I. Medication Description

Immune globulins are therapeutic preparations of pooled polyspecific IgG (Immunoglobulin G antibodies) obtained from the plasma of a large number of healthy individuals. The original use of these immunoglobulin preparations, which contain a broad range of antibody specificities, was in antibody replacement therapy. However, a number of other clinical benefits of immune globulin treatment have been demonstrated. Many of these other uses result from anti-inflammatory and immunomodulatory effects, which were not anticipated when these polyclonal preparations were first developed. Immune globulins are available as intravenous, subcutaneous and intramuscular dosage forms.

II. Position Statement

All formulations of immune globulin are available under the medical benefit.

Subcutaneous formulations of immune globulin are also available under the pharmacy benefit:

- Hizentra, Gamunex-C, Gammaked, Gammagard Liquid, HyQvia, Cuvitru

Coverage is determined through a prior authorization process with supporting clinical documentation for all requests.

III. Policy

Coverage for intravenous globulin products (J1459, J1556, J1561, J1566, J1568, J1569, J1572, J1557, J1599) is provided for the following:

- Primary immune and functional deficiency disorders (including, but not limited to agammaglobulinemia, hypogammaglobulinemia, common variable immunodeficiency, severe combined immunodeficiencies, Wiskott-Aldrich syndrome) OR B-cell chronic lymphocytic leukemia (CLL) when:
  - The member has a deficiency in producing antibodies OR
  - IgG pretreatment lab value is less than 600 mg/dL AND at least 1 bacterial infection is directly attributed to member's immunodeficiency
• Infection prophylaxis in hematopoietic cell transplantation (HCT) recipients OR HIV-infected members when:
  o IgG pretreatment lab value is less than 400 mg/dL
• Immune thrombocytopenia/Idiopathic thrombocytopenia purpura (ITP) (including HCV and HIV-associated):
  o For members unable to receive corticosteroids OR who need a rapid increase in platelet count
    (platelet counts usually less than 30,000/μl for newly diagnosed members)
  o To increase platelet counts prior to invasive major surgical procedures (i.e. splenectomy)
  o Post-splenectomy members with platelet counts less than 30,000/μl
• Fetal and neonatal alloimmune thrombocytopenia
• Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)
• Multifocal motor neuropathy (MMN)
• Myasthenia Gravis
  o Severe disease resistant to a trial with conventional therapies (i.e., cholinesterase inhibitors, corticosteroids, immunosuppressants, or plasma exchange)
• Myasthenic crisis (i.e. member is experiencing an acute episode of respiratory muscle weakness)
  o Member has a contraindication to plasma exchange
• Refractory dermatomyositis
  o Severe disease resistant to a trial of conventional therapy options (i.e., corticosteroids or immunosuppressant agents such as azathioprine, methotrexate, cyclophosphamide, cyclosporine) AND
  o Given in combination with immunosuppressant therapy
• Bone Marrow Transplant
• Solid Organ Transplant: prior to or following a transplant for prevention or treatment of antibody-mediated rejection
• Guillain-Barre Syndrome
• Kawasaki Disease
• West Nile virus treatment including meningitis and encephalitis
• Measles prophylaxis: for severely immune compromised or non-measles immune pregnant members
• Post transfusion purpura
• Autoimmune mucocutaneous blistering diseases (including, but not limited to pemphigus vulgaris): for members nonresponsive or intolerant to steroids or immunosuppressant therapy

Coverage for subcutaneous immune globulin (J1559, J1561, J1562, J1569, J1575) is provided for the following diagnoses:
• Primary immunodeficiency (including, but not limited to agammaglobulinemia, hypogammaglobulinemia, common variable immunodeficiency, severe combined immunodeficiencies, Wiskott-Aldrich syndrome) when:
  o The member is 2 years of age or older if using Hizentra, Gamunex-C, Gammagard Liquid, or Cuvitru OR the member is an adult if using Gammaked or HyQvia AND
The member has been receiving intravenous or subcutaneous immune globulin at regular intervals prior to switching to the requested subcutaneous product if using Gamunex-C, Gammagard Liquid, Gammaked, or Cuvitru OR

- The member has been receiving intravenous immune globulin at regular intervals for at least 3 months if using Hizentra AND
- The member has a deficiency in producing antibodies OR
- IgG pretreatment lab value is less than 600 mg/dL AND at least 1 bacterial infection is directly attributed to member's immunodeficiency

### IV. Quantity Limitations

- Dependent on diagnosis and product
- For the purposes of Max Unit editing, the dose of 1g/kg every day x 2 days given every 21 days is used for IVlg:
  - Max units (male): 460 units every 21 days
  - Max units (female): 400 units every 21 days

### V. Coverage Duration

- Initial coverage for multifocal motor neuropathy will be provided for 3 months to evaluate response and may be renewed.
- Initial coverage for all other diagnoses is provided for 6 months and may be renewed.

