



Clinical UM Guideline

Subject: Intravenous Immune Globulin Therapy (IVIG)
Guideline #: CG-DRUG-09 **Current Effective Date:** 01/13/2010
Status: Revised **Last Review Date:** 11/19/2009

Description

Intravenous Immunoglobulin (IVIG) is a blood product that is given intravenously for the treatment of inflammatory, autoimmune or other diseases featuring low antibody levels. IVIG is also used for removal of harmful antibodies and for blocking damage from immune cells.

This document does not pertain to use of Rho (D) Immune Globulin Injections and WinRho SD when used for prevention or treatment of Rh incompatibility or use of specific hyperimmune serum globulin after exposure to Botulinum, Cytomegalovirus, Diphtheria, Hepatitis B, Rabies, Tetanus, Vaccinia, or Varicella-Zoster.

Note: Please see the following related documents for additional information:

- [DRUG.00013 Intravenous Immunoglobulin as a Treatment of Recurrent Spontaneous Abortion and Associated Laboratory Tests](#)
- [CG-DRUG-01 Off-Label Drug and Approved Orphan Drug Use](#)

Clinical Indications

Medically Necessary:

Intravenous Immune Globulin Therapy (IVIG) is considered **medically necessary** for the U.S. Food and Drug Administration (FDA) *approved* indication:

- Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) for an initial trial (up to 12 weeks), when the medical record indicates that the clinical presentation is not consistent with other polyneuropathies (e.g. IgM neuropathy, hereditary neuropathy, diabetic neuropathy) and **ONE** of the following clinical and electrodiagnostic criteria are met:
 - There is proximal muscle weakness or sensory dysfunction caused by neuropathy and nerve conduction studies (NCS) confirm there is electrodiagnostic evidence of a demyelinating neuropathy in at least two limbs; OR
 - There is distal muscle weakness and results of diagnostic testing meet a recognized set of diagnostic criteria as established by the American Academy of Neurology (AAN), Saperstein, or Inflammatory Neuropathy Cause and Treatment (INTAC).
- Continued use of IVIG after initial trial for CIDP is medically necessary when the following criteria are met:
 - Clinically significant improvement in neurological symptoms is documented on physical examination; **and**
 - Continued need is demonstrated by documentation that attempts on an annual basis to titrate the dose or the interval of therapy result in worsening of symptoms.

The following FDA approved indications are also considered **medically necessary** for IVIG:

- Treatment of primary immunodeficiencies, including:
 - Hypogammaglobulinemia;
 - Congenital agammaglobulinemia (X-linked agammaglobulinemia);
 - Common variable immunodeficiency;
 - X-linked immunodeficiency with hyperimmunoglobulin M;
 - Severe combined immunodeficiency;
 - Wiskott-Aldrich syndrome.
- Treatment of idiopathic thrombocytopenic purpura (ITP);
- Treatment of Kawasaki Syndrome;
- Treatment of individuals with hypogammaglobulinemia and/or recurrent bacterial infection associated with B-cell chronic lymphocytic leukemia (CLL);

IVIG is considered **medically necessary** for the following *off-label* indication:

- Multifocal Motor Neuropathy (MMN) initial trial (up to 4 weeks), when **ONE** of the following criteria are met:
 - There is asymmetric weakness that predominantly affects distal muscles (without upper motor neuron signs) **AND** nerve conduction studies confirm a demyelinating neuropathy is present (conduction block, slowing, or abnormal temporal dispersion in at least one nerve); **or**
 - Clinical history and exam do not suggest upper motor neuron disease (no bulbar weakness, no upper motor neuron signs) and labs show that GM-1 antibody titers are elevated; **or**
 - After the initial exam and electrodiagnostic testing clinical presentation suggests MMN but the diagnosis remains uncertain.
- Continued use of IVIG after initial trial for MMN when the following criteria are met:
 - Clinical results document an improvement in strength and function within three weeks of the start of the infusion period;
 - Continued need is demonstrated by documentation that attempts on an annual basis to titrate the dose or the interval of therapy result in worsening of symptoms.

