

 Close Window

[Aetna.com Home](#) | [Help](#) | [Contact Us](#)



Search

Pharmacy Clinical Policy Bulletins

Aetna Non-Medicare Prescription Drug Plan

 [Print this Page](#)

Subject: IVIG

Additional Information
[> Clinical Policy Bulletin Notes](#)

Status	Drug	PR	PR-QL	PR-AL	ST	M	EX†
P	<i>carimune</i>	X					
P	<i>carimune nf</i>	X					
P	<i>gammar p</i>	X					
P	<i>iveegam en</i>	X					
P	<i>octagam</i>	X					
P	<i>panglobulin</i>	X					
P	<i>polygamy s/d</i>	X					
NP	Flebogamma® (<i>Immune Globulin (Human) IV</i>)	X					
NP	Gammagard SD® 0.5gm inj (<i>Immune Globulin (Human) IV</i>)	X					
NP	Gammunex® (<i>Immune Globulin (Human) IV</i>)	X					
NP	Panglobulin® 1gm inj; 12gm (<i>Immune Globulin (Human) IV</i>)	X					

*P = Preferred
 FE = Formulary Excluded
 NP = Nonpreferred
 PR = Precertification
 QL = Quantity Limits
 AL = Age Limits
 ST = Step-Therapy
 †M EX = [Medical Exception](#)

*The lists above are subject to change. Not all programs - for example step-therapy, precertification, and quantity limits - are available in all service areas.

Policy:

For the purpose of this policy, the criteria below apply to plans that have elected to use Aetna Pharmacy to manage the fulfillment and the precertification of specialty drugs.

I. Precertification Criteria

Under some plans, including plans that use an open or closed formulary,

Intravenous Immunoglobulins (IVIg) are subject to Precertification. If Precertification requirements apply Aetna considers Intravenous Immunoglobulins (IVIg) to be medically necessary for those members who meet the following Precertification criteria, see also **Appendix A**:

A. A documented diagnosis:

1. Immune or idiopathic thrombocytopenic purpura (ITP)
2. Guillain-Barré syndrome:
3. Multifocal motor neuropathy: (see Appendix)
4. Kawasaki disease (see Appendix)
5. HIV infected children: (see Appendix)
6. HIV-associated thrombocytopenia, pediatric or adult: (see Appendix)
7. Hemolytic disease of newborn(see Appendix)
8. Allogeneic bone marrow transplantation:
9. Secondary immunosuppression associated with major surgery (see Appendix)
10. Polymyositis in persons who are resistant to first and second line therapies (see Appendix)
11. Post-transfusion purpura (see Appendix)
12. Dermatomyositis in persons who are resistant to first and second line therapies (see Appendix)
13. Myasthenia gravis (see Appendix)
14. Multiple myeloma (see Appendix)
15. Moersch-Woltmann (Stiff-man) syndrome (unresponsive to other therapies) (see Appendix)
16. Neonatal alloimmune thrombocytopenia (NAIT) (also known as fetal alloimmune thrombocytopenia or FAIT) when criteria in Appendix are met
17. Parvovirus B19 infection, chronic, with severe anemia (see Appendix)
18. Lambert-Eaton myasthenic syndrome (see Appendix)
19. Hyperimmunoglobulinemia E syndrome (see Appendix)
20. Autoimmune mucocutaneous blistering diseases
21. Relapsing-remitting multiple sclerosis (MS) (see Appendix)
22. Systemic lupus erythematosus (SLE), (see Appendix)
23. Selective IgG subclass deficiencies (see Appendix)
24. Renal transplantation from live donor with ABO incompatibility or positive cross-match
25. Churg-Strauss Syndrome (CSS) (allergic granulomatosis),
26. Refractory autoimmune hemolytic anemia (see Appendix)
27. Toxic shock syndrome or toxic necrotizing fasciitis due to group A streptococcus (see Appendix.).

Aetna considers subcutaneously administered immunoglobulins as an alternative to intravenous immunoglobulin therapy medically necessary for members who meet the criteria for IVIG set forth above.

AND

B. Aetna considers certain experimental and investigational Intravenous Immunoglobulins (IVIg) uses noted under **Appendix B** not medically necessary and; therefore, not covered.

