

Medical Policy Manual **Approved: Do Not Implement Until 12/12/09**

Intravenous Immune Globulin (IVIG) Therapy

DESCRIPTION

Immune globulins or immunoglobulins (Ig) are specialized glycoproteins which function as antibodies. Produced by plasma cells, there are five human isotypes of immunoglobulins, IgA, IgD, IgE, IgG and IgM. Of these, IgG, IgA and IgM are referred to as natural antibodies as they are produced without deliberate immunization or antigen exposure. IgD and IgE are generally produced in response to the introduction of foreign antigens to which they bind and deactivate. Together, all immunoglobulin isotypes are vital components of the body's immune response.

IgG is the most common of the immunoglobulins, with multiple functions including placental antibody transfer, phagocytic cell surface binding and activating complement. Commercial preparations of intravenous immune globulins (IVIGs) are sterile, highly purified IgG products manufactured from large pools of human plasma, typically from 1000 or more healthy blood donors. They contain more than 95% unmodified IgG but only trace amounts of IgA and/or IgM. IVIGs are used in the treatment of multiple conditions.

Examples of preparations of intravenous immune globulins are: Carimune[®] NF, Gammagard[®] S/D, Gammagard[®] Liquid, Gamunex[®], Flebogamma[®], Privigen[®] and Octagam[®].

REFER TO DECISION SUPPORT TREE

POLICY

- Intravenous immune globulin (IVIG) for the treatment of the following is considered **medically necessary**:
 - Chronic inflammatory demyelinating polyneuropathies (CIDP)
 - Hyperimmunoglobulinemia E syndrome
 - Lambert-Eaton myasthenic syndrome
 - Primary humoral immunodeficiency, including, but not limited to, the following:
 - Congenital agammaglobulinemia (X-linked agammaglobulinemia)
 - Hypogammaglobulinemia
 - Common variable immunodeficiency
 - X-linked immunodeficiency with hyperimmunoglobulin M
 - Severe combined immunodeficiency (SCID)
 - Wiskott-Aldrich syndrome
- Intravenous immune globulin (IVIG) for the treatment of the following is considered **medically necessary** if the medical appropriateness criteria are met: **(See Medical Appropriateness below.)**
 - Bacterial infections associated with neonates
 - Dermatomyositis
 - Guillain-Barré syndrome
 - Immune/idiopathic thrombocytic purpura (ITP)
 - Kawasaki disease
 - Multifocal motor neuropathy (MMN)
 - Multiple sclerosis
 - Solid organ transplant recipients
 - Parvovirus B19
- Intravenous immune globulin (IVIG) for the prevention of serious bacterial infections in the following is considered **medically necessary**:
 - Individuals with pediatric human immunodeficiency virus (HIV)
 - Individuals with pediatric AIDS-related complex (ARC)
- Intravenous immune globulin (IVIG) for the prevention of the following is considered **medically necessary** if the medical appropriateness criteria are met: **(See Medical Appropriateness below.)**



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- Bacterial infections associated with the following:
 - Chronic lymphocytic leukemia (CLL)
 - Neonates
- Graft-versus-host disease
- Intravenous immune globulin (IVIG) for the treatment of other conditions/diseases, including, but not limited to the following is considered **investigational: (See Applicable Tennessee State Mandate Requirements below.)**
 - Alopecia universalis
 - Anemia
 - Antenatal and neonatal thrombocytopenia
 - Antiphospholipid antibody syndrome (APS)
 - Aplasia, pure red cell
 - Asthma
 - Autoimmune neutropenia
 - Behçet's syndrome
 - Bullous Pemphigoid
 - Burns
 - Chronic fatigue syndrome
 - Clostridium induced colitis
 - Crohn's disease
 - Cutaneous polyarteritis nodosa
 - Cystic fibrosis
 - Diabetic amyotrophy
 - Encephalomyelitis - acute, disseminated
 - Epidermolysis bullosa acquisita
 - Epilepsy
 - Epstein-Barr induced cerebellar ataxia
 - Hematopoietic stem cell recipients
 - Hemolytic uremic syndrome
 - Hemophagocytic syndrome
 - Hemophilia
 - Hopkins' syndrome
 - In vitro fertilization
 - Isaac's syndrome
 - Juvenile rheumatoid arthritis
 - Leukocytoclastic vasculitis
 - Linear immunoglobulin - A disease
 - Lysinuric protein intolerance
 - Malaria
 - Multiple Myeloma
 - Myasthenia gravis
 - Myocarditis
 - Myositis
 - Neonatal jaundice
 - Neuropathy
 - Nodular pemphigoid
 - Ocular cicatricial pemphigoid
 - Otitis media
 - Paraneoplastic pemphigus
 - Paraneoplastic visual loss
 - Pemphigus foliaceus
 - Pemphigus gestationis



