MEDICAL POLICY STATEMENT

Original Effective Date	Next Annual Review Date	Last Review / Revision Date
06/15/2011	09/22/2016	09/22/2015

Policy Name	Policy Number
Immune Globulin (IVIG, IGIV, or IMIG or SCIG)	**SRx-0036**

Medical Policy Statements prepared by CSMG Co. and its affiliates (including CareSource) are derived from literature based on and supported by clinical guidelines, nationally recognized utilization and technology assessment guidelines, other medical management industry standards, and published MCO clinical policy guidelines. Medically necessary services include, but are not limited to, those health care services or supplies that are proper and necessary for the diagnosis or treatment of disease, illness, or injury and without which the patient can be expected to suffer prolonged, increased or new morbidity, impairment of function, dysfunction of a body organ or part, or significant pain and discomfort. These services meet the standards of good medical practice in the local area, are the lowest cost alternative, and are not provided mainly for the convenience of the member or provider. Medically necessary services also include those services defined in any Evidence of Coverage documents, Medical Policy Statements, Provider Manuals, Member Handbooks, and/or other policies and procedures.

Medical Policy Statements prepared by CSMG Co. and its affiliates (including CareSource) do not ensure an authorization or payment of services. Please refer to the plan contract (often referred to as the Evidence of Coverage) for the service(s) referenced in the Medical Policy Statement. If there is a conflict between the Medical Policy Statement and the plan contract (i.e., Evidence of Coverage), then the plan contract (i.e., Evidence of Coverage) will be the controlling document used to make the determination.

For Medicare plans please reference the below link to search for Applicable National Coverage Descriptions (NCD) and Local Coverage Descriptions (LCD):

A. SUBJECT

Immune Globulin (IVIG, IGIV, or IMIG or SCIG)

- Gammaked
- Carimune NF
- Flebogamma, Flebogamma DIF
- GamaSTAN S/D
- Gammagard Liquid, Gammagard S/D Less IgA
- Gammaplex
- Gamunex
- Polygam
- Hizentra
- Octagam
- Privigen
- Bivigam

NOTE: See Medical policy on Synagis for RSV-IVG

B. BACKGROUND

The CareSource Medication Policies are therapy class policies that are used as a guide when determining health care coverage for our members with benefit plans covering prescription drugs. Medication Policies are written on selected prescription drugs requiring prior authorization or Step-Therapy. The Medication Policy is used as a tool to be interpreted in conjunction with the member's specific benefit plan.

The intent of the **Immune Globulin** (PA) Program is to encourage appropriate selection of patients for therapy according to product labeling and/or clinical guidelines and/or clinical studies, and also to encourage use of preferred agents.

C. DEFINITIONS

N/A

D. POLICY

CareSource will approve the use of and consider **Immune Globulin** (IVIG) use as medically necessary when the following criteria have been met for:

I. Acquired red cell aplasia, as indicated by **1 (one) or more** of the following:
   A. Acute disseminated encephalomyelitis – may be effective in patients contraindicated to or not responding to corticosteroids
   B. Allogeneic bone marrow or stem cell transplant and **ALL** of the following:
      1. Serum IgG less than 400 mg/dl (4 g/L)
      2. Severe infection
   C. Autoimmune bullous disease, as indicated by **ALL** of the following:
      1. Contraindications to, failure of (refractory to), or significant side effects from systemic corticosteroids or immunosuppressive treatment
      2. Dermatologic condition, as indicated by **1 (one) or more** of the following:
         2.1 Bullous pemphigoid
         2.2 Epidermolysis bullosa acquisita
         2.3 Linear IgA bullous dermatosis
         2.4 Mucous membrane (cicatricial) pemphigoid
         2.5 Pemphigoid gestationis
         2.6 Pemphigus foliaceus
         2.7 Pemphigus vulgaris
   D. Autoimmune encephalitis
   E. Autoimmune hemolytic anemia for severe life-threatening disease (not for routine use in acute or chronic disease)
   F. Chronic inflammatory demyelinating polyneuropathy
   G. Dermatomyositis or polymyositis refractory to other immunosuppressive therapy or if IVIG is being used as a steroid-sparing option
   H. Fetal-neonatal alloimmune thrombocytopenia, as indicated by **1 (one) or more** of the following:
      1. Newborn, if thrombocytopenia persists after transfusion of antigen-negative compatible platelets
      2. Pregnant woman and **1 (one) or more** of the following:
         2.1 Family history of disease
         2.2 Platelet alloantibodies found on screening
         2.3 Previously affected pregnancy
   I. Guillain-Barre syndrome, as indicated by **ALL** of the following:
      1. Diagnosis of Guiliain-Barre syndrome
      2. Four weeks or less have elapsed since symptom onset
      3. Symptom evaluation, as indicated by **1 (one) or more** of the following:
         3.1 Patient able to walk only with assistance, or worse symptom severity
         3.2 Progressive symptoms
   J. Hematologic malignancy as indicated by **1 (one) or more** of the following:
      1. Chronic lymphocytic leukemia and **ALL** of the following:
         1.1 History of recurrent or severe infection (eg, sinopulmonary infection requiring hospitalization)
         1.2 Serum IgG less than 500mg/dL (5g/L)