Appendix A

Condition

Indications

Autoimmune hemolytic anemia, refractory

IVIG may be considered medically necessary in persons with warm-type autoimmune hemolytic anemia that does not respond to corticosteroids or splenectomy, or those for whom the latter two treatments are contraindicated.

Bacterial infection in HIV-infected children

Consistent with recommendations of the Working Group on Antiretroviral Therapy of the National Pediatric HIV Resource Center IVIG is considered medically necessary in children with HIV-infection who meet ANY of the following criteria:

1. Those with hypogammaglobulinemia, i.e., serum IgG concentration less than 250 mg/dL;
2. Those with recurrent serious bacterial infections, i.e., defined as two or more infections such as bacteremia, meningitis, or pneumonia in a 1-year period;
3. Those who fail to form antibodies to common antigens, such as measles, pneumococcal, and/or Haemophilus influenzae type b vaccine;
4. Those living in areas where measles is highly prevalent and who have not developed an antibody response after two doses of measles, mumps, and rubella virus vaccine live;
5. Single dose for HIV-infected children who are exposed to measles;
6. HIV-infected children with chronic bronchiectasis that is suboptimally responsive to antimicrobial and pulmonary therapy.

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP), also known as Chronic Relapsing

Symmetric or focal neurologic deficits with slowly progressive or relapsing course over 2 months or longer with neurophysiological abnormalities).

Polyneuropathy, including diabetes mellitus-CIDP and multifocal acquired demyelinating sensory and motor neuropathy (MADSAM) variant

Note: IVIG is recommended under accepted guidelines as an equivalent alternative to plasma exchange in children and adults, or when there is difficulty with venous access for plasmapheresis.

Dermatomyositis, Polymyositis (includes Juvenile)

1. Diagnosis is established by biopsy; and
2. Member has severe active illness; and
3. Member is intolerant or refractory to 1st and 2nd line therapies:

Condition

Indications

- a. 1st line therapy - Corticosteroids (e.g. prednisone);
- b. 2nd line therapy - Immunosuppressants (e.g., methotrexate, azithioprine, cyclophosphamide, and cyclosporine).

Fetal Alloimmune Thrombocytopenia (FAIT)

Previous pregnancy affected by FAIT and father homozygous for HPA-1a; and

- 1. At 20 weeks cordocentesis reveals fetal platelets < 100 x 10⁹/L; or
- 2. Symptomatic neonates with severe thrombocytopenia, who are at high risk of developing intracranial hemorrhage when washed irradiated maternal platelets are not available, have not been successful, have become intolerable, or are contraindicated.

Guillain Barre Syndrome (GBS) - a.k.a. Acute Infective Polyneuritis (includes Miller-Fisher syndrome [MFS], Pan autonomic polyneuropathy

- 1. Severe GBS with significant weakness such as inability to stand or walk without aid, respiratory or bulbar weakness, or Miller-Fisher syndrome (MFS); and
- 2. The disorder has been diagnosed during the first 2 weeks of the illness; and
- 3. IVIG is initiated within one month of symptom onset. Note: Based on the 2003 AAN guidelines, IVIG should usually be initiated within 2 weeks and no longer than 4 weeks of onset of neuropathic symptoms.

Hematopoietic Stem Cell Transplant (HSCT) or Bone Marrow Transplant (BMT) - Allogeneic, matched, unrelated donor

Not Autologous (HSCT) or BMT

- 1. Transplantation was for an indication that Aetna considers medically necessary; and either of the following two criteria are met:
 - a. IVIG is medically necessary for treatment of severe GVHD in persons receiving matched HLA allogeneic BMT; or
 - b. IVIG is medically necessary for prophylaxis against infections (e.g., cytomegalovirus [CMV] infection, interstitial pneumonia, varicella-zoster virus infection, and recurrent bacterial infection) in persons with hypogammaglobulinemia (IgG level < 400 mg/dL), (The requirement for IgG levels less

Condition	Indications
	<p>than 400 mg/dL does not apply to persons undergoing transplantation for multiple myeloma or malignant macroglobulinemia because their total IgG level is affected by their underlying paraproteinemia)</p>

Notes: IVIG is not considered medically necessary in autologous HSCT and BMT, as these recipients do not benefit from IVIG treatment. Use of prophylactic immunoglobulin in allogeneic recipients of stem cell transplant from HLA-identical sibling donor is not considered medically necessary.

