Clinical Policy: Immunoglobulin for Idiopathic Guillain Barre Syndrome
Reference Number: CP.CPA.142
Effective Date: 11.16.16
Last Review Date: 11.17
Line of Business: Commercial

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
The following are immunoglobulins requiring prior authorization: Bivigam™, Carimune NF®, Cuvitru™, Flebogamma DIF®, Gammagard®, Gammagard S/D®, Gammaked®, Gammaplex™, Gamunex-C®, Octagam®, Privigen, Hizentra™, and Hyqvia. Immunoglobulins are sterile preparations of highly purified immunoglobulin G (IgG) derived from large pools of human plasma and administered intravenously or subcutaneously.

FDA approved indication
- For immune globulin intravenous (including Bivigam, Carimune NF, Flebogamma DIF, Gamunex-C, Gammaked, Gammagard, Liquid, Gammagard S/D, Gammaplex, Octagam, Privigen, when used intravenously)
  - Replacement therapy for primary humoral immunodeficiency (PI). This includes, but is not limited to, congenital agammaglobulinemia, common variable immunodeficiency (CVID), X-linked agammaglobulinemia, Wiskott-Aldrich syndrome, and severe combined immunodeficiencies.
  - Treatment of patients with idiopathic thrombocytopenic purpura (ITP) to raise platelet counts to prevent bleeding or to allow a patient with ITP to undergo surgery.
  - Maintenance therapy to improve muscle strength and disability in adult patients with Multifocal Motor Neuropathy (MMN)
  - 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.
  - Treatment of chronic inflammatory demyelinating polyneuropathy (CIDP) to improve neuromuscular disability and impairment and for maintenance therapy to prevent relapse.

- For immune globulin subcutaneous (including Cuvitru, Gamunex-C, Gammaked, Gammagard Liquid, Hizentra, and Hyqvia when used subcutaneously)
  - Treatment of/replacement therapy for patients with primary immunodeficiency (PI). This includes, but is not limited to, congenital agammaglobulinemia, common variable immunodeficiency (CVID), X-linked agammaglobulinemia, Wiskott-Aldrich syndrome, and severe combined immunodeficiencies.

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria
It is the policy of health plans affiliated with Centene Corporation® that Immunoglobulins are **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria**

**A. Guillain Barre Syndrome** (must meet all):

1. Diagnosis of Guillain Barre Syndrome (GBS), also referred to as acute inflammatory demyelinating polyneuropathy (AIDP);
2. The disorder has been diagnosed during the first 2 weeks of the illness;
3. One of the following (a or b):
   a. Patient has significant muscle weakness as evidenced by **any** of the following:
      i. Weakness is at least sufficient to preclude walking 30 feet without assistance;
      ii. Inability to stand or walk without aid;
      iii. Respiratory or bulbar weakness (i.e., deteriorating pulmonary function tests);
      iv. Miller-Fisher syndrome;
   b. Patient has an acutely worsening (<7 days) form of GBS as evidenced by **any** of the following:
      i. Inability to raise head against gravity;
      ii. Severe bulbar palsy (impaired gag reflex, dysarthria and/or dysphagia);
      iii. Patient has the need for intensive care unit (ICU) monitoring and/or elective intubation with mechanical ventilation;
      iv. Bilateral facial weakness;
      v. Significant autonomic dysfunction (unexplained dysrhythmia, blood pressure fluctuations, significant bowel involvement or bladder involvement);
      vi. Obvious aspiration;

   **Approval duration: 6 months or to renewal date, whichever is longer**

**B. Other diagnoses/indications**

1. Refer to CP.CPA.09 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized)

**II. Continued Therapy**

**A. Guillain Barre Syndrome** (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy.

   **Approval duration: 6 months or to renewal date, whichever is longer**

**B. Other diagnoses/indications** (must meet 1 or 2):

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

   **Approval duration: Duration of request or 12 months (whichever is less); or**

2. Refer to CP.CPA.09 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized)

**III. Diagnoses/Indications for which coverage is NOT authorized:**
A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – CP.CPA.09 or evidence of coverage documents.

B. A list of specific indications for which coverage is not authorized may be found in the PA guideline: CP.CPA.191 Immune Globulin Conditions Not Medically Necessary.

C. IVIG therapy for the following indications:
   1. The use of cerebral spinal fluid (CSF) filtration followed by IVIG
   2. The use of immunoabsorption followed by IVIG
   3. Sequential treatment of plasma exchange followed by IVIG
   4. The combined use of IV methylprednisolone and IVIG

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

<table>
<thead>
<tr>
<th>Abbreviation/Acronym</th>
<th>Definition</th>
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<tbody>
<tr>
<td>IgG</td>
<td>Immune globulin G</td>
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<tr>
<td>PI</td>
<td>Primary immunodeficiency</td>
</tr>
<tr>
<td>ITP</td>
<td>Idiopathic thrombocytopenic purpura</td>
</tr>
<tr>
<td>MMN</td>
<td>Multifocal Motor Neuropathy</td>
</tr>
<tr>
<td>CLL</td>
<td>Chronic Lymphocytic Leukemia</td>
</tr>
<tr>
<td>CIDP</td>
<td>Chronic inflammatory demyelinating polyneuropathy</td>
</tr>
<tr>
<td>demyelinating polyneuropathy</td>
<td></td>
</tr>
<tr>
<td>CVID</td>
<td>Common variable immunodeficiency</td>
</tr>
<tr>
<td>GBS</td>
<td>Guillain Barre Syndrome</td>
</tr>
<tr>
<td>AIDP</td>
<td>Acute inflammatory demyelinating polyneuropathy</td>
</tr>
<tr>
<td>AMAN</td>
<td>Acute motor axonal neuropathy</td>
</tr>
<tr>
<td>AMSAN</td>
<td>Acute motor-sensory axonal neuropathy</td>
</tr>
<tr>
<td>MFS</td>
<td>Miller Fisher Syndrome</td>
</tr>
<tr>
<td>CSF</td>
<td>Cerebrospinal fluid</td>
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<tr>
<td>PE</td>
<td>Plasma Exchange</td>
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<tr>
<td>IVIG</td>
<td>Intravenous immune globulin</td>
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</table>

