Prior Authorization Approval Criteria

**Intravenous immunoglobulin and subcutaneous immunoglobulin**

**Generic Name:** Intravenous immunoglobulin (IVIG), subcutaneous immunoglobulin (SCIG), Intramuscular immunoglobulin (IMIG)

**Brand Names:** Bivigam, Carimune NF, Cuvitru, Flebogamma DIF, GamaSTAN S/D, Gammagard Liquid, Gammagard S/D, Gammaked, Gammalex, Gamunex-C, Hizentra, HyQvia*, Octagam*, Privigen

*HyQvia & Octagam 10% are not FDA-approved for use in children under the age of 18

**Medication Class:** Immune globulin

**Criteria for approval (bullet points below are all inclusive unless otherwise noted):**

- For HyQvia and Octagam, patient must be 18 years old or older
- For HyQvia, must have a clinically documented severe intolerance to one IVIG product and one alternative SCIG product
- Medical services must meet nationally recognized standard for quality care and are provided at the appropriate level of care and place of service. The first dose may be given at the facility of choice by the physician; all subsequent doses will be given by home infusion. The following are some exceptions that may be acceptable for services outside the home:
  - Documented history of a severe reaction to IVIG or blood products. Severe reaction is defined as anaphylactic reaction. The patient should have a history of reactions and not be based on the potential of IVIG to induce such reactions
  - Documented intolerance to IVIG requiring constant telemetry monitoring of vitals.
  - Unsafe home environment
  - No access to 911 services
  - Documented presence of IGA auto antibodies
  - Patient is severely decompensated (e.g. respiratory failure in a myasthenic crisis)
- Must meet diagnostic criteria for one of the following indications:

**FDA-Approved Uses:**

- **B-cell chronic lymphocytic leukemia**
  - Reserved for patients who have recurrent serious infections due to hypogammaglobulinemia
  - Patients must have recurrent infections requiring intravenous (IV) antibiotics or hospitalization
  - Serum IgG <500 mg/dL
  - Recommended dosing**: 200 to 400 mg/kg IV every 3-4 weeks

The criteria listed above applies to Fallon Health Plan and its subsidiaries.
• **Hepatitis A virus (HAV) prophylaxis**
  - Pre-exposure protection is warranted for nonimmune individuals at risk for hepatitis A exposure in the following categories:
    - Individuals >40 years OR immunocompromised individuals OR individuals with chronic liver disease or other chronic medical conditions with insufficient time to receive the full two-dose vaccination series before traveling
    - Individuals who are allergic to the hepatitis A vaccine
    - Individuals <12 months of age
  - Recommended dosing**: 0.02 mL/kg IM (for anticipated risk of exposure <3 months) or 0.06 mL/kg (for anticipated risk of exposure ≥3 months); administration must be repeated if the travel period exceeds 5 months

• **Chronic inflammatory demyelinating polyneuropathy**
  - Diagnosis should be considered in patients with symmetric or asymmetric polyneuropathy who have a progressive or relapsing course for more than 2 months
  - Evidence of peripheral nerve demyelination demonstrated by either electrodiagnostic findings or by nerve biopsy
  - Other diagnostic studies may include: elevated CSF protein
  - Routine re-evaluation (eg, at least every 3 months when treatments are initiated or changed, and at least twice a year when on maintenance therapy) to determine response of therapy
  - Recommended dosing**: Loading dose: 2 g/kg IV over 2-5 days (eg, 0.4 g/kg/day for 5 days); Maintenance: 1g/kg every 3 weeks

• **Kawasaki disease**
  - Administered within the first 10 days of illness concomitantly with aspirin
  - Presence of fever lasting at least 5 days without any other explanation
  - At least 4 of the 5 following criteria must be present:
    - Bilateral bulbar conjunctival injection
    - Oral mucous membrane changes, including injected or fissured lips, injected pharynx, or strawberry tongue
    - Peripheral extremity changes, including erythema of palms or soles, edema of hands or feet (acute phase), and periungual desquamation (convalescent phase)
    - Polymorphous rash
    - Cervical lymphadenopathy (at least one lymph node >1.5 cm in diameter)
  - Recommended dosing**: 2 g/kg IV over 8 to 12 hours