HIV-associated Thrombocytopenia - Adult	<ol style="list-style-type: none"> 1. Significant bleeding in thrombocytopenic patients or platelet count less than 20,000/mm³; and 2. Failure of RhIG in Rh-positive patients.
--	--

HIV-associated Thrombocytopenia - Pediatric	<p>Infants and children < 13 years of age whose IgG level is < 400 mg/dL; and</p> <ol style="list-style-type: none"> 1. 2 or more bacterial infections in a 1-year period despite antibiotic chemoprophylaxis with TMP-SMZ or another active agent; or 2. Child has received 2 doses of measles vaccine and lives in a region with a high prevalence of measles; or 3. Member has HIV-associated thrombocytopenia despite antiretroviral therapy; or 4. Member has chronic bronchiectasis that is suboptimally responsive to antimicrobial and pulmonary therapy; or 5. T4 cell count is greater than or equal to 200/mm³
--	---

Hemolytic Disease of the Newborn	<p>Not responding to phototherapy to decrease the need for exchange transfusion. Physician discretion important in deciding.</p>
---	--

Hyperimmunoglobulin E Syndrome (Job's syndrome; Hyper IgE syndrome)	<p>Recurrent staphylococcal abscesses and markedly elevated serum IgE with normal IgG, IgA, and IgM concentrations.</p>
--	---

Idiopathic Thrombocytopenic Purpura (ITP) - Adult	<ol style="list-style-type: none"> 1. Other causes of thrombocytopenia have been ruled out by history and peripheral smear; and Unresponsive to corticosteroid therapy; and
--	--

Condition

Indications

- Management of acute bleeding due to severe thrombocytopenia (platelet counts less than 30,000/mm³); or
2. To increase platelet counts prior to invasive major surgical procedures (e.g., splenectomy), or
 3. To defer or avoid splenectomy; or
 4. In members with severe thrombocytopenia (platelet counts less than 20,000/mm³) considered to be at risk for intracerebral hemorrhage.

Idiopathic Thrombocytopenic Purpura (ITP) - Pediatric

Acute ITP:

1. IVIG as initial therapy if platelet count < 20,000/ul, especially when member has emergency bleeding or is at risk for severe life-threatening bleeding; or
2. Persons with severe thrombo-cytopenia (platelet counts less than 20,000/ul) considered to be at risk for intracerebral hemorrhage.

Note: IVIG not indicated if only mild manifestations of bleeding.

Chronic ITP:

In high risk persons when platelet count low or person symptomatic; and

1. Failure of other therapies or
2. Member is a high risk for post-splenectomy sepsis

Idiopathic Thrombocytopenic Purpura (ITP), Chronic Refractory

1. Age of 10 years or older; and
2. Duration of illness of greater than six months; and
3. No concurrent illness/disease explaining thrombocytopenia; and
4. Prior treatment with corticosteroids and splenectomy has failed or member is at high risk for post-splenectomy sepsis.

Immune Thrombocytopenic Purpura in Pregnancy

1. Refractory to steroids with platelet counts < 10,000/mL in the third trimester; or
2. Platelet counts < 30,000/mL associated with bleeding before vaginal delivery or C-section; or
3. Pregnant women who have previously delivered infants with autoimmune thrombocytopenia; or
4. Pregnant women who have platelet counts less than 75,000/mm³ during the current pregnancy; or
5. Pregnant women with past history of