Intravenous Immune Globulin Therapy (IVIG) is also considered **medically necessary** for the following *off-label* indications:

- Antenatal alloimmune thrombocytopenia;
- Autoimmune neutropenia;
- Dermatomyositis, refractory; (IVIG is used as a second line treatment of dermatomyositis. Corticosteroids are first-line treatments of dermatomyositis);
- Eaton-Lambert myasthenic syndrome treatment;
- Guillain-Barre Syndrome (acute demyelinating polyneuropathy) as an equivalent alternative to plasma exchange;
- Hyperimmunoglobulinemia E syndrome (HIE) treatment;
- Myasthenia Gravis, severe refractory;
- Polymyositis; routine use of IVIG is not recommended. IVIG may be considered in individuals with severe polymyositis for whom other treatments have been unsuccessful, have become intolerable, or are contraindicated;
- Prior to a medically necessary renal transplantation for suppression of panel reactive anti-HLA antibodies in individuals with high panel reactive antibody (PRA) levels to human leukocyte antigens (HLA);
- Prevention of infections in high-risk, preterm, low birth weight neonates;
- Stiff-person syndrome not controlled by other therapies;

- Toxic shock syndrome caused by staphylococcal or streptococcal organisms refractory to several hours of aggressive therapy;
- Solid organ transplant recipients at risk for CMV;
- Treatment of chronic parvovirus B19 infection and severe anemia associated with bone marrow suppression;
- To reduce the risk of graft-versus-host disease associated with interstitial pneumonia (infectious or idiopathic) and infections (cytomegalovirus infections, varicella-zoster virus infection, and recurrent bacterial infection) in allogeneic bone marrow transplant (BMT) recipients in the first 100 days after transplantation;
- Prevention of infection in HIV infected children;
- Refractory auto-immune mucocutaneous blistering diseases including: pemphigus vulgaris, pemphigus foliaceus, bullous pemphigoid, mucous membrane pemphigoid, and epidermolysis bullosa aquisita.

Not Medically Necessary:

Intravenous Immune Globulin Therapy (IVIG) is considered **not medically necessary** for all other indications not listed above as medically necessary.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

CPT

90283 Immune globulin, (IgIV), human, for intravenous use

HCPCS

J1459 Injection, immune globulin (Privigen), intravenous, non-lyophilized (e.g., liquid), 500 mg

J1561 Injection, immune globulin, (Gamunex), intravenous, non-lyophilized (e.g., liquid), 500 mg

J1566 Injection, immune globulin, intravenous lyophilized (e.g., powder), not otherwise specified, 500 mg

J1568 Injection, immune globulin, (Octagam), intravenous, non-lyophilized (e.g., liquid), 500 mg

J1569 Injection, immune globulin, (Gammagard liquid), intravenous, non-lyophilized (e.g., liquid), 500 mg

J1572 Injection, immune globulin, (Flebogamma/Flebogamma DIF), intravenous, non-lyophilized (e.g., liquid); 500 mg

S9338 Home infusion therapy; immunotherapy, administrative services, professional pharmacy services, care coordination, all necessary supplies and equipment, per diem

ICD-9 Diagnosis

Including, but not limited to, the following:

040.82 Toxic shock syndrome

041.00-041.9 Bacterial infection in conditions classified elsewhere

042 Human immunodeficiency virus (HIV) disease

052.0-052.9	Chickenpox (varicella zoster)
057.0	Erythema infectiosum (fifth disease; parvovirus B19 infection)
078.5	Cytomegaloviral disease
079.83	Other specified viral and chlamydial infections, parvovirus B19
204.10-204.92	Chronic lymphoid leukemia
279.00-279.09	Deficiency of humoral immunity
279.12	Wiskott Aldrich syndrome
279.2	Combined immunity deficiency
279.3	Unspecified immunity deficiency
287.30-287.39	Primary thrombocytopenia
287.5	Thrombocytopenia, unspecified
288.00-288.09	Neutropenia
333.91	Stiff-man syndrome
354.0-355.9	Mononeuritis of upper limb, multiplex, lower limb
356.4-356.9	Idiopathic peripheral neuropathy
357.0-357.7	Inflammatory and toxic neuropathy
357.81	Chronic inflammatory demyelinating polyneuritis (CIDP)
357.82	Critical illness polyneuropathy (acute motor neuropathy; MMN)
357.89-357.9	Other, unspecified polyneuropathy
358.00-358.01	Myasthenia gravis
358.1	Myasthenic syndromes in diseases classified elsewhere (e.g., Eaton-Lambert syndrome)
446.1	Acute febrile mucocutaneous lymph node syndrome (Kawasaki disease)
516.8	Other specified alveolar and parietoalveolar pneumonopathies (interstitial pneumonia)
694.4	Pemphigus (vulgaris, foliaceus)
694.5	Pemphigoid
694.60-694.61	Benign mucous membrane pemphigoid
710.3	Dermatomyositis
710.4	Polymyositis
757.39	Congenital pigmentary anomalies of skin (epidermolysis bullosa)
775.2	Myasthenia gravis, neonatal
776.1	Transient neonatal thrombocytopenia
996.80-996.89	Complications of transplanted organ
V07.2	Prophylactic immunotherapy
V21.30-V21.35	Low birth weight status
V42.0-V42.9	Organ or tissue replaced by transplant

Discussion/General Information

Our bodies naturally produce antibodies to fight and create immunity against disease-causing agents such as viruses and bacteria when infections occur. Once the body has been exposed to an infection, antibodies can sometimes protect us from becoming ill if we are exposed to the same infectious agents sometime in the future. Under many circumstances a person's ability to produce their own Immune globulin (Ig) is impaired and the use of other methods to boost the immune system becomes necessary. IVIG is a sterilized solution obtained from pooled human blood plasma, which contains the immunoglobulins (or antibodies) to prevent various infectious diseases. IVIG is sometimes used to aid in the prevention or progression of an illness by using a donor's antibodies to fight the illness. This process is referred to as passive immunity, as opposed to active immunity in

which the patient's body is making its own antibodies. Passive immunity conveys only temporary protection and should not be confused with getting an immunization, which provides longer-term protection. The duration of Ig treatment is extremely variable depending upon the condition being treated and the individual receiving the therapy. For some conditions retreatment may not be needed, however some individuals may require treatment every 3-4 weeks and others every 6-8 weeks.

Pooled IVIG preparations contain many different types of Igs (differentiated on the basis of structure and biological activity) that target different specific immune functions of the body. In this way, IVIG imparts several types of immune fighting antibodies simultaneously. The mechanism of IVIG action remains undetermined. The therapeutic mechanism and the short-and long-term effects may not be the same for each condition.

Since preparations of IVIG are derived from donor blood, concerns about the potential for contracting diseases, such as hepatitis and HIV, is a concern. The process used to prepare IVIG for use in humans is monitored by the manufacturer and the FDA for the presence of infectious agents. The monitoring process begins with the screening of potential donors. Next, all manufacturers use a multi-step process that extracts the desired immune globulins and attempts to remove all other substances. Finally, samples of each batch of Ig are tested for the presence of infectious particles. While all attempts are taken to reduce the risk of infection in the use of IVIG, some small risk still exists. Potential recipients of this treatment should take this risk into consideration when contemplating IVIG therapy.

The development of this document is based on the Food and Drug Administration (FDA) labeling, practice guidelines of medical specialty organizations and drug compendia off label indications.

The American Academy of Neurology (AAN) in their 2002 guideline, Disease modifying therapies in multiple sclerosis, addresses IVIG for the treatment of multiple sclerosis and states:

"The studies of intravenous immunoglobulin (IVIg), to date, have generally involved small numbers of patients, have lacked complete data on clinical and MRI outcomes or have used methods that have been questioned. It is, therefore, only possible that IVIg reduces the attack rate in RRMS (Type C recommendation*). The current evidence suggests that IVIg is of little benefit with regard to slowing disease progression (Type C recommendation*)." **Type C recommendation C—Possibly effective, ineffective or harmful for the given condition in the specified population.*

The American Academy of Allergy Asthma and Immunology (AAAAI), in their *Work Group Report on the appropriate use of intravenously administered immunoglobulin* (2005) states:

"IVIG may also be a potentially effective second line treatment in relapsing-remitting multiple sclerosis, although the optimal dosage remains to be established."