• **Measles**
  - Must be administered within 6 days of exposure to measles
  - Administration is appropriate for exposed individuals with increased risk of measles complications with contraindication for MMR vaccination as follows:
    - Pregnant women without evidence of immunity
    - Immunocompromised patients (such as individuals with severe immunodeficiency, bone marrow transplant recipients until at least 12 months after completing all immunosuppressive treatment (or longer in patients with graft-versus-host disease), patients on treatment for acute lymphoblastic leukemia until at least 6 months after completion of immunosuppressive chemotherapy, patients with HIV infection and CD4 percentage <15% (all ages) or CD4 count <200 cells/mm³ (age >5 years), and patients who have not received MMR vaccine since receiving effective antiretroviral therapy)
    - Infants aged <12 months

The criteria listed above applies to Fallon Health Plan and its subsidiaries.
- **Recommended dosing**: 400 mg/kg IV or 200 mg/kg SC or 0.5 mL/kg IM

- **Multifocal motor neuropathy**
  - Slowly progressive or stepwise progressive, focal, asymmetric limb weakness or motor involvement in the motor nerve distribution of at least 2 nerves for more than 1 month
  - No objective sensory abnormalities except for minor vibration sense abnormalities in the lower limbs
  - Medical documentation:
    - Diagnosis of MMN
    - EMG/NCS with interpretation; studies consistent with motor conduction block

- Recommended dosing**: 500-2400 mg/kg/month IV (400mg/kg over 2-5 days or 1 gm/kg/day x 2 days; maintenance should be lowest dose possible 1gm/kg or less) If patient does not respond to initial treatment, additional courses should be reconsidered)

- **Primary immune deficiency disorder** (includes congenital agammaglobulinemia (X-linked agammaglobulinemia), hypogammaglobulinemia, common variable immunodeficiency, IgG subclass deficiency, specific antibody deficiency (SAD), X-linked immunodeficiency with hyperimmunoglobulin M, severe combined immunodeficiency, and Wiskott-Aldrich syndrome)
  - Laboratory evidence of immunoglobulin deficiency may include one of the following definitions:
    - Agammaglobulinemia (total IgG <200 mg/dL)
    - Persistent hypogammaglobulinemia (total IgG <500 mg/dL, or at least 2 standard deviations below normal, on at least 2 occasions)
    - Absence of B lymphocytes
    - IgG subclass deficiency: Deficiency of 1 or more IgG subclasses. IgG1, IgG2, IgG3 ≥ 2 standard deviations below mean normal on at least 2 occasions when the patient is free of acute infections; normal IgG (total) and IgM levels, normal/low IgA levels.
    - Specific antibody deficiency: normal IgG, IgA and IgM levels
  - Medical documentation of one or more of the following:
    - Recurrent, severe, or unusual infections AND a poor response to antibiotics
    - Breakthrough bacterial infections in spite of prophylactic antibiotics if applicable
  - Documentation of an inadequate response to diagnostic vaccine administration unless IgG <200 mg/dL

- **Recommended dosing**: 400 to 600mg/kg IV every 3- 4 weeks

- **Idiopathic and chronic thrombocytopenic purpura**
  - Failed/intolerant/contraindicated to glucocorticoids
  - Management of severe, active bleeding and a platelet count <30,000/µL OR
  - To increase platelet count prior to an urgent invasive procedure OR
  - Severe thrombocytopenia <20,000 to 30,000/µL with or without bleeding
  - **Recommended dosing**: 1 g/kg daily for 1-2 days

- **Varicella prophylaxis** (when varicella-zoster immune globulin is unavailable)
  - IVIG considered if passive immunization (VariZIG) cannot be obtained
  - IVIG contains anti-varicella antibody titers that vary from lot to lot and limited data exist regarding efficacy
  - **Recommended dosing**: 0.6 to 1.2 mL/kg IM within 72 hours of exposure

The criteria listed above applies to Fallon Health Plan and its subsidiaries.
Off-Label Uses:

