Immune Globulins

**Intravenous Immune Globulin (IVIG):**
Bivigam, Carimune NF, Flebogamma DIF, Gammagard Liquid, Gammagard S/D, Gammaked, Gammaplex, Gamunex-C, Octagam, and Privigen

**Subcutaneous Immune Globulin:**
Hizentra and HyQvia

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**Line(s) of Business:**
HMO; PPO; QUEST Integration
Akamai Advantage

**Original Effective Date:**
05/21/1999

**Current Effective Date:**
10/01/2015

**POLICY**

**A. INDICATIONS**
The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

**FDA-APPROVED INDICATIONS**
- Primary immunodeficiency*
- Idiopathic thrombocytopenic purpura
- Chronic inflammatory demyelinating polyneuropathy
- Multifocal motor neuropathy
- Kawasaki syndrome
- B-cell chronic lymphocytic leukemia

*Subcutaneous immune (SCIG) globulin is covered only for the treatment of primary immunodeficiencies for members who are not able to tolerate intravenous immune globulin (IVIG).

**COMPENDIAL USES**
- Prevention of graft-versus-host disease and infections in bone marrow transplant (BMT)/hematopoietic stem cell transplant (HSCT) recipients
- Secondary immunodeficiency due to drugs/biologic agents, underlying disease, environmental exposure, or other causes
- Prevention of infections in pediatric human immunodeficiency virus (HIV) infection
- Dermatomyositis
- Guillain-Barre syndrome
- Fetal alloimmune thrombocytopenia
- Myasthenia gravis
• Autoimmune mucocutaneous blistering diseases: pemphigus vulgaris, pemphigus foliaceus, bullous pemphigoid, mucous membrane pemphigoid, and epidermolysis bullosa acquisita
B. REQUIRED DOCUMENTATION
The following information is necessary to initiate the prior authorization review:

- For subcutaneous immune globulin, documentation supporting the member’s inability to tolerate intravenously administered immune globulin
- For primary immunodeficiency
  - Laboratory evidence of immunoglobulin deficiency (see Appendix)
  - Laboratory evidence of inability to mount an adequate response to inciting antigens (see Appendix)
- For chronic inflammatory demyelinating polyneuropathy
  - Clinical notes documenting functional disability
  - Electromyography (EMG)/nerve conduction study (NCS) report
  - Spinal fluid protein and/or nerve biopsy report
- If therapy beyond the initial authorized duration is required, an extension request must be submitted with the physician’s updated orders, clinical information substantiating that IVIG is effective, and the need for the extension.
  - For CIDP following the initial treatment regimen, documentation that demonstrates significant improvement in clinical condition and, when relevant, a reduction in the level of sensory loss must be submitted.
  - For the long-term treatment of stable CIDP patients, documentation that the dose has been periodically reduced or withdrawn, and the effects measured, in order to validate continued use must be submitted.
- For Guillain-Barre syndrome
  - Pulmonary function test, or
  - Clinical notes documenting the patient’s functional status and course of illness
- Multifocal motor neuropathy
  - Anti-GM1 antibodies and conduction block
  - Conventional therapies that were tried and found to be ineffective, not tolerated or contraindicated

C. CRITERIA FOR APPROVAL – INTRAVENOUS IMMUNE GLOBULIN

1. Primary immunodeficiency (includes congenital agammaglobulinemia (X-linked agammaglobulinemia), hypogammaglobulinemia, common variable immunodeficiency, X-linked immunodeficiency with hyperimmunoglobulin M, severe combined immunodeficiency and Wiskott-Aldrich syndrome)
   a. Initial authorization for 12 months may be granted for members who meet the following criteria:
      i. Laboratory evidence of immunoglobulin deficiency (see Appendix)
      ii. Documented inability to mount an adequate response to inciting antigens (see Appendix)
      iii. Persistent and severe infections despite treatment with prophylactic antibiotics
   b. Authorization for 12 months may be granted for continuation of therapy.
2. **Secondary immunodeficiency due to drugs/biologic agents, underlying disease, environmental exposure, or other causes**
   a. Initial authorization for 12 months may be granted for members who meet the following criteria:
      i. Laboratory evidence of immunoglobulin deficiency (see Appendix)
      ii. Documented inability to mount an adequate response to inciting antigens (see Appendix)
      iii. Persistent and severe infections despite treatment with prophylactic antibodies
   b. Authorization for 12 months may be granted for continuation of therapy.

