IVIG (intravenous Immunoglobulin)  
SCIG Immune Globulin (subcutaneous immunoglobulin)

**Description**

IVIG / SCIG Immune Globulin – Bivigam, Carimune NF, Flebogamma, Gammagard, Gammagard S/D, Gammaked, Gammaplex, Gamunex-C, Hizentra, Hyqvia, Octagam, Privigen

**Background**

Immune globulin products from human plasma were first used in 1952 to treat immune deficiency. Intravenous immunoglobulin (IVIG) contains the pooled immunoglobulin G (IgG) immunoglobulins from the plasma of approximately a thousand or more blood donors (1).

IVIG is used to treat various autoimmune, infectious, and idiopathic diseases. IVIG is an approved treatment for graft versus host disease and ITP. It is accepted for use in persons with Kawasaki disease, Guillain-Barré syndrome, and polymyositis/dermatomyositis (1).

**Regulatory Status**

The immune globulins addressed by this policy are FDA-approved for use in one or more of the following conditions:

- Primary immune deficiency (PID)
- Acute and Chronic Thrombocytopenic Purpura (ITP)
- Prevention of bacterial infections in patients with hypogammaglobulinemia and/or recurrent bacterial infections associated with B-cell Chronic Lymphocytic Leukemia (CLL)
- Prevention of coronary artery aneurysms associated with Kawasaki syndrome
- Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)(2-13)
Immune globulin use is associated with increased risk of thrombosis, particularly in the elderly and patients with risk factors such as cardiovascular disease, hypercoagulopathy, those on estrogen therapy, and patients with central venous catheters. Patients should be monitored carefully for signs and symptoms of thrombosis both at the time of infusion and after infusion. For those patients who will be self-administering the medication, practitioners need to instruct the patients and caregivers on how to monitor for signs and symptoms of thrombosis. Thrombosis may occur regardless of the route of administration (2-13).

IVIG products have been associated with renal dysfunction, acute renal failure, osmotic nephrosis, and death. Patients predisposed to acute renal failure include patients with any degree of pre-existing renal insufficiency, diabetes mellitus, > 65 years of age, volume depletion, sepsis, paraproteinemia, or patients receiving known nephrotoxic drugs.(2-13)

Other potential complications to monitor include the following (2-13):

**Immunoglobulin A deficiency:** People with this condition have the potential for developing antibodies to IgA and could have anaphylactic reactions to subsequent administration of blood products that contain IgA.

**Aseptic meningitis syndrome (AMS):** Rare occurrences of AMS have been reported in association with IVIG treatment. AMS usually begins within several hours to 2 days following IVIG treatment and is characterized by symptoms including severe headache, drowsiness, fever, photophobia, painful eye movements, muscle rigidity, nausea, and vomiting. AMS may occur more frequently in association with high-dose (2 g/kg) IVIG treatment. Discontinuation of IVIG treatment has resulted in remission of AMS within several days without sequelae.

**Bleeding complications:** Bleeding complications may be encountered in patients with thrombocytopenia or other bleeding disorders.

**Severe reactions:** Severe reactions, such as anaphylaxis or angioneurotic edema, have been reported in association with IV immunoglobulins, even in patients not known to be sensitive to human immunoglobulins or blood products.

**Related policies**

Atgam, GamaSTAN

**Policy**

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.
IVIG / SCIG may be considered **medically necessary** for treatment of the following conditions: Primary Immunodeficiency Disease (PID) Including, but not limited to: hypogammaglobulinemia, agammaglobulinemia, SCID (severe combined immunodeficiency disease), Wiskott-Aldrich syndrome, CVID (common variable Immunodeficiency disease); also for idiopathic thrombocytopenic purpura, B-cell chronic lymphocytic leukemia, Kawasaki syndrome, Allogeneic Bone Marrow Transplantation (AlloBMT), Autologous Bone Marrow Transplantation (AuBMT), hematopoietic stem cell transplantation, peripheral blood progenitor cell (PBPC) collection, Umbilical Cord Stem Cell Transplantation, pediatric-HIV infections, polymyositis, dermatomyositis, inclusion-body myositis, fetal alloimmune thrombocytopenia, myasthenia gravis, multiple sclerosis, multifocal motor neuropathy, neoplastic disease, chronic inflammatory demyelinating polyneuropathy (CIDP), sinusitis, recurrent sinusitis, chronic sinusitis, or recurrent, chronic sinusitis if the patient has a deficiency of 1 or more of the following: IgA, IgG, or IgM; monitor patients carefully for signs and symptoms of thrombosis both at the time of infusion and after infusion, or patients / caregivers have been instructed on how to monitor for signs and symptoms of thrombosis when self-administering the medication.

IVIG / SCIG may be considered **investigational** for all other indications.

