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:

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

For claims payment purposes, coverage authorizations granted for products in this policy allow coverage for and are interchangeable with same coverage allowances as follows:

- For other immune globulin products when formulation and route of administration are the same AND
- When billable unit code parameters are equal, as listed under VII. Billing/Coding Information.

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:

- B-cell chronic lymphocytic leukemia (CLL) when:
  - IgG pretreatment lab value is less than 500 mg/dL AND
The member has a history of recurrent infections

- Primary immune and functional deficiency disorders (including, but not limited to agammaglobulinemia, hypogammaglobulinemia, common variable immunodeficiency, severe combined immunodeficiencies, Wiskott-Aldrich syndrome) when:
  - The member has a deficiency in producing antibodies (i.e. inability to mount an adequate antibody response to a polysaccharide [ex. pneumococcal] or protein [ex. Tetanus, diphtheria] vaccine challenge) OR
  - IgG pretreatment lab value is less than 500 mg/dL OR is below the lab reference range AND member has a history of recurrent infections directly attributed to immunodeficiency

- Infection prophylaxis in hematopoietic cell transplantation (HCT) recipients OR HIV-infected members when:
  - IgG pretreatment lab value is less than 400 mg/dL

- Immune thrombocytopenia/Idiopathic thrombocytopenia purpura (ITP) (including HCV and HIV-associated):
  - To increase platelet counts prior to invasive major surgical procedures (i.e. splenectomy) OR
  - Post-splenectomy members with platelet counts less than 30,000/μl OR
  - Platelet count is less than 30,000/μl AND
    - Member has not had an adequate response to corticosteroids OR
    - Member is unable to receive corticosteroids OR
    - A rapid increase in platelet count is needed that will not be achievable with corticosteroids

- Fetal and neonatal alloimmune thrombocytopenia

- Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)
  - Has a diagnosis of CIDP supported by progress notes or consultation reports from a pertinent specialist AND
  - Chart notes include a reference to, or a hardcopy of, electrodiagnostic studies with interpretation by a specialist that is consistent with CIDP

- Multifocal motor neuropathy (MMN)
  - Has a diagnosis of MMN supported by progress notes or consultation reports from a pertinent specialist AND
  - Chart notes include a reference to, or a hardcopy of, electrodiagnostic studies with interpretation by a specialist that is consistent with MMN

- Myasthenia gravis exacerbation
  - Member has had an inadequate response to corticosteroids (or use is contraindicated) AND
  - Member is currently receiving or will be starting an immunosuppressive maintenance therapy (i.e. azathioprine, cyclosporine, mycophenolate, methotrexate, tacrolimus, etc.), unless contraindicated

- Refractory myasthenia gravis
  - Member has had an inadequate response or contraindication to pyridostigmine AND
  - Member has had an inadequate response or contraindication to corticosteroids AND
  - Member has had an inadequate response or contraindication to at least TWO or more of the following:
    - Azathioprine
• Cyclosporine
• Mycophenolate mofetil
• Tacrolimus
• Methotrexate
• Cyclophosphamide
• Myasthenic crisis (e.g. member is experiencing an acute episode of respiratory muscle weakness)
• Refractory dermatomyositis
  - Severe disease resistant to a trial of conventional therapy options (i.e., corticosteroids or immunosuppressant agents such as azathioprine, methotrexate, cyclophosphamide, cyclosporine) AND
  - 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:
  - 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 (i.e. inability to mount an adequate antibody response to a polysaccharide [ex. pneumococcal] or protein [ex. Tetanus, diphtheria] vaccine challenge) OR
  - IgG pretreatment lab value is less than 500 mg/dL OR is below the lab reference range AND member has a history of recurrent infections directly attributed to immunodeficiency

Coverage for subcutaneous immune globulin (J1559) is also provided for the following diagnoses for adults only:
• Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)
  o The member has been receiving intravenous immune globulin at regular intervals for at least 3 months if using Hizentra AND
  o Has a diagnosis of CIDP supported by progress notes or consultation reports from a specialist AND
  o Chart notes include a reference to, or a hardcopy of, electrodiagnostic studies with interpretation by a specialist that is consistent with CIDP

IV. Quantity Limitations

Coverage is available for a quantity sufficient to allow for FDA-approved dosing. Dosing will vary based on diagnosis and specific medication being used.

V. Coverage Duration

• Initial coverage for myasthenic exacerbation will be provided for 1 month (one treatment course) and may not be renewed.
• Initial coverage for refractory myasthenia gravis will be provided for up to 3 months and may be renewed in up to 6 month intervals.
• Initial coverage for multifocal motor neuropathy will be provided for 3 months to evaluate response and may be renewed.
• Initial coverage for ITP will be provided for one treatment course:
  o Duration of treatment course ranges from 1-5 days and is dependent upon product-specific labeling
• Initial coverage for Fetal and neonatal alloimmune thrombocytopenia will be provided for one treatment course and may be renewed:
  o Duration of treatment course is dependent upon product-specific labeling
• Initial coverage for all other diagnoses is provided for 6 months and may be renewed.