The American Academy of Otolaryngology–Head and Neck Surgery Foundation guideline, *Clinical practice guideline: Adult sinusitis* (2007) concluded that treatment with intravenous immune globulin (IVIG) for chronic sinusitis or recurrent acute rhinosinusitis in patients with humoral immune deficiency requires more research.

Chronic inflammatory demyelinating polyneuropathy (CIDP) is a neurological disorder characterized by progressive weakness and impaired sensory function in the legs and arms. The disorder, which is sometimes called chronic relapsing polyneuropathy, is caused by damage to the

myelin sheath (the fatty covering that wraps around and protects nerve fibers) of the peripheral nerves. This myelin damage is often documented by nerve conduction study or nerve biopsy and there is often evidence of elevated CSF protein during the course of the disease. CIDP is difficult to diagnose due to its heterogeneous presentation (both clinical and electrophysiological). Sander and Latov (2003) acknowledged the diagnostic difficulty of CIDP. They attributed this in part to the lack of clarity with the diagnostic criteria for CIDP. Without proper diagnostic criteria, many patients might remain untreated. In their publication, Sander and Latov presented the American Academy of Neurology (AAN), Saperstein Diagnostic Criteria and the Inflammatory Neuropathy Cause and Treatment (INCAT) electrodiagnostic criteria.

Although CIDP can occur at any age and in both genders, it is more common in young adults, and in men more so than women. CIDP is closely related to Guillain-Barre syndrome and it is considered the chronic counterpart of that acute disease. The Food and Drug Administration (FDA) approved Gamunex® for the treatment of CIDP in September 2008. The FDA based its approval on clinical trials that showed Gamunex® was effective at improving certain motor functions for up to 48 weeks after the initial treatment.

Off label use of IVIG has been proposed for treatment for renal transplant rejection. Based upon drug compendia evaluation, IVIG for this indication is assigned as category C: the evidence is based on data derived from expert opinion or consensus, case reports or case series and Class IIb: evidence is inconclusive.

References

Peer Reviewed Publications:

1. Achiron A, Barak Y, Miron S, Sarova-Pinhas I. Immunoglobulin treatment in refractory myasthenia gravis. *Muscle Nerve*. 2000; 23(4):551-555.
2. Ahmed AR. Intravenous immunoglobulin therapy for patients with bullous pemphigoid unresponsive to conventional immunosuppressive treatment. *J Am Acad Dermatol*. 2001; 45(6):825-835.
3. Ahmed AR. Intravenous immunoglobulin therapy in the treatment of patients with pemphigus vulgaris unresponsive to conventional immunosuppressive treatment. *J Am Acad Dermatol* 2001; 45:679-690.
4. Ahmed AR. Intravenous immunoglobulin therapy in the treatment of patients with pemphigus foliaceus unresponsive to conventional therapy. *J Am Acad Dermatol*. 2002; 46:42-49.
5. Ancona KG, Parker RI, Atlas MP, Prakash D. Randomized trial of methylprednisolone versus intravenous immunoglobulin for the treatment of acute idiopathic thrombocytopenic purpura in children. *J Ped Hematol Oncol*. 2002; 24(7):540-544.
6. Bachot N, Revuz J, Roujeau J. Intravenous immunoglobulin treatment for Stevens-Johnson syndrome and toxic epidermal necrolysis. *Arch Dermatol*. 2003; 139:33-36.
7. Cavaletti G. Current status and future prospective of immunointervention in multiple sclerosis. *Curr Med Chem*. 2006; 13(19):2329-2343.
8. Cherin P, Pelletier S, Teixeira A, et al. Results and long-term follow-up of intravenous immunoglobulin infusions in chronic, refractory polymyositis: an open study with thirty-five adult patients. *Arthritis Rheum*. 2002; 46(2):467-474.
9. Dalakas MC, Fujii M, Li M, et al. High-dose intravenous immune globulin for stiff-person syndrome. *N Engl J Med*. 2001; 345(26):1870-1876.
10. Darabi K, Abdel-Wahab O, Dzik WH. Current usage of intravenous immune globulin and the rationale behind it: the Massachusetts General Hospital data and a review of the literature. *Transfusion*. 2006; 46(5):741-53.