3. **Chronic inflammatory demyelinating polyneuropathy (CIDP)**
   a. Initial authorization for 3 months may be granted for members who meet the following criteria:
      i. Significant functional disability
      ii. Slowing of nerve conduction velocity on EMG or NCS
      iii. Elevated spinal fluid protein on lumbar puncture or a nerve biopsy confirming the diagnosis
   b. Authorization of 12 months for continuation of treatment may be granted when member demonstrates significant improvement in clinical condition and, when relevant, a reduction in the level of sensory loss.
   c. For members receiving treatment with IVIG for 2 years or more, authorization of 6 months may be granted when IVIG dose reduction or withdrawal has been periodically attempted and the effects measured to validate continue use.

4. **Multifocal motor neuropathy**
   a. Initial authorization for 6 months may be granted for members who meet the following criteria:
      i. Conduction block on EMG/NCS
      ii. Elevated anti-GM1 antibody titers
      iii. Conventional therapy was ineffective or not tolerated.
   b. Authorization of 12 months for continuation of therapy may be granted for members who experience significant improvement in disability and maintenance of improvement with IVIG therapy.

5. **Guillain-Barre syndrome**
   a. Authorization for 6 months may be granted for members who meet the following criteria:
      i. Plasma exchange is not available or is not an appropriate treatment option
      ii. Member has one of the following clinical features
         1) Deteriorating pulmonary function tests
         2) Rapid deterioration with symptoms for less than 2 weeks
         3) Rapidly deteriorating ability to ambulate
         4) Frank inability to ambulate independently for 10 meters
6. Dermatomyositis
   a. Initial authorization for 6 months may be granted for members whose condition has failed to respond to first-line treatment with corticosteroids.
   b. Authorization of 12 months for continuation of therapy may be granted for members who experience significant improvement in disability and maintenance of improvement with IVIG therapy.

7. Myasthenia gravis
   a. Authorization for 3 months may be granted for members who are experiencing a myasthenic crisis (ie, acute episode of respiratory muscle weakness) and plasma exchange is not available or is not an appropriate option.
   b. Initial authorization for 6 months may be granted for members with chronic debilitating myasthenia gravis who have experienced an inadequate response or toxicity from treatment with cholinesterase inhibitors, corticosteroids, and/or azathioprine.
   c. For chronic debilitating disease, authorization of 12 months for continuation of therapy may be granted for members who experience significant improvement in disability and maintenance of improvement with IVIG therapy.

8. Autoimmune mucocutaneous blistering disease
   a. Authorization for 6 months may be granted for members who meet both of the following criteria (i. and ii.):
      i. Member has one of the following:
         a) Pemphigus vulgaris
         b) Pemphigus foliaceus
         c) Bullous pemphigoid
         d) Mucous membrane pemphigoid (cicatrical pemphigoid, benign mucous membrane pemphigoid), with or without mention of ocular involvement
         e) Epidermolysis bullosa acquisita
      ii. Member has severe progressive disease despite treatment with conventional therapy (eg, corticosteroids, azathioprine, or cyclophosphamide).

9. Kawasaki syndrome
   a. Authorization for 6 months may be granted for members with Kawasaki syndrome and IVIG will be used in conjunction with aspirin.

10. Bone marrow/hematopoietic stem cell transplant recipients (BMT/HSCT)
    a. Authorization for up to 100 days after BMT/HSCT may be granted for members who meet the following criteria:
       i. IVIG is prescribed for prevention of graft-versus-host disease after allogeneic BMT/HSCT, or for prevention of infection after BMT/HSCT
       ii. Member is age 20 years or older
       iii. IVIG is requested for use within 100 days after transplantation (the date of transplantation must be documented)
11. **Pediatric HIV infection**
   a. Initial authorization for 6 months may be granted for members who meet the following criteria:
      i. IVIG is prescribed for prevention of infections associated with HIV infection
      ii. Members is less than or equal to 12 years of age
   b. Authorization of 6 months for continuation of therapy may be granted for members who experience a reduction in infections with IVIG therapy.