- **Autoimmune Mucocutaneous Blistering Diseases** (*Pemphigus vulgaris*, *Pemphigus Foliaceus*, Bullous Pemphigoid, Mucous Membrane Pemphigoid, Epidermolysis Bullosa Acquisita)
  - Meets diagnostic criteria for an Autoimmune Mucocutaneous Blistering Disease
  - Failed or intolerant/contraindicated to oral/topical corticosteroids
  - If steroid sparing is needed: Failed or intolerant/contraindicated to adjuvant nonsteroidal immunosuppressants (ie, azathiprone, mycophenylate, dapsone)
  - Or
  - Patients with rapidly progressive disease in whom a clinical response could not be affected quickly enough using conventional agents. In such situations IVIg therapy would be given along with conventional treatment(s) and the IVIg would be used only until the conventional therapy could take effect.

- **Autoimmune neutropenia**
  - Meets diagnostic criteria for Autoimmune neutropenia
  - Failed/intolerant/contraindicated to corticosteroids
  - Recommended dosing**: 1-3 g/kg over 2-5 days

- **Systemic dermatomyositis**
  - Meets diagnostic criteria for Systemic dermatomyositis
  - Failed or intolerant/contraindicated to corticosteroids
  - Failed or intolerant/contraindicated to azathioprine or methotrexate
  - Recommended dosing**: 400 mg/kg/day for 5 days

- **Fetal/Neonatal Alloimmune Thrombocytopenia (FAIT/NAIT)**
  - Meets diagnostic criteria for FAIT or NAIT
  - Medical documentation of one or more of the following
    - Pregnant women with a previously affected pregnancy
    - Family history of disease
    - Platelet alloantibodies found on screening
  - Recommended dosing**: 0.8 to 1 g/kg as a single dose

- **Guillain-Barré Syndrome**
  - Meets diagnostic criteria for Guillain-Barre syndrome
  - For nonambulatory adult patients with GBS who are within 4 weeks of neuropathic symptom onset
  - For ambulatory adult patients with GBS who are not yet recovering within 4 weeks of neuropathic symptom onset
  - Recommended dosing**: 0.4 g/kg/day for 5 days

- **HIV infection**
  - Meets diagnostic criteria for HIV infection and low platelet counts
  - Severe thrombocytopenia (<30,000/µL)
  - Recommended dosing**: 400 mg/kg every 3-4 weeks

- **Lambert-Eaton Myasthenic Syndrome**
  - Meets diagnostic criteria for Lambert-Eaton Myasthenic Syndrome
  - Failed or intolerant/contraindicated to acetylcholisterase inhibitors (eg. Pyridostigmine)
  - Failed or intolerant/contraindicated to immunosuppressants (eg. prednisone, azathioprine)
  - Recommended dosing**: total dose of 2 g/kg over 2-5 days; maintenance therapy with repeat infusions at 4 to 12 week intervals based upon symptoms

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- **Myasthenia gravis**
  - Meets diagnostic criteria for Myasthenia gravis in acute myasthenic crisis
  - OR
  - Periodic use to maintain remission if not controlled with chronic immunomodulating drugs.
  - OR
  - Pre-operative management (e.g., prior to thymectomy)
  - AND
  - Failed or intolerant/contraindicated to at least two first-line immunotherapies (e.g., prednisone, azathioprine, cyclosporine, and/or mycophenolate)
  - Recommended dosage**: 2 g/kg over 2-5 days

- **Parovirus B19-induced Pre Red Cell Aplasia (PRCA)**
  - Meets diagnostic criteria for PRCA
  - Clinically diagnosed with severe, chronic refractory anemia.

- **Polymyositis**
  - Meets diagnostic criteria for Polymyositis
  - Failed or intolerant/contraindicated to corticosteroids OR if condition responded to glucocorticoids, patient has failed or intolerant to azathioprine, methotrexate, mycophenolate, or cyclosporine as steroid sparing agent.
  - Recommended dose**: 2g/kg over 2-5 consecutive days