2. Multiple myeloma and recurrent life-threatening infection

K. Hemolytic disease of newborn, as indicated by **1 (one) or more** of the following:
   1. Total serum bilirubin level within 2 mg/dl (34 micromoles/L) of age-adjusted and gestation-adjusted threshold for initiation of exchange transfusion
   2. Total serum bilirubin still rising despite intensive phototherapy

L. Hemolytic transfusion reaction and **1 (one) or more** of the following:
   1. After incompatible blood transfusion for severe life-threatening disease unresponsive to other therapies
   2. Sickle cell disease and severe life-threatening post-transfusion hemolysis

M. Hemolytic uremic syndrome or thrombotic thrombocytopenic purpura and inability to tolerate first-line therapy, including **1 (one) or more** of the following:
   1. For hemolytic uremic syndrome, hemodialysis and supportive care
   2. For thrombotic thrombocytopenic purpura, plasma exchange

N. Hemophagocytic syndrome, for severe life-threatening disease unresponsive to other therapies

O. HIV positive status with **1 (one) or more** of the following:
   1. Active bleeding and platelet count less than 10,000/mm^3 ($10x10^9$/L)
   2. Hypogammaglobulinemia, (primary or secondary) following allogeneic stem cell transplant **AND**
      2.1 Low serum IgG (level less than 400mg/dL or 4g/L)
      2.2 Age 18 years or younger
      2.3 Recurrent bacterial infection despite treatment with antiretroviral and antibacterial agents

P. Idiopathic (immune) thrombocytopenic purpura and need for rapid rise in platelet count to prevent or control bleeding or allow a patient with ITP to undergo surgery

Q. Chronic idiopathic immune thrombocytopenic purpura

R. Kawaskai disease – reduced the incidence of coronary artery aneurysms

S. Kidney transplant and **1 (one) or more** of the following:
   1. Postoperative IVIG needed for **ALL** of the following:
      1.1 Antibody-mediated transplant rejection
      1.2 Planned plasmapheresis
   2. Preoperative and perioperative IVIG needed for **ALL** of the following:
      2.1 Kidney transplant recipient has baseline anti-HLA antibody titer less than 1:16 to donor kidney
      2.2 Living donor transplant

T. Lambert-Eaton syndrome, when steroids and other immunosuppressive treatments do not control symptoms

U. Multifocal motor neuropathy

V. Myasthenia gravis, as indicated by **ALL** of the following:
   1. IVIG not to be used for chronic maintenance therapy
   2. Need for treatment of myasthenia gravis, as indicated by **1 (one) or more** of the following:
      2.1 Adult or juvenile myasthenia gravis and **1 (one) or more** of the following:
         a. Acute crisis
         b. Need for stabilization before surgery
         c. Severe exacerbation
         d. Symptomatic patient resistant to or intolerant of immunosuppressive therapy
      2.2 Neonatal myasthenia gravis

W. Opsoclonus-myoclonus syndrome

X. Post-transfusion purpura

Y. Pregnancy-associated idiopathic (immune) thrombocytopenic purpura, as indicated by **1 (one) or more** of the following:

1. Any bleeding during pregnancy
2. Platelet count less than 10,000/mm^3 ($10x10^9$/L) at any time during pregnancy
3. Platelet count between 10,000/mm^3 ($10x10^9$/L) and 30,000/mm^3 ($30x10^9$/L) in second or third trimester

Z. Primary humoral immunodeficiency as indicated by **1 (one) or more** of the following:
1. Agammaglobulinemia (e.g., less than 0.2 g/dL (2g/L))
2. Combined variable immunodeficiency (CVID)
3. Hyper-IgM syndrome (HIM)
4. Primary hypogammaglobulinemia
5. Serum IgG less than 400 mg/dL (4 g/L) and inadequate immunization response (i.e., 4-fold increase in titers) to protein and polysaccharide antigens

AA. Rasmussen encephalitis, chronic focal encephalitis (CFE), for short-term amelioration prior to definitive surgical therapy

BB. Stevens-Johnson syndrome or toxic epidermal necrolysis for severe life-threatening disease

CC. Stiff Person syndrome, with failure of, or inability to receive or tolerate, GABA agonist medication

DD. Systemic lupus erythematosus – severely ill patients not responding to standard therapy, in those with concomitant infections

ALL other uses of IVIG are considered experimental/investigational and therefore, will follow CareSource's Off-Label policy.

