Clinical Policy: Immunoglobulin for Myasthenia Gravis

Reference Number: CP.CPA.46
Effective Date: 11.16.16
Last Review Date: 11.17
Line of Business: Commercial

Revision Log

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. Myasthenia gravis (MG) or Lambert Eaton myasthenic syndrome (LEMS) (must meet all)**:**

1. Diagnosis of myasthenia gravis (MG) or Lambert Eaton myasthenic syndrome (LEMS);
2. Failure or clinically significant adverse effects to cholinesterase inhibitors (i.e., Mestinon) or corticosteroids (i.e., prednisone);
3. Treatment is for reversing an acute life-threatening or disabling muscle weakness defined by ONE of the following:
   a. Vital capacity less than 1L/min;
   b. Dysphagia associated with aspiration;
   c. Inability to walk 100 feet without assistance;
   d. Acutely worsening disease for which rapid improvement and strength is necessary to minimize the risk for bulbar or respiratory failure.

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. Myasthenia gravis (MG) (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.

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.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

IVIG: Intravenous immunoglobulin
MG: Myasthenia gravis
IgG: Immune globulin G
PI: Primary immunodeficiency
ITP: Idiopathic thrombocytopenic purpura
MMN: Multifocal Motor Neuropathy
CLL: Chronic Lymphocytic Leukemia
CIDP: Chronic inflammatory demyelinating polyneuropathy
CVID: Common variable immunodeficiency
EFNS: the European Federation of Neurological Studies
LEMS: Lambert Eaton myasthenic syndrome

Appendix B: General Information

- Myasthenia gravis (MG) is a disorder of neuromuscular function that is characterized by fatigue and weakness of the muscular system without atrophy or sensory deficits.
- Myasthenia "Crisis" refers to exacerbation sufficient to endanger life, and usually involves respiratory failure in MG, therefore would not include disabled patients who are able to walk with or without assistance.
- Intravenous Immunoglobulin (IVIG) has not been shown to be superior to plasmapheresis in the treatment of life-threatening myasthenia gravis.
- High-dose IVIG may temporarily modify the immune system and suppress autoantibody production to improve severe myasthenia gravis symptoms. The effect of IVIG is seen typically in less than a week, and the benefit can last for three to six weeks. IVIG is used to quickly reverse an exacerbation of myasthenia.
- According to the European Federation of Neurological Studies (EFNS) guidelines on the use of intravenous immunoglobulin in treatment of neurological diseases, the efficacy of IVIG has been proven acute exacerbations of myasthenia gravis and short-term treatment of severe MG (level A recommendation).
- A small clinical trial conducted by Wegner and Ahmed showed that long-term IVIG was effective. This trial included six patients who were anti-AChR-Ab-positive. These patients received IVIG at a dosage of 400 mg/kg/day for 5 days then a maintenance therapy of 400 mg/kg for 1 day every 3 to 4 months. After a 2 year follow up all patients maintained a good functional status and side effects from IVIG did not increase.

Appendix C: Therapeutic Alternatives

Drug	Dosing Regimen	Dose Limit/Maximum Dosage
pyridostigmine (Mestinon®); Mestinon® Timespan (pyridostigmine extended release)	**Immediate Release tablets and syrup** Average dosage, 600 mg PO QD, spaced throughout the day to provide maximum relief when maximum strength is needed; mild cases may respond to 60 to 360 mg/day **Extended Release** 180 to 540 mg PO QD-BID	Size and frequency of dosing must be individualized for the patient. **Immediate Release** 1,500 mg/day **Extended Release** 1,080 mg/day; doses should be at least 6 hours apart.

systemic glucocorticoid (Various - prednisone, prednisolone, or methylprednisolone)	An equivalent dose of prednisone 1 mg/kg per day.	2 mg/kg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

*Requires prior authorization

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
IVIG (Various Brand names)	Myasthenia Gravis	The total dose is 2 gm/kg , usually in five consecutive 0.4 gm/kg daily infusions	2 gm/kg/day

VI. Product Availability

Drug	Availability
Intravenous Immunoglobulin	
Bivigam	10% (1 g/10 mL) in 50 mL, 100 mL vials
Carimune NF powder for injection	3 g, 6 g, 12 g bottles
Flebogamma DIF	5% (50 mg/mL) in 10 mL, 50 mL, 100 mL, 200 mL, 400 mL vials; 10% (5 g/50 mL) in 50 mL, 100 mL, 200 mL vials
Gammagard	10% (1 g/10 mL) in 10 mL, 25 mL, 50 mL, 100 mL, 200 mL, 300 mL vials
Gammagard S/D	powder for injection5 g, 10 g bottles
Gammaked 10%	(1 g/10 mL) in 10 mL, 25 mL, 50 mL, 100 mL, 200 mL vials
Gammaplex 5%	(50 mg/mL) in 50 mL, 100 mL, 200 mL, 400 mL vials
Gamunex-C:	10% (1 g/10 mL) in 10 mL, 25 mL, 50 mL, 100 mL, 200 mL, 400 mL vials
Octagam 5%	(50 mg/mL) in 20 mL, 50 mL, 100 mL, 200 mL, 500 mL
Octagam 10%	(100 mg/mL) in 20 mL, 50 mL, 100 mL, 200 mL
Privigen:	10% (100 mg/mL) in 50 mL, 100 mL, 200 mL, 400 mL vials
Subcutaneous Immunoglobulin	
Cuvitru 20% (200 mg/mL)	Solution: 5 mL, 10 mL, 20 mL, 40 mL vials
Gammagard:	10% (1 g/10 mL) in 10 mL, 25 mL, 50 mL, 100 mL, 200 mL, 300 mL vials
Gammaked	10% (1 g/10 mL) in 10 mL, 25 mL, 50 mL, 100 mL, 200 mL vials

Gamunex-C	10% (1 g/10 mL) in 10 mL, 25 mL, 50 mL, 100 mL, 200 mL, 400 mL vials
Hizentra	20% (0.2 g/mL) in 5 mL, 10 mL, 20 mL, 50mL vials
HyQvia	10% (1 g/10 mL) in 25 mL, 50 mL, 100 mL, 200 mL, 300 mL vials and 160 U/mL recombinant human hyaluronidase in 1.25 mL, 2.5 mL, 5 mL, 10 mL, 15 mL vials

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
Converted to new template. Minor changes to verbiage and grammar. References updated.	01.24.17	11.17
Cuvitru added to criteria	02.03.17	11.17

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.

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