### VI. Coverage Renewal Criteria

Coverage can be renewed for up to 12 months at a time based upon the following criteria:

- For multifocal motor neuropathy: If member is a responder to initial therapy, renewal may be given.
- For all other indications:
  - Documented improvement of disease symptoms AND
  - Documentation of improvement or stabilization of IgG level (if applicable)

### VII. Billing/Coding Information

- J Codes:
  - J1459- Privigen (500mg per 1 billable unit)
  - J1556- BIVIGam (500mg per 1 billable unit)
  - J1557- Gammaplex (500mg per 1 billable unit)
  - J1559- Hizentra (100mg per 1 billable unit)
  - J1561- Gammaked, Gamunex-C (500mg per 1 billable unit)
  - J1566- IVlg lyophilized: Gammagard S/D, Carimune NF, Panglobulin NF (500mg per 1 billable unit)
  - J1568- Octagam (500mg per 1 billable unit)
  - J1569- Gammagard (500mg per 1 billable unit)
  - J1572- Flebogamma, Flebogamma DIF (500mg per 1 billable unit)
VIII. Summary of Policy Changes

- 6/1/11:
  - Gamunex-C (subcutaneous) added to policy indications and contraindications
  - Autopay grid edited for intravenous products only
  - Criteria added for specific diagnoses (primary immune deficiencies, ITP, CIDP, myasthenic crisis/myasthenia gravis, refractory dermatomyositis, solid organ transplant, multifocal motor neuropathy, and prevention of infection in HIV positive members.

- 6/15/12:
  - allow coverage in situations where the member has a documented inability to produce adequate amounts of antibody
  - extend coverage duration for renewals

- 12/15/12:
  - Removed requirement for IVIg use prior to coverage consideration of SCIg based on current practices and dosing capabilities

- 6/15/13:
  - Addition of IMIg to policy with criteria for approved indications
  - Addition of approvable diagnoses for SCIg to mirror IVIg indications
  - Addition of dosing limitations for all product formulations
  - Removal of autopay for Guillain-Barre Syndrome and Kawasaki Disease
  - Addition of Gammaked, BIVIGam, BayGam, and GamaSTAN S/D to the policy
  - Addition of renewal criteria

- 1/1/14: BIVIGam code update documented

- 6/15/14:
  - Clarification of West Nile Virus treatment scenario
  - Measles prophylaxis criteria added
  - autoimmune mucocutaneous blistering diseases criteria added excluded uses updated

- 1/12/15: HyQvia added to policy

- 7/1/15: formulary distinctions made

- 9/15/15: no policy changes

- 1/1/16: updated HyQvia drug code

- 9/15/16: no policy changes

- 7/19/16:
  - Update of ITP criteria according to guidelines
  - Addition of coverage for infection prophylaxis in hematopoietic cell transplantation

- 1/1/17:
  - Cuvitru added to policy; Vivaglobin and Baygam removed due to product discontinuation
  - Clarified criteria for products with different routes of administration
  - clarified no PA required for IMIg products
• 6/21/17: removed Gamunex as product is off-market

IX. References

5. Gammagard® package insert, Revised June 2012.
13. BLIGam® package insert, Revised April 2012.
15. HyQvia® package insert, September 2014.

The Plan fully expects that only appropriate and medically necessary services will be rendered. The Plan reserves the right to conduct pre-payment and post-payment reviews to assess the medical appropriateness of the above-referenced therapies.

The preceding policy applies only to members for whom the above named pharmacy benefit medications are included on their covered formulary. Members with closed formulary benefits are subject to trying all appropriate formulary alternatives before a coverage exception for a non-formulary medication will be considered. The preceding policy is a guideline to allow for coverage of the pertinent medication/product, and is not meant to serve as a clinical practice guideline.