Immune Globulins **Policy Number: M-0028**
Revision: 1 **Last Update: 3/19/2013**

Payment will not be made for any use of these drugs outside of the criteria without prior authorization. The member may not be billed unless the member explicitly agrees in writing to be responsible for the charges in accordance with the contract/provider manual. Prior authorization will only be given if the provider demonstrates the intended use meets Medicare coverage guidelines.

Indications and Limitations:

Immune serums (immune globulin) provide passive immunity to infectious disease. The protection will be of rapid onset, but of short duration (1-3 months). Immune sera are obtained from pooled human plasma of either general population donors or hyperimmunized donors. It may be administered either by intravenous (IV) or intramuscular (IM) injection.

A. Immune globulin is available in broad-spectrum form, or disease-specific hyperimmune serum.

1. Gamma Globulin; intramuscular (IM) (IG, Gamma Globulin, ISG, Gamastan, Gammar, (J1460, J1560) is indicated for the following conditions:

a. Hepatitis A exposure (V01.79).

b. Measles (Rubeola): for a susceptible patient (has not been vaccinated and has not had measles and is at high risk for complication) who has been exposed less than three days prior to treatment (ICD-9 V04.2).

c. Rubella: for a woman in early pregnancy, who is exposed to the virus and does not have immunity. (V22.2 and
V01.4; or 647.50; or 647.53)

d. Varicella: for passive immunization in immunosuppressed patients when varicella zoster immunoglobulin is not available (V05.4).
e. Immunoglobulin deficiency: for prevention of serious infection when circulating IgG levels are low. Prophylactic therapy, especially against infections due to encapsulated bacteria, is often effective in Bruton-type, sex-linked congenital agammaglobulinemia, agammaglobulinemia associated with thymoma and acquired agammaglobulinemia (279.00-279.06, 279.2).

2. Specific hyperimmune serum globulin includes several different disease-specific drugs.

a. Hepatitis B serum (CPT 90371) is indicated post-exposure for transient prevention of hepatitis B infection. (V15.85)

b. Rabies serum (CPT 90375, 90376) is indicated post-exposure for transient prevention of rabies infection when the patient has not been completely immunized with the vaccination. (V01.5)

c. Vaccinia serum (CPT 90393) is indicated for transient prevention of or modification of aberrant infections induced by vaccinia (smallpox) vaccine, the vaccinia virus, such as eczema vaccinatum, some cases of progressive vaccinia, and possibly ocular vaccinia. (V01.4)

d. Varicella-zoster serum (CPT 90396) is indicated for transient prevention of varicella-zoster infection in exposed, susceptible individuals who have a greater risk of complications from varicella (V01.71). Documentation in the progress notes must indicate one of the following complicating conditions to verify medical necessity:
- Personal history of leukemia or lymphoma
- HIV infection
- Current immunosuppressive therapy
- a newborn with exposure to chickenpox (the documentation must indicate why the newborn is at increased risk; e.g., if the mother was exposed within 5 days of delivery).

e. Tetanus serum (J1670) is indicated for transient protection against tetanus post-exposure to tetanus (V03.7).
Documentation in the progress notes must identify the following:
- The wound is other than a clean minor wound, and the date of the injury;
- The active immunization with tetanus toxoid is unknown or uncertain; or
- The patient has received either less than 2 prior doses of tetanus toxoid; or two prior doses of tetanus toxoid, but there has been a delay of 24 hours or more between the time of injury and the initiation of tetanus prophylaxis.

f. Cytomegalovirus immune globulin intravenous (human) per vial (J0850) is indicated for the prophylaxis of cytomegalovirus disease associated with transplantation of kidney, lung, liver, pancreas and heart. In transplants of these organs other than kidney from CMV seropositive donors into seronegative recipients, prophylactic CMV-IGIV should be considered in combination with ganciclovir. (V42.0, V42.1, V42.6, V42.7, V42.81, V42.82, V42.83)

B. Intravenous immune globulin (Sandoglobulin, Venoglobulin-I, Privigen, Gamunex, Octagam, Gammagard liquid, Flebogamma/Flebogamma DIF, Carimune, Gammaplex) (J1459, J1557, J1561, J1566, J1568, J1569, J1572, J1599) provides immediate antibody levels. IVIG may be indicated for the following conditions:

1. Immunodeficiency Syndrome: to include congenital agammaglobulinemia such as x-linked agammaglobulinemia, common variable hypoglobulinemia, x-linked immunodeficiency with hyper IGM, combined immunodeficiency (279.00-279.06, 279.2).

