Clinical Policy: Immunoglobulin for Multiple Sclerosis

Reference Number: CP.CPA.45
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 (IVIG) (including Gamunex-C, Gammaked and Gammagard when used intravenously)
  - Replacement therapy for primary immunodeficiency (PI) This includes, but is not limited to, congenital agammaglobulinemia, common variable immunodeficiency, 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. Multiple Sclerosis (must meet all)**:**

1. Diagnosis of relapsing remitting multiple sclerosis (MS) as defined by the all of the following Posner criteria:
   a. Onset of symptoms between 10 and 50 years of age;
   b. There is a consistent course of relapsing/remitting type of MS with objective evidence of at least 2 attacks (also known as an exacerbation, flare, or relapse) within the last year clinically defined as the sudden appearance or worsening of an MS symptom or symptoms;
   c. Each attack lasts at least 24 hours;
   d. Evidence of inflammation and/or damage in different areas of the central nervous system;
   e. Attacks separated by at least 1 month;
   f. Documented neurologic signs of lesions on MRIs in more than one area of the brain or spinal cord white matter;
   g. Patient has severely impaired function secondary to relapsing-remitting MS as measured by a standard clinical scale;
2. Failure or clinically significant adverse effect or patient is refractory to at least a three month trial (at therapeutic doses) of other standard therapies [i.e., Avonex, Aubagio, Betaseron, Rebif, Copaxone, Tecfidera, or Gilenya];
3. There must be no other explanation for these attacks or the symptoms the person is experiencing.

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. Multiple Sclerosis (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 (fewer relapses and/or improvement in level of disability).

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

Abbreviation: translation
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
IVIG: Intravenous immunoglobulin
MS: Multiple Sclerosis

Appendix B: General Information

- The clinical course of MS usually falls within one of the following categories, with the potential for progression from one pattern to a more serious one:
  - Relapsing-remitting MS: This form of MS is characterized by clearly defined acute attacks with full recovery or with some remaining neurological signs/symptoms and residual deficit upon recovery. The periods between disease relapses are characterized by a lack of disease progression.
  - Secondary progressive MS: The disease begins with an initial relapsing-remitting course, followed by progression at a variable rate that may also include occasional relapses and minor remissions.
  - Progressive-relapsing MS: Persons with progressive-relapsing MS experience progressive disease from onset, with clear, acute relapses that may or may not resolve with full recovery. Unlike relapsing-remitting MS, the periods between relapses are characterized by continuing disease progression.
  - Primary progressive MS: The disease shows gradual progression of disability from its onset, without plateaus or remissions or with occasional plateaus and temporary minor improvements.

Appendix C: Therapeutic Alternatives

Drug	Dosing Regimen	Dose Limit/Maximum Dose
Avonex® (interferon Beta-1a)*	30 mcg IM Q Wk Avonex may be titrated to reduce the incidence of flu-like symptoms, starting with 7.5 mcg for the first week and increasing the dose by 7.5 mcg each week for the next 3 weeks until the recommended dose of 30 mcg Q Wk is obtained.	30 mcg Q Wk
Rebif® (interferon Beta-1a)*	22 mcg or 44 mcg SC TIW titrated over a 4 week period.	44 mcg TIW
Betaseron® (interferon Beta -1b)* Extavia™ (interferon Beta-1b)*	250 mcg SC QOD. Generally, start at 0.0625 mg (0.25 mL) SC QOD, and increase over a six week period to 0.25 mg (1 mL) SC QOD.	250 mcg QOD
Copaxone® (glatiramer acetate) *	20 mg SC QD or 40 mg SC TIW For SC injection only, doses are not interchangeable	20 mg QD or 40 mg TIW
Aubagio® (teriflunomide) *	7 mg or 14 mg PO QD	14 mg QD
Gilenya™ (fingolimod)*	0.5 mg PO QD	0.5 mg QD
Tecfidera™ (dimethyl fumarate)*	120 mg PO BID for 7 days followed by 240 mg PO BID Administration with food may reduce the incidence of flushing	240 mg BID
Plegridy (peginterferon beta-1a)*	125 mcg SC every 14 days Dose should be titrated, starting with 63 mcg SC on day 1, 94 mcg SC on day 15, 125 mcg (full dose) SC on day 29	125 mcg Q 2 Wk

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)	Relapsing Remitting Multiple Sclerosis	2 g/kg followed by 0.4 g/kg bimonthly OR 1 g/kg QD for 2 days at 4-week intervals for 6 months OR 0.2 g/kg	Not Available

		Q month for 2 years OR 400 mg/kg × 5 days, followed by 0.4 g/kg Q 2 months for 2 years	

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

VII. References

1. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed January 27,2017.