Condition	Indications
Immunosuppressed Patients	<p>splenectomy.</p> <p>To prevent or modify recurrent bacterial or viral infections (e.g., CMV) in members with iatrogenically induced, or disease associated immunosuppression (IgG < 400 mg.dL) with one of the following:</p> <ol style="list-style-type: none"> 1. Solid organ transplants or extensive surgery with immunosuppression (<u>Note</u>: In particular, IVIG may be medically necessary in persons undergoing multiple courses of plasmapheresis as a treatment for allograft rejection or for other indications; these persons may receive IVIG at the completion of therapy if their IgG level is less than 400 mg/dL); or 2. Hematological malignancy; or 3. Extensive burns; or 4. Collagen-vascular disease.
Kawasakidisease (Mucocutaneous Lymph Node Syndrome [MCLS])	<p>Diagnosis must be established - no specific lab test - diagnosis is established by meeting the following criteria:</p> <ol style="list-style-type: none"> 1. Fever present for at least five days; and 2. Four of the following five conditions are met: <ol style="list-style-type: none"> a. Mucous membrane changes such as a red tongue and dry fissured lips; b. Swelling of the hands and feet; c. Enlarged lymph nodes in the neck; d. Diffuse red rash covering most of the body; e. Redness of the eyes.
Lambert-Eaton Myasthenic Syndrome (LEMS)	<p>No response to anticholinesterases and Diaminopyridine); and</p> <ol style="list-style-type: none"> 1. Used as an alternative to plasma exchange if weakness is severe; or 2. When there is difficulty with venous access for plasmapheresis
Myasthenia Gravis	<ol style="list-style-type: none"> 1. Treatment of acute myasthenic crisis with decompensation (respiratory failure, or disabling weakness requiring hospital admission); and 2. Other treatments have been unsuccessful or are contraindicated (e.g., azathioprine, cyclosporine, and cyclophosphamide).

Condition	Indications
Moersch-Woltmann (Stiff-man) Syndrome	<p><u>Note:</u> For management of myasthenic crises, IVIG is administered over 2 to 5 days. Use of IVIG as maintenance therapy is considered experimental and investigational.</p> <ol style="list-style-type: none"> 1. Presence of Anti-GAD antibody; and 2. Benzodiazepines (e.g., Valium) and/or Baclofen, phenytoin, clonidine, tizanidine have failed.
Multifocal Motor Neuropathy with Conduction Block	<p>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 IVIG treatment).</p>
Multiple Myeloma (MM)	<ol style="list-style-type: none"> 1. "Plateau Phase" MM (> 3 months since diagnosis); and 2. IgG level < 600mg/dL; and 3. 2 or more significant infections in last year or a single life threatening infection; or <p>Evidence of specific antibody deficiency</p>
Multiple Sclerosis (MS) - Relapsing-remitting <i>(not primary or secondary progressive MS)</i>	<ol style="list-style-type: none"> 1. Severe manifestations of relapsing-remitting MS (not primary or secondary progressive MS); and 2. Standard approaches (i.e., interferons - Betaseron, Avonex, Rebif) have failed, become intolerable, or are contraindicated.
Parvovirus B19 Infection, Chronic, with Severe Anemia (Pure Red Cell Aplasia)	<p>Severe, refractory anemia with documented parvovirus B19 viremia.</p>
Pemphigus Vulgaris (Autoimmune Mucocutaneous Blistering Diseases) - includes Pemphigus Foliaceus, Bullous Pemphigoid, Mucous Membrane Pemphigoid (a.k.a. Cicatricial Pemphigoid), and Epidermolysis bullosa aquisita	<ol style="list-style-type: none"> 1. The diagnosis has been proven by biopsy and confirmed by pathology report; and 2. The condition is rapidly progressing, extensive or debilitating; and 3. Corticosteroids, immuno-suppressive agents have failed or the member has experienced significant complications from standard treatment, such as diabetes or steroid-induced osteoporosis.
Post-transfusion purpura (PTP)	<ol style="list-style-type: none"> 1. Decreased platelets (usually < 10,000/mm³); and 2. 2 - 14 days post transfusion with bleeding

Condition

Indications

Selective IgG Subclass Deficiency

1. Member has unexplained recurrent or persistent severe bacterial infections; and
2. Infections fail to respond adequately to conservative measures, including meticulous hygiene and prophylactic antibiotics; and
3. Member has demonstrated an inability to mount an adequate response to protein and polysaccharide antigens, as determined by the following criteria, derived from Buckley (2002):
 - a. Member has documented inability to mount an antibody response to protein antigens: Serum antibody titres to tetanus and/or diphtheria should be obtained prior to immunization with diphtheria and/or tetanus vaccine and two to four weeks after immunization. An inadequate response is defined as less than a fourfold rise in antibody titre; and
 - b. Member has documented inability to mount an adequate antibody response to polysaccharide antigens. Serum antibody titres to pneumococcus should be measured prior to immunization and three to six weeks after immunization with polyvalent pneumococcal polysaccharide vaccine (e.g., Pneumovax). An inadequate response is defined as less than a 2-fold rise in titer over baseline in at least one serotype tested.