11. Engineer L, Ahmed AR. Role of intravenous immunoglobulin in the treatment of bullous pemphigoid: analysis of current data. *J Am Acad Dermatol.* 2001; 44(1):83-88.
12. Engineer L, Bhol KC, Ahmed AR. Analysis of current data on the use of intravenous immunoglobulins in management of pemphigus vulgaris. *J Am Acad Dermatol.* 2000; 43(6):1049-1057.
13. Genevay S, Saudan-Kister A, Guerne PA. Intravenous gammaglobulins in refractory polymyositis: lower dose for maintenance treatment is effective. *Ann Rheum Dis.* 2001; 60(6):635-636.
14. Gerschlager W, Brown P. Effect of treatment with Intravenous immunoglobulin on quality of life in patients with stiff-person syndrome. *Movement Disord.* 2002;17(3):590-593.
15. Gold R, Stangel M, Dalakas MC. Drug Insight: the use of intravenous immunoglobulin in neurology-therapeutic considerations and practical issues. *Nat Clin Pract Neurol.* 2007; 3(1):36-44.
16. Hedlund-Treutiger I, Henter J, Elinder G. Randomized study of IVIG and high-dose dexamethasone therapy for children with chronic idiopathic thrombocytopenic purpura. *J Ped Hematol Oncol.* 2003; 25(2):139-144.
17. Hughes R, Donofrio P, Bril V, et al. Intravenous immune globulin (10% caprylatechromatography purified) for the treatment of chronic inflammatory demyelinating polyradiculoneuropathy (ICE study): a randomized placebo-controlled trial. *Lancet Neural* 2008; 7:136–144
18. Jolles S. Clinical uses of intravenous immunoglobulin. *Clinical and Experimental Immunology.* 2005; 142:1–11.
19. Jordan S, Cunningham-Rundles C, McEwan R. Utility of intravenous immune globulin in kidney transplantation: Efficacy, safety, and cost implications. *Am J of Transplantation.* 2003; 3(6):653-664.
20. Jordan SC, Vo A, Bunnapradist S, et al. Intravenous immune globulin treatment inhibits crossmatch positivity and allows for successful transplantation of incompatible organs in living-donor and cadaver recipients. *Transplantation.* 2003; 76(4):631-636.
21. Pescovitz M. Drugs for the hypersensitized patient. *Current Opinion in Organ Transplantation.* 2005; 10(4):279-283.
22. Petereit HF, Reske D, Pukrop R, et al. No effect of intravenous immunoglobulins on cytokine-producing lymphocytes in secondary progressive multiple sclerosis. *Mult Scler.* 2006; 12(1):66-71.
23. Qureshi AI, Choudhry MA, Akbar M, et al. Plasma exchange versus intravenous immunoglobulin treatment in myasthenic crisis. *Neurology.* 1999; 52(3):629-632.
24. Sami N, Bhol KC, Ahmen AR. Treatment of oral pemphagoid with intravenous immunoglobulins as monotherapy. Long term follow-up: Influence of treatment on antibody titers to human $\alpha 6$ integrin. *Clin Exp Immunol.* 2002; 129(3):533-540.
25. Sander H, Latov N. Research criteria for defining patients with CIDP. *Neurology* 2003; 60(Suppl 3):S8–S15.
26. Saperstein DS, Katz JS, Amato AA, Barohn RJ. Clinical spectrum of chronic acquired demyelinating polyneuropathies. *Muscle Nerve.* 2001; 24:311–324.
27. Selcen D, Dabrowski ER, Michon AM, Nigro MA. High-dose intravenous immunoglobulin therapy in juvenile myasthenia gravis. *Pediatr Neurol.* 2000; 22(1):40-43.
28. Strasser-Fuchs S, Fazekas F, et al. The Austrian Immunoglobulin in MS (AIMS) study: final analysis. *Mult Scler.* 2000; 6 Suppl 2:S9-S13.
29. Teksam M, Tali T, Kocer B, Isik S. Qualitative and quantitative volumetric evaluation of the efficacy of intravenous immunoglobulin in multiple sclerosis: preliminary report. *Neuroradiology.* 2000; 42(12):885-889.
30. Wolfe GI, Barohn RJ, Foster BM et al. Randomized, controlled trial of intravenous immunoglobulin in myasthenia gravis. *Muscle Nerve.* 2002; 26(4):549-552.

