Aetna Better Health®

Pharmacy Prior Authorization
Clinical Guidelines – Immune Globulins

Formulary Immune Globulins: Gamunex-C, Gammagard (liquid), Privigen, Hizentra

Non-formulary Immune Globulins: Asceniv, Bivigam, Cutaquig, Cuvitru, Gamastan, Gammaplex, Gammagard SD, Gammaked, Hyqvia, Octagam, Panzyga, Xembify

Authorization Guidelines:

Documentation of ALL 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. Requests for formulary subcutaneous Hizentra require previous trial with formulary Intravenous Immune Globulin (IVIG), or inadequate response, or contraindication to the formulary Intravenous Immune Globulin (IVIG) product
V. 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

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Effective: 6/7/2022

2. B-cell chronic lymphocytic leukemia (prevention of recurrent bacterial infections)
   - Immunoglobulin G (IgG) level less than 500 mg/dl; and
   - Member has a history of recurrent sinopulmonary infections requiring intravenous antibiotics or hospitalization

3. Multiple myeloma
   - Immunoglobulin G (IgG) less than 400 mg/dl and recurrent bacterial infections should be documented for immune globulin treatment

4. 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:
       - Platelet counts less than 20,000/µl; or
       - Rapid increase to platelet counts required (for example, prior to invasive major surgical procedures); or
       - Member is experiencing significant bleeding or is at high risk of bleeding
   - Idiopathic Thrombocytopenic Purpura (ITP) (Chronic Refractory)
     - Duration of illness of greater than 6 months; and
     - No concurrent illness/disease explaining thrombocytopenia; and
     - One of the following:
       - Platelet counts less than 20,000/µl; or
       - Rapid increase to platelet counts required (for example, prior to invasive major surgical procedures); or
       - Member is experiencing significant bleeding or is at high risk of bleeding
       - Relapse after previously responding to IVIG or inadequate response/intolerance/contraindication to corticosteroid or anti-D
   - Idiopathic Thrombocytopenic Purpura (ITP) (Pediatrics)
     - Acute Idiopathic Thrombocytopenic Purpura (ITP), one of the following:
       - Platelet count less than 20,000/µl, life-threatening bleeding, or moderate or severe bleeding; or
       - Member is a neonate born to a woman with ITP and has intracranial hemorrhage, platelet count less than 30,000/µl, or symptomatic bleeding
       - Rapid increase in platelets is required
     - Chronic Idiopathic Thrombocytopenic Purpura (ITP):

        - Medication is being used as rescue therapy or member is experiencing significant bleeding or is at high risk of bleeding
    - Idiopathic Thrombocytopenic Purpura (ITP) (Pregnancy)
        - Platelet count less than 20,000/µl, the member has symptoms of bleeding, or a procedure is planned; or
        - The member is late in the third trimester and a platelet count of 50,000/µl or more is needed for delivery

5. Chronic inflammatory demyelinating polyneuropathy
    - Member has symmetric or asymmetrical polyradiculoneuropathy with slowly progressive or relapsing and remitting course over 2 months or longer
    - Documentation showing diagnosis was confirmed by electrodiagnostic studies

6. Multifocal motor neuropathy

7. Kawasaki disease – for the prevention of coronary artery aneurisms in pediatric members

8. Human Immunodeficiency Virus – for the prophylaxis of serious opportunistic infections in pediatric members
    - Primary prophylaxis: Immunoglobulin G (IgG) level is less than 400 mg/dl; or
    - Secondary prophylaxis: member experienced greater than 2 infections in a one-year period and both combination antiretroviral therapy and antibiotic prophylaxis were ineffective

9. 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

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

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

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

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

14. Moersch-Woltmann (Stiff-man) syndrome
    - Documentation of trial and failure with benzodiazepines and/or baclofen
15. Myasthenia Gravis
    - One of the following:
        - Documentation medication is being used for treatment of acute myasthenic crisis with decompensation (respiratory failure or disabling weakness requiring hospital admission) or in preparation for surgery (for example thymectomy); or
        - Treatment of refractory disease and documentation of trial and failure of at least 2 other therapies, such as corticosteroids, azathioprine, cyclosporine mycophenolate mofetil, methotrexate, and tacrolimus

16. Birdshot (vitiligenous) retinochoroidopathy
    - Documentation of trial and failure to 2 or more immunosuppressive agents (for example, corticosteroids, methotrexate, cyclosporine)

17. Enteroviral meningoencephalitis

18. Fetal/neonatal alloimmune thrombocytopenia

19. Neonatal hemochromatosis prophylaxis
    - Documentation that member is pregnant with a history of pregnancy that ended in neonatal hemochromatosis

20. Autoimmune mucocutaneous blistering diseases
    - Documentation showing one of the following has been proven by biopsy: 1) Pemphigus vulgaris 2) Pemphigus foliaceus 3) Bullous pemphigoid 4) Mucous membrane pemphigoid 5) Epidermolysis bullosa acquisita

- The condition is rapidly progressing, extensive or debilitating; and
- Failure on corticosteroids or immuno-suppressive agents or the member has experienced significant complications from standard treatment, such as diabetes or steroid-induced osteoporosis.

21. Acquired red cell aplasia

22. Parvovirus B19 infection, chronic, with severe anemia

23. Human Immunodeficiency Virus (HIV)-associated thrombocytopenia:
    - Active bleeding in thrombocytopenic members or platelet count less than 10,000/µl

24. Toxic epidermal necrolysis and Steven-Johnson syndrome

25. Opsoclonus-myoclonus

26. Paraneoplastic opsoclonus-myoclonus-ataxia associated with neuroblastoma

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

28. Lambert-Eaton myasthenic syndrome
    - No response to anticholinesterases (for example, pyridostigmine) and amifampridine; and
    - Used as an alternative to plasma exchange if weakness is severe or there is difficulty with venous access for plasmapheresis

29. 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

30. Prophylaxis of bacterial infections in hematopoietic stem cell/bone marrow transplantation:
    - Prophylaxis within the first 100 days post-transplant;
    - After 100 days post-transplant, member has Immunoglobulin G (IgG) level less than 400 mg/dL and recurrent bacterial infection

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

32. Hemolytic disease of the newborn with severe hyperbilirubinemia in neonates

33. Post-transfusion purpura
    - Severe thrombocytopenia with platelet counts less than 10,000/μl approximately 1 week post-transfusion

34. 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)

35. Acute disseminated encephalomyelitis
    - Documentation of trial and failure of intravenous corticosteroid treatment

36. Autoimmune encephalitis, Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS), or Pediatric Acute-onset Neuropsychiatric Syndrome (PANS)

Criteria for Renewal:

- Supporting documentation showing clinical improvement or stabilization of the disease state.
- For autoimmune encephalitis, Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS), or Pediatric Acute-onset Neuropsychiatric Syndrome (PANS):
    - There have not been more than 2 infusions within a 12-month period

General Approval Duration:

- 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): 1 month
- Idiopathic thrombocytopenic purpura in pregnant women: Entire pregnancy duration
- Post-transfusion purpura: 5 days
- Chronic inflammatory demyelinating polyneuropathy: 3 months
- Myasthenia Gravis – acute use: 1 month
- Autoimmune encephalitis, Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS), or Pediatric Acute-onset Neuropsychiatric Syndrome (PANS): 5 days

Renewal Approval Duration for Specific Indications:

- Autoimmune encephalitis, Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS), or Pediatric Acute-onset Neuropsychiatric Syndrome (PANS): 5 days

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
- Alzheimer's disease

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