- **Prophylaxis of bacterial infections in bone marrow transplant (BMT)/hematopoietic stem cell transplant (HCST) recipients**
  - Meets diagnostic criteria for prophylaxis of bacterial infections in patients with BMT or HCST
  - Medication (IVIG) is requested within the first 100 days post-transplant
  - OR
  - Member has pre-treatment serum IgG < 400mg/dL after 100 days post-transplant
  - Recommended dosing**: 500 mg/kg IV on days 7 and 2 pretransplant or at the time conditioning therapy for transplantation is begun, then weekly through day 90 posttransplant

- **Renal transplant rejection**
  - Used as desensitization of acute humoral rejection in kidney transplant patients to reduce anti-HLA antibodies
  - Recommended dosing**: Induction therapy: 0.4 g/kg/day for 4 days every 4 weeks for 6 months; maintenance therapy: 1.2 to 1.6 g/kg over 2 to 4 days at 6 to 8 week intervals

- **Stiff-person syndrome**
  - Meets diagnostic criteria for Stiff-person syndrome
  - Failed or intolerant/contraindicated to benzodiazepines (e.g., diazepam) and/or baclofen
  - Recommended dosing**: 2 g/kg, administered over two to three infusions, each usually separated by three to five days

- **Von Willebrand disorder (VMD)**
  - Meets diagnostic criteria for acquired VWD associated with autoimmune disease or a monoclonal gammopathy
  - Recommended dosing**: 1 g/kg/day for 2 days

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The criteria listed above applies to Fallon Health Plan and its subsidiaries.
Criteria for Continuation of Therapy:

- Patient’s therapy has been re-evaluated within the last 12 months, unless a re-evaluation is not clinically appropriate for the patient’s condition at this time
- There continues to be a medical need for the medication or medication is clinically appropriate
- Patient has disease stabilization or improvement in disease (as defined by standard parameters for the patient’s condition)
- Medical services must continuously meet nationally recognized standard for quality care and are provided at the appropriate level of care and place of service. The following are some exceptions that may be acceptable for services outside the home:
  - Documented history of a severe reaction to IVIG or blood products. Severe reaction is defined as anaphylactic reaction. The patient should have a history of reactions and not be based on the potential of IVIG to induce such reactions.
  - Documented intolerance to IVIG requiring constant telemetry monitoring of vitals
  - Unsafe home environment
  - No access to 911 services
  - Documented presence of IGA auto antibodies.
  - Patient is severely decompensated (e.g. respiratory failure in a myasthenic crisis)

Caution:

- Hypersensitivity and anaphylactic reactions can occur, especially in patients with anti-IgA antibodies or corn allergy
- Acute renal dysfunction may occur. Use with caution in the elderly, patients with renal disease, diabetes mellitus, overweight, hypovolemia, volume depletion, sepsis, paraproteinemia, and nephrotoxic medications.
- Thrombosis may occur with immune globulin products even in the absence of risk factors for thrombosis
- Ensure adequate hydration before administration. Monitor for signs and symptoms of thrombosis and assess blood viscosity in patients at risk for hyperviscosity
- Infectious agent transmission may occur

Contraindications:

- Anaphylaxis or severe systemic reaction to human immunoglobulins or to any component of the product, including polysorbate 80
- Hereditary intolerance to fructose, including infants and neonates for whom sucrose or fructose tolerance has not been established (Gammaplex)
- Hyperprolinemia (type I or II); Hizentra and Privigen contain the stabilizer L-proline
- IgA deficiency with antibodies against IgA, and a history of hypersensitivity; IG products contain trace amounts of IgA
- Severe thrombocytopenia or any coagulation disorder which would contraindicate IM injections (GammSTAN S/D)

Special Considerations:

- Pregnancy category C
- Use with caution in the elderly; may be at increased risk for renal dysfunction/failure and thromboembolic events
- Concurrent use with live virus vaccines may result in interference with the immune response to the live vaccine

** Please provide medical rationale for doses above the recommended dose

The criteria listed above applies to Fallon Health Plan and its subsidiaries.
Approval Duration:

- Varies for individual disease states depending on clinical responses, trough IgG levels, and patient tolerability

Benefit Type:

- Medical

Adopted: 11/16/04
Revised: 6/13/07, 9/8/10, 3/14/12

Reviewed: 6/14/2017 – updated criteria for use & contraindications, added continuation of therapy criteria, approval duration & benefit type