31. Yarmohammadi H, Estrella L, Doucette J, et al. Recognizing primary immune deficiency in clinical practice. *Clinical and Vaccine Immunology*. 2006; 13(3):329–332.

Government Agency, Medical Society, and Other Authoritative Publications:

1. American Academy of Allergy, Asthma and Immunology (AAAAI). Practice parameter for the diagnosis and management of primary immunodeficiency. *Ann Allergy* 2005; 94(suppl):S1-63.
2. American Academy of Neurology (AAN). Research criteria for diagnosis of chronic inflammatory demyelinating polyneuropathy (CIDP). Report from an Ad Hoc Subcommittee of the AAN AIDS Task Force. *Neurology*. 1991; 41(5):617-618.
3. American Academy of Otolaryngology–Head and Neck Surgery Foundation. Clinical practice guideline: Adult sinusitis. *Otolaryngology–Head and Neck Surgery*. 2007; 137:S1-S31.
4. Alcock GS, Liley H. Immunoglobulin infusion for isoimmune haemolytic jaundice in neonates. *Cochrane Database of Systematic Reviews* 2002, Issue 3. Art. No.: CD003313. DOI: 10.1002/14651858.CD003313.
5. Association of Community Cancer Centers. *Oncology Drug Information*. US PDI 20th Edition, 2000:257-264.
6. American College of Obstetricians and Gynecologists (ACOG). Practice Bulletin No. 6, Sept 1999.
7. American Society of Health-System Pharmacists® (AHFS) Hospital Formulary Service® (AHFS). Immune Globulin. AHFS Drug Information 2008®. Bethesda, MD.
8. Centers for Medicare and Medicaid Services. National Coverage Determination for Intravenous Immune Globulin for the Treatment of Autoimmune Mucocutaneous Blistering Diseases. NCD #250.3. Effective October 1, 2002. Available at: http://www.cms.hhs.gov/mcd/index_chapter_list.asp. Accessed on September 30, 2009.
9. Centers for Medicare and Medicaid Services. National Coverage Determination for Lymphocyte Immune Globulin, Anti-Thymocyte Globulin (Equine). NCD# 260.7. Effective (longstanding national coverage determination). Available at: http://www.cms.hhs.gov/mcd/index_chapter_list.asp. Accessed on September 30, 2009.
10. Donofrio PD, Berger A, Brannagan TH, et al. Consensus statement: The use of intravenous immunoglobulin in the treatment of neuromuscular conditions report of the AANEM AD HOC committee. *American Association of Neuromuscular and Electrodiagnostic Medicine (AANEM)*. *Muscle Nerve*. 2009; 40: 890–900.
11. Gamunex® [Product Information], Triangle Park, NC. Talecris Biotherapeutics, Inc.: September 2008.
12. Gajdos P, Chevret S, Toyka K. Intravenous immunoglobulin for myasthenia gravis. *Cochrane Database of Systematic Reviews* 2006, Issue 2. Art. No.: CD002277. DOI: 10.1002/14651858.CD002277.pub2.
13. Goodin DS, Frohman EM, Garmany GP, et al. Disease modifying therapies in multiple sclerosis: Subcommittee of the American Academy of Neurology and the MS Council for Clinical Practice Guidelines. *Neurology* 2002; 58:169-178. Reaffirmed October 9, 2008.
14. Hayes Inc. Hayes Medical Technology Directory. *Intravenous Immune Globulin for Acquired Immune Deficiency Syndrome (AIDS) in Adults*; Lansdale, PA: Hayes, Inc.; February 28, 2005. Search updated February 15, 2009.
15. Hayes Inc. Hayes Medical Technology Directory. *Intravenous Immune Globulin for Children with HIV Infection*; Lansdale, PA: Hayes, Inc.; April 13, 2006. Search updated April 20, 2009.
16. Hayes Inc. Hayes Medical Technology Directory. *Intravenous Immune Globulin for Pulmonary Diseases*; Lansdale, PA: Hayes, Inc.; July 18, 2006. Search updated August 19, 2009.