VI. Coverage Renewal Criteria

• Coverage for Fetal and neonatal alloimmune thrombocytopenia may be renewed for one additional treatment course if 4 weeks have elapsed since the initial treatment course
• Coverage for ITP may be renewed for subsequent treatment courses if initial coverage criteria is met
• Coverage for multifocal motor neuropathy may be renewed if the member is a responder to initial therapy
• Coverage for the treatment of refractory myasthenia gravis may be renewed for up to 6 months at a time based upon the following criteria:
  o Member displays improvement of symptoms or shows stabilization of disease AND
  o Continuation of treatment is warranted (medical necessity shown with provided documentation) AND
  o Absence of unacceptable toxicity from the drug has been documented
• Coverage for Primary immune and functional deficiency disorders may be renewed for up to 12 months at a time if the following criteria are met:
• Documentation of improvement or stabilization of IgG level (if applicable) OR
• Documentation of improvement in the frequency of infections

• Coverage for all other indications can be renewed for up to 12 months at a time based upon the following criteria:
  o Documented improvement of disease symptoms AND
  o Documentation of improvement or stabilization of IgG level (if applicable)

VII. Billing/Coding Information

• J Codes:
  o J1459- Privigen (500mg per 1 billable unit)
  o J1556- BIVIGam (500mg per 1 billable unit)
  o J1557- Gammaplex (500mg per 1 billable unit)
  o J1559- Hizentra (100mg per 1 billable unit)
  o J1561- Gammaked, Gamunex-C (500mg per 1 billable unit)
  o J1566- IVIg lypholized: Gammagard S/D, Carimune NF, Panglobulin NF (500mg per 1 billable unit)
  o J1568- Octagam (500mg per 1 billable unit)
  o J1569- Gammagard (500mg per 1 billable unit)
  o J1572- Flebogamma DIF (500mg per 1 billable unit)
  o J1599- IVIg NOS (500mg per 1 billable unit)
  o J1575- HyQvia (100mg per 1 billable unit)
  o J1555- Cuvitru (100 mg per 1 billable unit)
  o J1599 – Panzyga (500mg per 1 billable unit)
  o J1599 – Asceniv (500 mg per 1 billable unit)
  o J1558 - Xembify (100 mg per 1 billable unit)

VIII. Summary of Policy Changes

• 6/1/11:
  o Gamunex-C (subcutaneous) added to policy indications and contraindications
  o Autopay grid edited for intravenous products only
  o 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:
  o allow coverage in situations where the member has a documented inability to produce adequate amounts of antibody
  o extend coverage duration for renewals

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

• 6/15/13:
o Addition of IMIg to policy with criteria for approved indications
o Addition of approvable diagnoses for SCIg to mirror IVIg indications
o Addition of dosing limitations for all product formulations
o Removal of autopay for Guillain-Barre Syndrome and Kawasaki Disease
o Addition of Gammaked, BIVIGam, BayGam, and GamaSTAN S/D to the policy
o Addition of renewal criteria
• 1/1/14: BIVIGam code update documented
• 6/15/14:
  o Clarification of West Nile Virus treatment scenario
  o Measles prophylaxis criteria added
  o 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:
  o Update of ITP criteria according to guidelines
  o Addition of coverage for infection prophylaxis in hematopoietic cell transplantation
• 1/1/17:
  o Cuvitru added to policy; Vivaglobin and Baygam removed due to product discontinuation
  o Clarified criteria for products with different routes of administration
  o clarified no PA required for IMIg products
• 6/21/17: removed Gamunex as product is off-market
• 1/1/18: updated billing/coding information
• 5/1/18: updated criteria, quantity limits, and coverage duration for myasthenia gravis treatment
• 8/15/18:
  o created separate coverage criteria for CLL
  o updated coverage criteria for PID and ITP
  o added requirement for specialist involvement in diagnosis and electrodiagnostic studies confirming CIDP or MMN
  o updated coverage duration
  o updated renewal criteria
  o updated billing/coding information
• 8/15/19: removed Flebogamma as product is off-market; updated billing/coding information
• 11/15/19: added Xembify to policy; updated billing/coding information
• 5/1/20: added Asceniv and Panzyga to policy; updated billing/coding information
• 7/1/20: updated billing/coding information
• 8/1/20: Primary immune and functional deficiency disorders renewal duration clarified as up to 12 months

IX. References

*These guidelines are not applicable to benefits covered under Medicare Advantage. Medicare Advantage benefit coverage requests are reviewed in accordance with the guidance set forth in Chapter 15 Section 50 of the Centers for Medicare & Medicaid Services Medicare Benefit Policy Manual.

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.