Note: Response to polysaccharide antigens is not reliable in children less than 2 years of age.

4. IVIG should be discontinued and the medical necessity of IVIG should be reevaluated 1 year after initiating therapy and every two years thereafter by reassessing immune response to protein and polysaccharide antigens.

Condition

Indications

Systemic Lupus Erythematosus

Members with severe active SLE for whom first- and second-line therapies have been unsuccessful, have become intolerable, or are contraindicated.

Note: Standard first-line therapy of active SLE include non-steroidal anti-inflammatory drugs, followed by low-dose corticosteroids and antimalarial compounds. Second-line therapeutic alternatives are the cytotoxic agents methotrexate, azathioprine, or cyclophosphamide.

Toxic shock syndrome or toxic necrotizing fasciitis due to group A streptococcus

IVIg is considered medically necessary in persons who are sufficiently ill to require critical care unit support and have documented presence of fasciitis and microbiological data consistent with invasive streptococcal infection (culture or Gram stain).

Place of Service:



Outpatient

The above policy is based on the following references:

1. Drug Facts and Comparisons on-line. (www.drugfacts.com), Wolters Kluwer Health, St. Louis, MO. 2006.
2. USP DI® Drug Information For The Health Care Professional - 26th Ed. (online from www.statref.com) Thomson Micromedex, Greenwood Village, CO. 2006.
3. AHFS Drug Information® with AHFSfirstReleases®. (online from www.statref.com), American Society Of Health-System Pharmacists®, Bethesda, MD. 2006.
4. DRUGDEX® System: Klasco RK (Ed): DRUGDEX® System. Online edition. Thomson Micromedex, Greenwood Village, CO.
5. PDR® Electronic Library, Thomson Micromedex, Greenwood Village, Colorado (Edition expires 2006).
6. Dudesek A, Zetl UK. Intravenous immunoglobulins as therapeutic option in the treatment of multiple sclerosis. J Neurol. 2006;253 Suppl 5:v50-v58.
7. Fergusson D, Hutton B, Sharma M, et al. Use of intravenous immunoglobulin for treatment of neurologic conditions: a systematic review. Transfusion. 2005;45(10):1640-57.
8. Gajdos P, Chevret S, Toyka K. Intravenous immunoglobulin for myasthenia gravis. Cochrane Database Syst Rev. 2006;(2):CD002277.
9. Joint Task Force of the EFNS and the PNS. European Federation of Neurological Societies/Peripheral Nerve Society Guideline on management of multifocal motor neuropathy. Report of a joint task force of the European Federation of Neurological Societies and the Peripheral Nerve Society. J Peripher Nerv Syst. 2006;11(1):1-8.
10. Kumar A, Teuber SS, Gershwin ME. Intravenous immunoglobulin: striving for appropriate use. Int Arch Allergy Immunol. 2006;140(3):185-98.

Copyright Aetna Inc. All rights reserved. Pharmacy Clinical Policy Bulletins are developed by Aetna to assist in administering plan benefits and constitute neither offers of coverage nor medical advice. This Clinical Policy Bulletin contains only a partial, general description of plan or program benefits and does not constitute a contract. Aetna does not provide health care services and, therefore, cannot guarantee any results or outcomes. Participating providers are independent contractors in private practice and are neither employees nor agents of Aetna or its affiliates. Treating providers are solely responsible for medical advice and treatment of members. This Clinical Policy Bulletin may be updated and therefore is subject to change.

January 01, 2007

 [Email this Page](#)  [Print this Page](#)

[Company Information](#) | [Site Map](#)
[Web Privacy Statement](#) | [Legal Statement](#) | [Privacy Notices](#) | [Member Disclosure](#)

[Aetna.com Home](#) | [Help](#) | [Contact Us](#) | [Search](#)
Copyright © 2001-2010 Aetna Inc.