12. **Chronic lymphocytic leukemia (CLL)**
   a. Initial authorization for 6 months may be granted for members who meet the following criteria:
      i. IVIG is prescribed for prevention of infections associated with CLL
      ii. Member has hypogammaglobulinemia prior to starting IVIG therapy
      iii. Member has a history or recurrent bacterial infections prior to starting IVIG therapy
   b. Authorization of 6 months for continuation of therapy may be granted for members who experience a reduction in infections with IVIG therapy.

D. **CRITERIA FOR APPROVAL – SUBCUTANEOUS IMMUNE GLOBULIN**
   1. **Primary immunodeficiency** (includes congenital agammaglobulinemia (X-linked agammaglobulinemia), hypogammaglobulinemia, common variable immunodeficiency, X-linked immunodeficiency with hyperimmunoglobulin M, severe combined immunodeficiency and Wiskott-Aldrich syndrome)
      a. Initial authorization for 12 months may be granted for members who meet the following criteria:
         i. Member is unable to tolerate intravenously administered immune globulin
         ii. Laboratory evidence of immunoglobulin deficiency (see Appendix)
         iii. Documented Inability to mount an adequate response to inciting antigens (see Appendix)
         iv. Persistent and severe infections despite treatment with prophylactic antibiotics
      b. Authorization for 12 months may be granted for continuation of therapy.

E. **APPENDIX - Primary Immunodeficiency Syndromes.**
The diagnosis of immunodeficiency and post immunization titers must be taken in context with the clinical presentation of the patient and may vary dependent on the type of vaccine given and the prior immunization history of the patient. The following parameters are examples of criteria for diagnosis of the primary immunodeficiency syndromes.

1. Laboratory evidence of immunoglobulin deficiency may include the following definitions:
   a. Agammaglobulinemia (total IgG less than 200 mg/dL)
   b. Persistent hypogammaglobulinemia (total IgG less than 400 mg/dL, or at least two standard deviations below normal, on at least two occasions)
   c. Absence of B lymphocytes

2. Inability to mount an adequate antibody response to inciting antigens may include the following definitions:
   a. Lack of appropriate rise in antibody titer following provocation with a polysaccharide antigen. For example, an adequate response to the pneumococcal vaccine may be defined as at least a 4-fold increase in titers for at least 50% of serotypes tested.
b. Lack of appropriate rise in antibody titer following provocation with a protein antigen. For example, an adequate response to tetanus/diphtheria vaccine may be defined as less than a 4-fold rise in titers 3-4 weeks after vaccine administration.

F. CONTINUATION OF THERAPY

Members starting therapy as well as new members not previously authorized by CVS/HMSA must meet ALL initial authorization criteria.

G. DOSAGE AND ADMINISTRATION

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

H. PROGRAM EXCEPTION – AKAMAI ADVANTAGE

For Akamai Advantage members, the following Local Coverage Determination (LCD) applies:

- Intravenous Immune Globulin (IVlg) (L33532)

I. IMPORTANT REMINDER

The purpose of this Medical Policy is to provide a guide to coverage. This Medical Policy is not intended to dictate to providers how to practice medicine. Nothing in this Medical Policy is intended to discourage or prohibit providing other medical advice or treatment deemed appropriate by the treating physician.

Benefit determinations are subject to applicable member contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

This Medical Policy has been developed through consideration of the medical necessity criteria under Hawaii’s Patients’ Bill of Rights and Responsibilities Act (Hawaii Revised Statutes §432E-1.4), generally accepted standards of medical practice and review of medical literature and government approval status. HMSA has determined that services not covered under this Medical Policy will not be medically necessary under Hawaii law in most cases. If a treating physician disagrees with HMSA's determination as to medical necessity in a given case, the physician may request that CVS/caremark reconsider the application of the medical necessity criteria to the case at issue in light of any supporting documentation.

J. REFERENCES