2. Primary thrombocytopenia (287.30-287.39).

3. Alloimmune thrombocytopenia, refractoriness to platelet transfusions (287.49). Routine use is not indicated. IVIG may have a role in patients with severe thrombocytopenia of documented immune basis for whom other modalities are unsuccessful or contraindicated.
4. Post-transfusion purpura (287.41). IVIG may be considered as first-line therapy in severely affected patients.
5. Lymphoid Leukemia (204.10, 204.12, 204.20, 204.22) with either hypogammaglobulinemia or recurrent bacterial infections.

6. Autoimmune hemolytic anemia (283.0). Routine use is not indicated. IVIG may have a role in patients with warm-type AIHA that does not respond to corticosteroids.

7. Immune-mediated neutropenia (288.09). Routine use is not indicated. IVIG may have a role in severe illness that does not respond to other modalities or when the latter are contraindicated.

8. Multiple Myeloma (203.00-203.02, 203.10-203.12, 203.80, 203.82). Routine use is not indicated. It may have a role in patients with stable (plateau phase) disease and high risk of recurrent infections.

9. Pediatric intractable epilepsy (345.11, 345.3, 345.61). Routine use is not indicated. IVIG may have a role in certain syndromes as a last resort, especially in patients who may be candidates for surgical resection.

10. Guillian-Barré syndrome (357.0) IVIG is recommended as an equivalent alternative to plasma exchange in children and adults.

11. Myasthenia gravis (MG) (358.00, 358.01). Routine use is not indicated. IVIG may be considered in patients with severe MG to treat acute severe decompensation when other treatments have been unsuccessful or are contraindicated.

12. Eaton-Lambert Syndrome (358.1)
This is an immune-mediated, myasthenia-like syndrome. Treatment with IVIG is directed at decreasing the autoimmune response.

13. Polyneuropathy, chronic inflammatory demyelinating (357.81). IVIG is recommended as an equivalent alternative to plasma exchange in adults.

14. Multifocal motor neuropathy (357.9). The routine use of IVIG is not usually recommended. IVIG may be considered in patients who have progressive, symptomatic

multifocal motor neuropathy that has been diagnosed on the basis of electrophysiologic findings that rule out other possible conditions that may not respond to this treatment.

15. Dermatomyositis (710.3). Routine use is not indicated. IVIG may be used for patients with severe active illness for whom other interventions have been unsuccessful or intolerable.

16. Polymyositis (710.4). Routine use is not indicated. IVIG may be used for patients with severe active illness for whom other interventions have been unsuccessful or intolerable.

17. Systemic lupus erythematosus (SLE) (710.0). Routine use is not indicated. IVIG may be used for patients with severe active SLE for whom other interventions have been unsuccessful or intolerable.

18. Systemic sclerosis dermatomyositis overlap syndrome (710.8). Routine use is not indicated. IVIG may be used for patients with severe active illness for whom other interventions have been unsuccessful or intolerable.

19. Kawasaki disease (446.1).

20. Severe Vasculitic Syndromes, systemic (polyarteritis nodosa) (446.0), Churg-Strauss Vasculitis (446.4) and livedoid vasculitis (atrophie blanche) (701.3). Evidence does not support routine use of IVIG. IVIG may be used for patients with severe active illness for whom other interventions have been unsuccessful or intolerable.

21. Toxic Epidermal Necrolysis (695.15) and Stevens-Johnson Syndrome (695.13, 695.14). Evidence does not support routine use of IVIG. It will be covered if it is refractory to conventional therapy.

22. Pemphigoid gestationis (646.83, 646.84) that is refractory to conventional therapy.

23. Pyoderma gangrenosum (686.01) that is refractory to conventional therapy.

24. Neonatal alloimmune thrombocytopenia (776.1). Routine use of IVIG is not recommended. It is recommended in severely thrombocytopenic, symptomatic neonates who are at high risk of developing intracranial hemorrhage when other interventions have been unsuccessful become intolerable or are contraindicated.

25. IVIG may be indicated for high-risk pregnant women (V23.89) who have had a history of a previously affected infant with fetal-neonatal thrombocytopenia.

26. Wiskott-Aldrich Syndrome (279.12)

27. Anemia due to pure red cell aplasia (284.81, 284.89)

28. Human Immunodeficiency Virus (HIV) infection (042) IVIg will be covered for patients infected with HIV to reduce significant bacterial infection when all of the following coverage indicators are present: a) age less than 13 years old; b) evidence of either qualitative or quantitative humoral immunologic defects and c) current bacterial infections, despite appropriate antimicrobial prophylaxis. Dosage Guidelines: 400 mg/kg body weight given every 28 days.