**Prior-Approval Requirements**

**Diagnoses**

Patient must have **ONE** of the following

1. Primary Immunodeficiency Disease (PID) Including, but not limited to:
   a. Hypogammaglobulinemia
   b. Agammaglobulinemia
   c. SCID (severe combined immunodeficiency disease)
   d. Wiskott-Aldrich syndrome
   e. CVID (common variable Immunodeficiency disease)

2. Idiopathic thrombocytopenic purpura
3. B-cell chronic lymphocytic leukemia
4. Kawasaki syndrome
5. Allogeneic Bone Marrow Transplantation (AlloBMT)
6. Autologous Bone Marrow Transplantation (AuBMT)
7. Hematopoietic stem cell transplantation
8. Peripheral blood progenitor cell (PBPC) collection
9. Umbilical Cord Stem Cell Transplantation
10. Pediatric-HIV infections
11. Polymyositis  
12. Dermatomyositis  
13. Inclusion-body myositis  
14. Fetal alloimmune thrombocytopenia  
15. Myasthenia gravis  
16. Multiple sclerosis  
17. Multifocal motor Neuropathy  
18. Neoplastic disease  
19. Chronic inflammatory demyelinating polyneuropathy (CIDP).  
20. Sinusitis, recurrent sinusitis, chronic sinusitis, or recurrent, chronic sinusitis if the patient has a deficiency of 1 or more of the following: IgA, IgG, or IgM.

AND ONE of the following:
   a. Monitor patients carefully for signs and symptoms of thrombosis both at the time of infusion and after infusion  
   b. Patients or caregivers have been instructed on how to monitor for signs and symptoms of thrombosis when self-administering the medication

Prior – Approval Renewal Requirements
Same as above

Policy Guidelines

Pre - PA Allowance
None

Prior - Approval Limits
Duration 12 months

Prior – Approval Renewal Limits
Same as above

Rationale

Summary
IVIG is used to provide immediate passive immunity after suspected exposure to an organism for which no active immunization exists or if there is inadequate time to develop active immunization, and as replacement therapy for patients with antibody deficiencies. The passive immunity imparted by IVIG is capable of attenuating or preventing infectious diseases or deleterious reactions from toxins, mycoplasma, parasites, bacteria, and viruses. The IVIG products differ in the preparation method, viral inactivation steps, stabilizing agent, osmolality, and IgA content (1).

Prior approval is required to ensure the safe, clinically appropriate and cost effective use of IVIG / SCIG while maintaining optimal therapeutic outcomes.

References

Policy History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
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<tbody>
<tr>
<td>September 2008</td>
<td>FDA approved Gamunex for the treatment of chronic inflammatory demyelinating polyneuropathy (CIDP) on 9/12/08. CIDP is approvable as off-label use for all Immune Globulins</td>
</tr>
<tr>
<td>March 2009</td>
<td>Added PriVIGen to Immune Globulins and updated format.</td>
</tr>
<tr>
<td>November 2009</td>
<td>Off-label uses clarified; removed Gamimune, Gammar PIV, Venoglobulin-1 and Venoglobulin-S; all of which are no longer on the market.</td>
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### 5.20.03

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<tr>
<th><strong>Section:</strong></th>
<th>Prescription Drugs</th>
<th><strong>Effective Date:</strong></th>
<th>July 1, 2016</th>
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<tr>
<td><strong>Subsection:</strong></td>
<td>Biologicals</td>
<td><strong>Original Policy Date:</strong></td>
<td>March 8, 2002</td>
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<tr>
<th>Date</th>
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<tr>
<td>September 2011</td>
<td>Line extension of Gamunex-C, FDA approved 10/14/2011, for primary immunodeficiency.</td>
</tr>
<tr>
<td>September 2011</td>
<td>Line extension of Gammaked, FDA approved 8/3/2011, for the treatment of primary humoral immunodeficiency disease (PI), idiopathic thrombocytopenic purpura (ITP) and chronic inflammatory demyelinating polyneuropathy (CIDP).</td>
</tr>
<tr>
<td>December 2012</td>
<td>Annual editorial review and update</td>
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<tr>
<td>February 2013</td>
<td>Line addition of BIVIGam</td>
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<tr>
<td>June 2013</td>
<td>Annual editorial review and reference update</td>
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<tr>
<td>June 2013</td>
<td>FDA: New Boxed Warning for Clot Risk with Immune Globulin, reference update</td>
</tr>
<tr>
<td>December 2013</td>
<td>Annual editorial review and reference update</td>
</tr>
<tr>
<td>February 2014</td>
<td>Revision to criteria requirements that self-administering patients are instructed to how to monitor for signs and symptoms of thrombosis.</td>
</tr>
<tr>
<td>November 2014</td>
<td>Addition of HyQvia for all indications</td>
</tr>
<tr>
<td>December 2014</td>
<td>Annual editorial review and reference update</td>
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<tr>
<td>March 2015</td>
<td>Annual editorial review and reference update</td>
</tr>
<tr>
<td>June 2016</td>
<td>Annual editorial review and reference update</td>
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**Addition of CVID (common variable Immunodeficiency disease)**  
**Policy code changed from 5.05.03 to 5.20.03**

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**Keywords**

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This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 24, 2016 and is effective on July 1, 2016.

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