Appendix B: General Information

- GBS subtypes: Acute inflammatory demyelinating polyneuropathy (AIDP), Acute motor axonal neuropathy (AMAN), Acute motor-sensory axonal neuropathy (AMSAN), and Miller Fisher Syndrome (MFS).
- Miller Fisher syndrome is a rare, acute polyneuropathy characterized by ataxia (abnormal muscle coordination), ophthalmoplegia (paralysis of the eye muscles), and areflexia (absence of the reflexes). Serum IgG antibodies to GQ1b (a ganglioside component of nerve) is useful for diagnosis of MFS.
- Elevated CSF protein, with a normal CSF white blood cell count, is often present; fifty to 66 percent the first week of symptoms and ≥75 percent the third week.
- Initiation of IVIG within 2 weeks of symptom onset appears to be as effective as Plasma Exchange (PE).
- The combination of IVIG and plasmaphoresis used together is not better than either treatment used alone.
- The combination of IVIG and IV methylprednisolone was not more effective than IVIG alone.
- Immunoabsorption is an alternative technique to PE that removes immunoglobulins. There is insufficient evidence to recommend the use of immunoabsorption for GBS.
- CSF filtration is as effective as PE for treatment of GBS.
- Pulmonary function risk factors include one or more of the following:
  - Forced vital capacity < 20 mL/kg
  - Maximal inspiratory pressure < 30 cm H2O
CLINICAL POLICY
Immunoglobulin for Idiopathic Guillain Barre Syndrome

- Maximal inspiratory pressure < 40 cm H2O
- 30% reduction in vital capacity from baseline

Appendix C: Therapeutic Alternatives - N/A

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVIG (Cuvitru, Bivigam, Gammaplex Flebogamma, Gammagard, Gammagard S/D, Gammaked, Gamunex-C, Octagam, Cariumune NF, Privigen)</td>
<td>Guillain Barre Syndrome</td>
<td>400 mg/kg IV QD for 5 days OR 1g/kg IV daily for 2 days</td>
<td>Not available</td>
</tr>
</tbody>
</table>

VI. Product Availability

<table>
<thead>
<tr>
<th>Drug</th>
<th>Availability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bivigam 10% Vial</td>
<td>Solution: 5 gm/50ml, 10 gm/100ml</td>
</tr>
<tr>
<td>Carimune NF Vial</td>
<td>Lyophylized Powder: 6gm, 12gm</td>
</tr>
<tr>
<td>Cuvitru 20% (200 mg/mL)</td>
<td>Solution: 5 mL, 10 mL, 20 mL, 40 mL vials</td>
</tr>
<tr>
<td>Flebogamma DIF 5% Vial 10% vial</td>
<td>Solution: 0.5gm, 2.5gm, 5gm, 10gm, 20gm</td>
</tr>
<tr>
<td>Gammagard 10% Vial</td>
<td>Solution: 1 gm, 2.5 gm, 5 gm, 10 gm, 20 gm, 30 gm</td>
</tr>
<tr>
<td>Gammagard S/D vial</td>
<td>Freeze-dried: 5 gm, 10 gm</td>
</tr>
<tr>
<td>Gammaked vial</td>
<td>Solution: 1 gm, 2.5 gm, 5 gm, 10 gm, 20 gm</td>
</tr>
<tr>
<td>Gammaplex 5% vial</td>
<td>Solution: 2.5 gm, 5 gm, 10 gm, 20 gm</td>
</tr>
<tr>
<td>Gammunex-C vial</td>
<td>Solution: 1 gm, 2.5 gm, 5 gm, 10 gm, 20 gm, 40 gm</td>
</tr>
<tr>
<td>Octagam 5% vial</td>
<td>Solution: 1 gm, 2.5 gm, 5 gm, 10 gm, 25 gm</td>
</tr>
<tr>
<td>Octagam 10% vial</td>
<td>Solution: 2 gm, 5 gm, 10 gm, 20 gm</td>
</tr>
<tr>
<td>Privigen 10% vial</td>
<td>Solution: 5 gm, 10 gm, 20 gm, 40 gm</td>
</tr>
<tr>
<td>Hizentra 20% vial</td>
<td>Solution: 1 gm, 2 gm, 4 gm, 10 gm</td>
</tr>
<tr>
<td>HyQvia 10% vial w/ Hyaluronidase recombinant</td>
<td>Solution: 2.5 gm, 5 gm, 10 gm, 20 gm, 30 gm 160 u/ml</td>
</tr>
</tbody>
</table>

VII. References
11. Flebogamma DIF Prescribing Information. Los Angeles, CA; Grifols Biologicals: January 2016.
15. Octagam 10% Prescribing Information. Hoboken, NJ; Octapharma USA: January 2015.
**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

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