29. Autoimmune mucocutaneous blistering disease is covered by a National Coverage Determination (See PUB 100-3: Medicare National Coverage Determination Manual Chapter1, Part 4 Section 250.3)(694.4, 694.5, 694.60, 694.61, 694.8)

30. Stiff-man syndrome (333.91) IVIG may be used for patients with severe active illness for whom other interventions have been unsuccessful or intolerable.

Coding Information:

CPT/HCPCS Code(s)

90371	HEPATITIS B IMMUNE GLOBULIN (HBIG), HUMAN, FOR INTRAMUSCULAR USE
90375	RABIES IMMUNE GLOBULIN (RIG), HUMAN, FOR INTRAMUSCULAR AND/ OR SUBCUTANEOUS USE
90376	RABIES IMMUNE GLOBULIN, HEAT-TREATED (RIG-HT), HUMAN, FOR INTRAMUSCULAR AND/OR SUBCUTANEOUS USE
90393	VACCINIA IMMUNE GLOBULIN, HUMAN, FOR INTRAMUSCULAR USE
90396	VARICELLA-ZOSTER IMMUNE GLOBULIN, HUMAN, FOR INTRAMUSCULAR USE
96365	INTRAVENOUS INFUSION, FOR THERAPY, PROPHYLAXIS, OR DIAGNOSIS (SPECIFY SUBSTANCE OR DRUG); INITIAL, UP TO 1 HOUR
96366	INTRAVENOUS INFUSION, FOR THERAPY, PROPHYLAXIS, OR DIAGNOSIS (SPECIFY SUBSTANCE OR DRUG); EACH ADDITIONAL HOUR (LIST SEPARATELY IN ADDITION TO CODE FOR PRIMARY PROCEDURE)
96372	THERAPEUTIC, PROPHYLACTIC, OR DIAGNOSTIC INJECTION (SPECIFY SUBSTANCE OR DRUG); SUBCUTANEOUS OR INTRAMUSCULAR
J0840	INJECTION, CROTALIDAE POLYVALENT IMMUNE FAB (OVINE), UP TO 1 GRAM
J0850	INJECTION, CYTOMEGALOVIRUS IMMUNE GLOBULIN INTRAVENOUS (HUMAN), PER VIAL
J1459	INJECTION, IMMUNE GLOBULIN (PRIVIGEN), INTRAVENOUS, NON-LYOPHILIZED (E.G. LIQUID), 500 MG
J1460	INJECTION, GAMMA GLOBULIN, INTRAMUSCULAR, 1 CC
J1557	INJECTION, IMMUNE GLOBULIN, (GAMMAPLEX), INTRAVENOUS, NON-LYOPHILIZED (E.G. LIQUID), 500 MG
J1560	INJECTION, GAMMA GLOBULIN, INTRAMUSCULAR, OVER 10 CC
J1561	INJECTION, IMMUNE GLOBULIN, (GAMUNEX/GAMUNEX-C/GAMMAKED), 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
J1571	INJECTION, HEPATITIS B IMMUNE GLOBULIN (HEPAGAM B), INTRAMUSCULAR, 0.5 ML
J1572	INJECTION, IMMUNE GLOBULIN, (FLEBOGAMMA/FLEBOGAMMA DIF), INTRAVENOUS, NON-LYOPHILIZED (E.G. LIQUID), 500 MG
J1573	INJECTION, HEPATITIS B IMMUNE GLOBULIN (HEPAGAM B), INTRAVENOUS, 0.5 ML
J1599	INJECTION, IMMUNE GLOBULIN, INTRAVENOUS, NON-LYOPHILIZED (E.G. LIQUID), NOT OTHERWISE SPECIFIED, 500 MG
J1670	INJECTION, TETANUS IMMUNE GLOBULIN, HUMAN, UP TO 250 UNITS

ICD-9 Code(s):