Note: Documented diagnosis must be confirmed by portions of the individual's medical record which will confirm the presence of disease and will need to be supplied with prior authorization request. These medical records may include, but are not limited to test reports, chart notes from provider's office or hospital admission notes.

Refer to the product package insert for dosing, administration and safety guidelines.

For Medicare Plan members, reference the Applicable National Coverage Descriptions (NCD) and Local Coverage Descriptions (LCD).

CONDITIONS OF COVERAGE
PLACE OF SERVICE
Office, Outpatient, Home
**Preferred place of service is in the home
This medication can be self-administered and can be billed through the pharmacy benefit.
Note: CareSource supports administering injectable medications in various settings, as long as those services are furnished in the most appropriate and cost-effective setting and that are supportive of the patient's medical condition and unique needs and condition. The decision on the most appropriate setting for administration is based on the member's current medical condition and any required monitoring or additional services that may coincide with the delivery of the specific medication.

HCPCS
J1561 Gammaked
J1569 Gammagard Liquid
J1566 Gammagard S/D
J1561 Gamunex
J1568 Octagam
J1566 Polygam S/D
J1459 Privigen

J1566 Carimune
J1572 Flebogamma
J1560 GamaSTAN S/D
J1557 Gammaplex
J1559 Hizentra
J1599 Immune Globulin (non-lyophilized), not otherwise specified
J1460, J1560 Gamma Globulin Injection
J1556 Bivigam

CPT

Step Therapy
Under some plans, including plans that use an open or closed formulary, some of the medications in this policy may be subject to step-therapy. Refer to the CareSource formulary tool or PDL for further guidance.

AUTHORIZATION PERIOD
Approved initial authorizations are valid for **3 (three)** months. Continued treatment may be considered when the member has shown biological response to treatment. A reauthorization after successful initiation period will be placed for 1 year. **ALL** authorizations are subject to continued eligibility.

E. RELATED POLICIES/RULES

F. REVIEW/REVISION HISTORY

Date Issued:	06/15/2011
Date Reviewed:	06/15/2011, 03/14/2013, 09/26/2014
Date Revised:	03/14/2013, 09/26/2014 09/22/2015 – Policy revision: add Bivigam, criteria changes for HIV, autoimmune encephalitis, and hematologic malignancy

G. REFERENCES

1. Immune Globulin Intravenous (IVIG). (2014, January 1). Retrieved January 1, 2014, from http://careweb.careguidelines.com/ed18/index.html
2. Lexi-Comp Online. (2014). AHFS DI. *IVIG*. Retrieved May 30, 2014 from Lexi-Comp Online with AHFS.
3. Vo AA, Petrozzino J, Yeung K, Sinha A, Kahwaji J, Peng A, Villicana R, Mackowiak J, Jordan SC. Efficacy, outcomes, and cost-effectiveness of desensitization using IVIG and rituximab. *Transplantation*. 2013 Mar 27;95(6):852-8. doi: 10.1097/TP.0b013e3182802f88.
4. Gammaked (Immune Globulin (Human), 10% Caprylate/Chromatography Purified). [Prescribing Information] Grifols Therapeutics, Inc.,; Research Triangle Park, NC: Revised September 2013.
5. Gammagard Liquid (Immune Globulin (Human), 10% solution). [Prescribing Information] Baxter International, Inc.; Westlake Village, CA: Revised April 2014.
6. Gammgard S/D (Immune Globulin (Human). [Prescribing Information] Baxter International, Inc.; Westlake Village, CA: Revised September 2013.
7. Carimune NF (Immune Globulin Intravenous (Human), Nanofiltered) [prescribing information] CLS Behring, LLC; Kankakee, IL: Revised September 2013.
8. Flebogamma [Prescribing Information] Grifols Biologicals, Inc.; Los Angeles, CA: Revised December 2011.
9. GamaSTAN S/D [Package Insert] Grifols Biologicals, Inc.; Los Angeles, CA: Revised September 2013.

10. Gammaplex [Prescribing Information] BPL, Inc.; Raleigh, NC: Revised February 2014.
11. Polygam [Prescribing Information] Baxter Healthcare Corporation; Westlake Village, CA: Revised September 2013.
12. Hizentra [Prescribing Information] CLS Behring, LLC; Kankakee, IL: Revised January 2015.
13. Octagam [Prescribing Information] Octapharma USA, Inc.; Hoboken, NJ: Revised July 2014.
14. Privigen [Prescribing Information] CLS Behring, LLC; Kankakee, IL: Revised November 2013.
15. Bivigam [Prescribing information] Biotest Pharmaceuticals Corporation; Boca Raton, FL: 2012 Apr.

This guideline contains custom content that has been modified from the standard care guidelines and has not been reviewed or approved by MCG Health, LLC.

The medical Policy Statement detailed above has received due consideration as defined in the Medical Policy Statement Policy and is approved.