Clinical Policy: Immunoglobulin for Kidney Transplant
Reference Number: CP.CPA.48
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. Kidney Transplant (must meet all):
      1. One of the following (a or b):
         a. If prescribed prior to kidney transplant, patient has high levels of “anti-donor” antibodies (i.e. patients highly sensitized to the tissue of the majority of living or cadaveric donors because of “non-self” human leukocyte antigen (HLA) or ABO incompatibility;
         b. If prescribed following kidney transplant, used for the treatment of antibody-mediated rejection;
      2. Dose does not exceed 140g/infusion.
      Approval duration: 6 months or 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. Kidney Transplant (must meet all):
      1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
      2. Documentation of positive response to therapy;
      3. Dose does not exceed 140g/infusion.
      Approval duration: 6 months or 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 used in combination with Rituxan® (rituximab) for desensitization prior to renal transplantation.

IV. Appendices/General Information
   Appendix A: Abbreviation/Acronym Key
Appendix B: General Information

- Health Net, Inc. considers the combination of intravenous immunoglobulin (IVIG) and Rituxan (rituximab) for desensitization prior to renal transplantation, investigational at this time. Larger, prospective, randomized controlled trials are needed to evaluate the long-term efficacy and safety of this treatment and to compare this protocol with the current treatment of IVIG alone.

- In a retrospective analysis of 50 kidney transplant patients at Johns Hopkins Hospital, all patients were live donor HLA incompatible recipients. Desensitization included plasmapheresis with low dose IVIG, mycophenolate and tacrolimus, and intraoperative induction therapy with anti-IL2 receptor antibodies. Twenty five of the higher risk patients also received rituximab (375 mg/m²) the day prior to transplant. There was no significant difference in the incidence of acute rejection within the first 3 months of transplant between the two groups. Further randomized, controlled trials are still needed.

Appendix C: Therapeutic Alternatives: N/A

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Various Brand Names IVIG</th>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Prior to Kidney Transplant, Antibody-Mediated Rejection</td>
<td>Monthly IV infusions of 2g/kg</td>
<td>140g/infusion</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>Liquid: 5gm/50ml, 10gm/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>Liquid: 0.5gm, 2.5gm, 5gm, 10gm, 20gm</td>
</tr>
<tr>
<td>Gammagard 10% Vial</td>
<td>Liquid: 1gm, 2.5gm, 5gm, 10gm, 20gm, 30gm</td>
</tr>
<tr>
<td>Gammagard S/D vial</td>
<td>Freeze-dried: 5gm, 10gm</td>
</tr>
<tr>
<td>Gammaked vial</td>
<td>1gm, 2.5gm, 5gm, 10gm, 20gm</td>
</tr>
<tr>
<td>Gammaplex 5% vial</td>
<td>Liquid: 2.5gm, 5gm, 10gm, 20gm</td>
</tr>
<tr>
<td>Gammunex-C vial</td>
<td>Liquid: 1gm, 2.5gm, 5gm, 10gm, 20gm, 40gm</td>
</tr>
<tr>
<td>Octagam 5% vial</td>
<td>Liquid: 1gm, 2.5gm, 5gm, 10gm, 25gm</td>
</tr>
<tr>
<td>Octagam 10% vial</td>
<td>Liquid: 2gm, 5gm, 10gm, 20gm</td>
</tr>
</tbody>
</table>
VII. References

<table>
<thead>
<tr>
<th>Immunoglobin for Kidney Transplant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Privigen 10% vial</td>
</tr>
<tr>
<td>Hizentra 20% vial</td>
</tr>
<tr>
<td>HyQvia 10% vial w/</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>
18. Flebogamma DIF Prescribing Information. Los Angeles, CA; Grifols Biologicals: January 2016.

<table>
<thead>
<tr>
<th>Reviews, Revisions, and Approvals</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Converted to new template. Minor changes to verbiage and grammar. References updated.</td>
<td>01.24.17</td>
<td>11.17</td>
</tr>
<tr>
<td>Cuvitru added to criteria</td>
<td>02.03.17</td>
<td>11.17</td>
</tr>
</tbody>
</table>

**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.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

©2016 Centene Corporation. All rights reserved. All materials are exclusively owned by Centene Corporation and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Centene Corporation. You may not alter or remove any trademark, copyright or other notice contained herein. Centene® and Centene Corporation® are registered trademarks exclusively owned by Centene Corporation.