042	HUMAN IMMUNODEFICIENCY VIRUS (HIV) DISEASE
070.20-070.23	VIRAL HEPATITIS B WITH HEPATIC COMA ACUTE OR UNSPECIFIED WITHOUT HEPATITIS DELTA - CHRONIC VIRAL HEPATITIS B WITH HEPATIC COMA WITH HEPATITIS DELTA
070.30-070.33	VIRAL HEPATITIS B WITHOUT HEPATIC COMA ACUTE OR UNSPECIFIED WITHOUT HEPATITIS DELTA - CHRONIC VIRAL HEPATITIS B WITHOUT HEPATIC COMA WITH HEPATITIS DELTA
070.42	HEPATITIS DELTA WITHOUT ACTIVE HEPATITIS B DISEASE WITH HEPATIC COMA HEPATITIS DELTA WITH HEPATITIS B CARRIER STATE
203.00-203.80	MULTIPLE MYELOMA, WITHOUT MENTION OF HAVING ACHIEVED REMISSION – OTHER IMMUNOPROLIFERATIVE NEOPLASMS, WITHOUT MENTION OF HAVING ACHIEVED REMISSION
203.82	OTHER IMMUNOPROLIFERATIVE NEOPLASMS, IN RELAPSE
204.10	CHRONIC LYMPHOID LEUKEMIA, WITHOUT MENTION OF HAVING ACHIEVED REMISSION
204.12	CHRONIC LYMPHOID LEUKEMIA, IN RELAPSE
204.20	SUBACUTE LYMPHOID LEUKEMIA, WITHOUT MENTION OF HAVING ACHIEVED REMISSION
204.22	SUBACUTE LYMPHOID LEUKEMIA, IN RELAPSE
279.00-279.06	HYPOGAMMAGLOBULINEMIA UNSPECIFIED - COMMON VARIABLE IMMUNODEFICIENCY

279.12	WISKOTT-ALDRICH SYNDROME
279.2	COMBINED IMMUNITY DEFICIENCY
283.0	AUTOIMMUNE HEMOLYTIC ANEMIAS
284.81	RED CELL APLASIA (ACQUIRED) (ADULT) (WITH THYMOMA)
284.89	OTHER SPECIFIED APLASTIC ANEMIAS
287.30-287.39	PRIMARY THROMBOCYTOPENIA,UNSPECIFIED - OTHER PRIMARY THROMBOCYTOPENIA
287.41	POSTTRANSFUSION PURPURA
287.49	OTHER SECONDARY THROMBOCYTOPENIA
288.09	OTHER NEUTROPENIA
333.91	STIFF-MAN SYNDROME
345.11	GENERALIZED CONVULSIVE EPILEPSY WITH INTRACTABLE EPILEPSY
345.3	GRAND MAL STATUS EPILEPTIC
345.61	INFANTILE SPASMS WITH INTRACTABLE EPILEPSY
357.0	ACUTE INFECTIVE POLYNEURITIS
357.81	CHRONIC INFLAMMATORY DEMYELINATING POLYNEURITIS
357.9	UNSPECIFIED INFLAMMATORY AND TOXIC NEUROPATHIES
358.00	MYASTHENIA GRAVIS WITHOUT (ACUTE) EXACERBATION
358.01	MYASTHENIA GRAVIS WITH (ACUTE) EXACERBATION
358.1	MYASTHENIC SYNDROMES IN DISEASES CLASSIFIED ELSEWHERE
446.0	POLYARTERITIS NODOSA
446.1	ACUTE FEBRILE MUCOCUTANEOUS LYMPH NODE SYNDROME (MCLS)
446.4	WEGENER'S GRANULOMATOSIS
646.83	OTHER SPECIFIED ANTEPARTUM COMPLICATIONS
646.84	OTHER SPECIFIED POSTPARTUM COMPLICATIONS
647.50	RUBELLA OF MOTHER COMPLICATING PREGNANCY CHILDBIRTH OR THE PUERPERIUM UNSPECIFIED AS TO EPISODE OF CARE
647.53	ANTEPARTUM RUBELLA
686.01	PYODERMA GANGRENOSUM
694.4	PEMPHIGUS
694.5	PEMPHIGOID
694.60	BENIGN MUCOUS MEMBRANE PEMPHIGOID WITHOUT OCULAR INVOLVEMENT
694.61	BENIGN MUCOUS MEMBRANE PEMPHIGOID WITH OCULAR INVOLVEMENT
694.8	OTHER SPECIFIED BULLOUS DERMATOSES
695.13-695.15	STEVENS-JOHNSON SYNDROME - TOXIC EPIDERMAL NECROLYSIS
701.3	STRIAE ATROPHICAE
710.0	SYSTEMIC LUPUS ERYTHEMATOSUS