17. Hayes Inc. Hayes Medical Technology Directory. *Intravenous Immunoglobulin for Multiple Sclerosis*; Lansdale, PA: Hayes, Inc.; October 14, 2005. Search updated October 24, 2008.
18. Hayes Inc. Hayes Medical Technology Directory. *Intravenous Immunoglobulin for Rheumatic Diseases*; Lansdale, PA: Hayes, Inc.; February 21, 2006. Search updated August 15, 2009.
19. Hayes Inc. Hayes Medical Technology Directory. *Intravenous Immunoglobulin for Neurological Diseases*; Lansdale, PA: Hayes, Inc.; February 2, 2006. Search updated August 19, 2009.
20. Hughes RA, Bouche P, Cornblath DR, et al. European Federation of Neurological Societies/Peripheral Nerve Society guideline on management of chronic inflammatory demyelinating polyradiculoneuropathy: report of a joint task force of the European Federation of Neurological Societies and the Peripheral Nerve Society. *Eur J Neurol*. 2006; 3(4):326-332.
21. Hughes RAC, Raphaël J-C, Swan AV, van Doorn PA. Intravenous immunoglobulin for Guillain-Barré syndrome. *Cochrane Database of Systematic Reviews* 2006, Issue 1. Art. No.: CD002063. DOI: 10.1002/14651858.CD002063.pub3.
22. Immune Serum Globulin. In: DrugPoints® System [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Available at: <http://www.thomsonhc.com>. Accessed on September 30, 2009.
23. Joint Task Force of the EFNS and the PNS. European Federation of Neurological Societies/Peripheral Nerve Society guideline on management of paraproteinemic demyelinating neuropathies. Report of a joint task force of the European Federation of Neurological Societies and the Peripheral Nerve Soc. *J Peripher Nerv Syst* 2006; 11(1):9-19. Available at: http://www.guidelines.gov/summary/summary.aspx?ss=15&doc_id=9656&nbr=&string=#s28. Accessed on September 30, 2009.
24. Lunn MPT, Nobile-Orazio E. Immunotherapy for IgM anti-myelin-associated glycoprotein paraprotein-associated peripheral neuropathies. *Cochrane Database of Systematic Reviews* 2006, Issue 2. Art. No.: CD002827. DOI: 10.1002/14651858.CD002827.pub2.
25. National Institutes of Health (NIH). National Institute of Neurological Disorders and Stroke (NINDS). NINDS Chronic inflammatory demyelinating polyneuropathy (CIDP) information page. 2008. Available at: <http://www.ninds.nih.gov/disorders/cidp/cidp.htm>. Accessed on September 30, 2009.
26. Oates-Whitehead RM, Baumer JH, Haines L, et al. Intravenous immunoglobulin for the treatment of Kawasaki disease in children. *Cochrane Database of Systematic Reviews* 2003, Issue 4. Art. No.: CD004000. DOI: 10.1002/14651858.CD004000.
27. Ohlsson A, Lacy JB. Intravenous immunoglobulin for preventing infection in preterm and/or low-birth-weight infants. *Cochrane Database of Systematic Reviews* 2004, Issue 1. Art. No.: CD000361. DOI: 10.1002/14651858.CD000361.pub2.
28. Rosenfeld R, Andes D, Bhattacharyya N, et al. Clinical practice guideline: Adult sinusitis. *Otolaryngology–Head and Neck Surgery*. 2007; 137:S1-S31.
29. van Schaik IN, Winer JB, de Haan R, Vermeulen M. Intravenous immunoglobulin for chronic inflammatory demyelinating polyradiculoneuropathy. *Cochrane Database of Systematic Reviews* 2002, Issue 2. Art. No.: CD001797. DOI: 10.1002/14651858.CD001797.
30. van Schaik IN, van den Berg LH, de Haan R, Vermeulen M. Intravenous immunoglobulin for multifocal motor neuropathy. *Cochrane Database of Systematic Reviews* 2005, Issue 2. Art. No.: CD004429. DOI: 10.1002/14651858.CD004429.pub2.
31. U.S. Food and Drug Administration (FDA). Center for Biologics Evaluation and Research. Product approval: Gamunex®. Available at: <http://www.fda.gov/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/LicensedProductsBLAs/FractionatedPlasmaProducts/ucm064976.htm>. Accessed on: September 30, 2009.

