Clinical UM Guideline

Subject:	Intravenous Immune Globulin Therapy (IVIG)		
Guideline #:	CG-DRUG-09	**Current Effective Date:**	04/01/2008
Status:	Revised (Coding updated 10/01/2008)	**Last Review Date:**	02/21/2008

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.

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

Clinical Indications

Medically Necessary:

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

- 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 patients with hypogammaglobulinemia and/or recurrent bacterial infection associated with B-cell chronic lymphocytic leukemia (CLL).

Intravenous immune globulin therapy (IVIG) is considered **medically necessary** for the following off-label indications:

- Antenatal alloimmune thrombocytopenia;
- Autoimmune neutropenia;
- Chronic inflammatory demyelinating polyneuropathy (CIDP); (IVIG should be considered as a first-line treatment for CIDP. IVIG is used alone or following therapeutic plasma exchange to prolong its effect. IVIG is considered easier to use than repeated therapeutic plasma exchange and to have fewer complications than long-term glucocorticoid therapy);
- 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;
- Multifocal motor neuropathy in patients with anti GM1 antibodies and conduction block;
- Myasthenia Gravis, severe refractory;
- Polymyositis; routine use of IVIG is not recommended. IVIG may be considered in patients 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 patients 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) patients in the first 100 days after transplantation;
- Prevention of infection in HIV infected pediatric patients;
- Refractory auto-immune mucocutaneous blistering diseases including: pemphigus vulgaris, pemphigus foliaceous, bullous pemphigoid, mucous membrane pemphigoid, and epidermolysis bullosa aquisita.

Not Medically Necessary:
Intravenous Immune Globulin Therapy (IVIG) is considered **not medically necessary** for indications not listed as medically necessary.

Place of Service

Inpatient or outpatient, depending on the concurrent acuity of the clinical situation.

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

J1561	Injection, immune globulin, (Gamunex), intravenous, non-lyophilized (e.g., liquid), 500 mg
J1566	Injection, immune globulin, intravenous lyophilized (eg, 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), intravenous, non-lyophilized (e.g., liquid); 500 mg
Q4097	Injection, immune globulin (Privigen), 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	Erythemia infectiosum (fifth disease; parvovirus B19 infection)
078.5	Cytomegaloviral disease
079.83	Other specified viral and chlamydial infections, parvovirus B19
199.1	Malignant neoplasm
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
357.0-357.9	Inflammatory and toxic neuropathy
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, foliaceous)
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 patients 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, in part, on the practice guideline positions of the American Academy of Neurology (AAN), American Academy of Otolaryngology (AAO) and the American Academy of Allergy Asthma and Immunology (AAAAI). These professional organizations base recommendations primarily on the available evidence for diagnosis and treatment. For example, the AAN in their 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:

> IGIV 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.

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Government Agency, Medical Society, and Other Authoritative Publications:

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Intravenous Immune Globulin, Human (IVIG)
Iveegam®
IVIG
Polygam®
Polygam S/D®
Sandoglobulin®
Venoglobulin-I®
Venoglobulin-S®

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
Reviewed	10/01/2008	Updated coding section with 10/01/2008 ICD-9 changes.
Reviewed	02/21/2008	Medical Policy & Technology Assessment Committee (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.
Reviewed	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.
Reviewed	07/01/2007	Updated coding section with 07/01/2007 HCPCS changes.
Reviewed	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.
Reviewed	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