2. Immune Globulin. American Hospital Formulary Service Drug Information. Available at: http://www.medicinescomplete.com/mc/ahfs/current/. Accessed January 27,2017
3. Gammagard-SD [Prescribing Information], Westlake Village, CA; Baxter: September 2013.
4. Gammaplex [Prescribing Information], United Kingdom ; Bio Products Laboratory Ltd. September 2013.
5. Gamunex-C [Prescribing Information]. Research Triangle Park, NC. Grifolis Therapeutics Inc: July 2014.
6. Hizentra [Prescribing Information], Bern, Switzerland; CSL Behring AG, January 2015.
7. Carimune [Prescribing Information], Bern, Switzerland ; CSL Behring AG, September 2013.
8. Privigen [Prescribing Information], Bern, Switzerland ; CSL Behring AG, November 2013.
9. Gammagard Liquid [Prescribing Information], Westlake Village, CA; Baxter: April 2014.
10. Buttmann M, Rieckmann P. Treating multiple sclerosis with monoclonal antibodies. Expert Rev Neurother. 2008 Mar;8(3):433-55
11. Zohren F, Toutzaris D, Klärner V, et al. The monoclonal anti-VLA-4 antibody natalizumab mobilizes CD34+ hematopoietic progenitor cells in humans. Blood. 2008 Apr 1;111(7):3893-5.
12. Clerico M, Rivoiro C, Contessa G, et al. The therapy of multiple sclerosis with immune-modulating or immunosuppressive drug A critical evaluation based upon evidence based parameters and published systematic reviews. Clin Neurol Neurosurg. 2007 Dec 27;
13. Fiore D. Multiple sclerosis and Natalizumab. Am J Ther. 2007 Nov-Dec;14(6):555-60.
14. Engelhardt B, Kappos L. Natalizumab: targeting alpha4-integrins in multiple sclerosis. Neurodegener Dis. 2008;5(1):16-22.
15. Mareckova H, Havrdova E, Krasulova E, et al. Natalizumab in the treatment of patients with multiple sclerosis: first experience. Ann N Y Acad Sci. 2007 Sep;1110:465-73.
16. Horga A, Horga de la Parte JF. Natalizumab in the treatment of multiple sclerosis. Rev Neurol. 2007 Sep 1-15;45(5):293-303.
17. Greenberg BM, Balcer L, Calabresi PA, et al. Interferon Beta Use and Disability Prevention in Relapsing-Remitting Multiple Sclerosis. Arch Neurol. 2012 Nov 5:1-4.
18. Miller AE, Rhoades RW. Treatment of relapsing-remitting multiple sclerosis: current approaches and unmet needs. Curr Opin Neurol. 2012 Feb;25 Suppl:S4-10
19. Flebogamma [Prescribing Information], Barcelona, Spain; Institutio Grifols, S.A: September 2013.
20. Gammaked [Prescribing Information], Research Triangle Park, NC; Grifolis Therapeutics Inc; : September 2013.
21. Octagam 5%[Prescribing Information]. Hoboken, NJ; Octapharmac USA: October 2013.
22. Bivigam [Prescribing Information], Boca Raton, FL; Biotest Pharmaceuticals Corp: May 2015
23. Octagam 10%[Prescribing Information]. Hoboken, NJ; Octapharma USA: December 2014.
24. HyQvia [Prescribing Information]. Westlake Village, CA; Baxter: September 2014.
25. Cuvitru [Prescribing Information]. Westlake Village, CA: Baxalta US Inc.; September 2016.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Converted to new template. Minor changes to verbiage and grammar. References updated.	01.27.17	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.

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.

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