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Carimune Nanofiltered[®]
 Flebogamma[®]
 Gammagard S/D[®]
 Gamma Globulin
 Gamunex[®]
 Immune Globulin
 Intravenous Immune Globulin, Human (IVIG)
 IVIG
 Octagam
 Polygam[®]
 Panglobulin[®]
 Polygam S/D[®]
 Privigen[®]
 Sandoglobulin[®]
 Venoglobulin-I[®]

The use of specific product names is illustrative only. It is not intended to be a recommendation of one product over another, and is not intended to represent a complete listing of all products available.

Document History

Status	Date	Action
Revised	11/19/2009	Medical Policy & Technology Assessment Committee (MPTAC) review. Diagnostic criteria added for CIDP and MMN. Place of service removed. Discussion and references updated.
Revised	11/20/2008	MPTAC review. CIDP moved from off label indications to medically necessary criteria. Discussion and references updated. Updated coding section with 01/01/2009 HCPCS changes.
Reviewed	10/01/2008	Updated coding section with 10/01/2008 ICD-9 changes.
	02/21/2008	MPTAC review. Discussion/General Information updated with AAN and AAAAI IVIG for MS position; AAO Head and Neck Surgery IVIG for PID position. References updated. Updated coding section with 04/01/2008 HCPCS changes.
	01/01/2008	Updated coding section with 01/01/2008 HCPCS changes; removed HCPCS J1567, Q4087, Q4088, Q4091, Q4092 deleted 12/31/2007.
Reviewed	10/01/2007	Updated coding section with 10/01/2007 ICD-9 changes.
	07/01/2007	Updated coding section with 07/01/2007 HCPCS changes.
	03/08/2007	MPTAC review. References updated. Coding updated; removed HCPCS J1563, J1564, Q9941, Q9942, Q9943, and Q9944, deleted 12/31/2005.
Revised	03/23/2006	MPTAC review.
	01/01/2006	Updated coding section with 01/01/2006 CPT/HCPCS changes
	11/18/2005	Added reference for Centers for Medicare & Medicaid Services (CMS) -National Coverage Determination (NCD).
Revised	07/14/2005	MPTAC review. Revision based on Pre-merger Anthem and Pre-merger WellPoint Harmonization.

Pre-Merger Organizations	Last Review Date	Document Number	Title
Anthem, Inc.	09/18/2003	DRUG.00013	Intravenous Immune Globulin Therapy
WellPoint Health Networks, Inc.	04/28/2005	2.09.17	Intravenous Immunoglobulin as a Treatment of Recurrent Spontaneous Abortion and Associated Laboratory Tests
	12/02/2004	Pharmacology Toolkit	Intravenous Immune Globulin

Federal and State law, as well as contract language including definitions and specific coverage provisions/exclusions, and Medical Policy take precedence over Clinical UM Guidelines and must be considered first in determining eligibility for coverage. The member's contract benefits in effect on the date that services are rendered must be used. Clinical UM Guidelines, which address medical efficacy, should be considered before utilizing medical opinion in adjudication. Medical technology is constantly evolving, and we reserve the right to review and update Clinical UM Guidelines periodically. Clinical UM guidelines are used when the plan performs utilization review for the subject. Due to variances in utilization patterns, each plan may choose whether or not to implement a particular Clinical UM Guideline. To determine if review is required for this Clinical UM Guideline, please contact the customer service number on the back of the member's card.

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