710.3	DERMATOMYOSITIS
710.4	POLYMYOSITIS
710.8	OTHER SPECIFIED DIFFUSE DISEASES OF CONNECTIVE TISSUE
776.1	TRANSIENT NEONATAL THROMBOCYTOPENIA
989.5	TOXIC EFFECT OF VENOM
V01.4	CONTACT WITH OR EXPOSURE TO RUBELLA
V01.5	CONTACT WITH OR EXPOSURE TO RABIES
V01.71	CONTACT OR EXPOSURE TO VARICELLA
V01.79	CONTACT OR EXPOSURE TO OTHER VIRAL DISEASES
V02.61	CARRIER OR SUSPECTED CARRIER OF HEPATITIS B
V03.7	NEED FOR PROPHYLACTIC VACCINATION WITH TETANUS TOXOID ALONE
V04.2	NEED FOR PROPHYLACTIC VACCINATION AND INOCULATION AGAINST MEASLES ALONE
V05.4	NEED FOR PROPHYLACTIC VACCINATION AND INOCULATION AGAINST VARICELLA
V15.85	PERSONAL HISTORY OF CONTACT WITH AND (SUSPECTED) EXPOSURE TO POTENTIALLY HAZARDOUS BODY FLUIDS
V22.2	PREGNANT STATE INCIDENTAL
V23.89	SUPERVISION OF OTHER HIGH-RISK PREGNANCY
V42.0	KIDNEY REPLACED BY TRANSPLANT
V42.1	HEART REPLACED BY TRANSPLANT
V42.6	LUNG REPLACED BY TRANSPLANT
V42.7	LIVER REPLACED BY TRANSPLANT
V42.83	PANCREAS REPLACED BY TRANSPLANT

Background:

This medication is used to strengthen the body's natural defense system (immune system) to lower the risk of infection in persons with a weakened immune system. This medication is made from healthy human blood that has a high level of certain defensive substances (antibodies), which help fight infections. It is also used to increase the blood count (platelets) in persons with a certain blood disorder (idiopathic thrombocytopenia purpura-ITP).

Black Box Warning

Injection (Solution)

Renal dysfunction, acute renal failure, osmotic nephrosis, and death may occur with immune globulin intravenous (IGIV) products. Renal dysfunction and acute renal failure occur more commonly in patients receiving IGIV products containing sucrose. Gammagard Liquid(R) and Gamunex(R)-C, do not contain sucrose. For patients at risk of renal dysfunction or failure, administer at the minimum rate of infusion practicable.

Intravenous (powder for Solution; Solution)

Immune globulin intravenous (IGIV) products have been reported to be associated with renal dysfunction, acute renal failure, osmotic nephrosis, and death. Use caution in patients predisposed to acute renal failure and administer at the minimum concentration available and the minimum rate of infusion practicable in such patients. Higher rates of renal failure were associated with IGIV products containing sucrose. Flebogamma(R) 5%, Flebogamma(R) 5% DIF, Flebogamma(R) 10% DIF, and Privigen(R) do not contain sucrose.

Definitions:

HCPCS Code—Healthcare Common Procedure Coding System - A system of letter and number codes assigned to procedures, medications, supplies and equipment used for pricing and billing.

ICD-9 Code—International Classification of Disease, 9th edition. A standardized classification of disease, injuries, and causes of death, by etiology and anatomic localization and codified into a 6-digit number, which allows clinicians, statisticians, politicians, health planners and others to speak a common language, both US and internationally.

References:

1. Local Coverage Determination (LCD) for Immune Globulins (L30147). Revision X. Available at: http://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=30147&ContrId=212&ver=32&ContrVer=1&Date=01%2f01%2f2012&DocID=L30147&bc=iAAAAAgAIAAAAA%3d%3d&. Accessed March 19, 2013.
2. Immune Globulin. Available at: http://www.thomsonhc.com/micromedex2/librarian/ND_T/evidencexpert/ND_PR/evidencexpert/CS/E70303/ND_AppProduct/evidencexpert/DUPLICATIONSHIELDSYNC/9E8232/ND_PG/evidencexpert/ND_B/evidencexpert/ND_P/evidencexpert/PFActionId/evidencexpert.IntermediateToDocumentLink?docId=298670&contentSetId=100&title=Immune+Globulin&servicesTitle=Immune+Globulin. Accessed August 31, 2012.

Document History:

Date Written: 8/31/2012
Effective Date: 4/1/13
Revision 1: 3/19/2013
Internal review: 3/24/2013
External Review: 3/26/2013

For the Archived Policy, please go to http://www.vivaprovider.com/Resources/CoveragePolicies.aspx and click on the Archived Policies Link.