, Skin changes (POEMS) syndrome
- Paraneoplastic cerebellar degeneration, sensory neuropathy or encephalopathy
- Brachial plexopathy
- Autistic disorders
- Non-steroid dependent asthma
- Dilated cardiomyopathy
- Prevention of infection and acute graft-versus-host disease after bone marrow transplantation
- Cystic fibrosis without hypogammaglobulinemia

- Chronic sinusitis
- Crohn's disease

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