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- Pemphigus vulgaris
- Polymyositis
- Post transplant lymphoproliferative disorder
- Posttransfusion purpura
- Pyoderma gangrenous
- Recurrent fetal loss
- Respiratory syncytial virus
- Rheumatoid arthritis
- Stevens-Johnson syndrome
- Stiff person syndrome
- Still's disease
- Systemic lupus erythematosus (SLE)
- Systemic vasculitis
- Nonimmune thrombocytopenia
- Quinine-induced thrombocytopenia
- Refractory to platelet transfusion
- Septic thrombocytopenia
- Thrombotic thrombocytopenic purpura
- Toxic shock syndrome
- Uveitis
- Von Willebrand's syndrome
- Wegener's granulomatosis

See also:

- [Cytomegalovirus Immune Globulin Intravenous, Human \(CMV-IVIG\)](#)
- [Palivizumab](#)
- [Rho \(D\) Immune Globulins](#)
- [Subcutaneous Immune Globulin](#)

MEDICAL APPROPRIATENESS

- Intravenous immune globulin (IVIG) for the treatment of **ANY ONE** of the following is considered **medically appropriate** if the criteria are met:
 - Bacterial infections associated with neonates if treatment is adjunctive (i.e., to increase efficacy of primary treatment regimen)
 - Dermatomyositis if **ALL** of the following criteria are met:
 - Agent is used as second-line therapy (i.e., after failure of initial treatment of choice)
 - Corticosteroid therapy is **ANY ONE** of the following:
 - Contraindicated
 - Ineffective due to proven resistance
 - Guillain-Barré syndrome (GBS) if **ALL** the following criteria are met:
 - Individual is 18 years of age or older
 - Disease is acute
 - GBS diagnosis is made within the first two weeks of the illness
 - Individual requires assistance to walk due to severity of GBS impairment
 - Immune/idiopathic thrombocytopenic purpura (ITP) if a rise in platelet count is required (e.g., prior to surgery, to control excessive bleeding, to defer or avoid a splenectomy, or to prevent bleeding post-splenectomy)
 - Kawasaki disease if administered with aspirin
 - Multifocal motor neuropathy (MMN) as second-line therapy (i.e., after failure of initial treatment of choice)
 - Multiple sclerosis if **ALL** of the following criteria are met:



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- Disease is relapsing-remitting
- Treatment is second-line treatment therapy (i.e., after failure of initial treatment of choice)
- Solid organ transplant recipients if **ANY ONE** of the following criteria are met:
 - Pre-transplant, individual is at high risk for antibody-mediated rejection, (e.g., highly sensitized individuals or those receiving an ABO/blood type incompatible organ)
 - Post-transplant, for treatment of an antibody-mediated rejection
- Parvovirus B19 if **ALL** the following criteria are met:
 - Disease is chronic
 - Individual has severe anemia secondary to bone marrow suppression
- Intravenous immune globulin (IVIG) for the prevention of **ANY ONE** of the following is considered **medically appropriate** if the criteria are met:
 - Bacterial infections associated with **ANY ONE** of the following:
 - Chronic lymphocytic leukemia (CLL) if **ALL** of the following criteria are met:
 - Infections are recurrent
 - Treatment is adjunctive (i.e., to increase efficacy of primary treatment regimen)
 - Neonates if the if treatment is adjunctive (i.e., to increase efficacy of primary treatment regimen)
 - Graft-versus-host disease (GVHF) if **ALL** of the following criteria are met:
 - Treatment is adjunctive (i.e., to increase efficacy of primary treatment regimen)
 - Individual is 20 years of age or older
 - GVHF is acute
 - IVIG is administered in the first 100 days after bone marrow transplantation
 - GVHF is associated with **ANY ONE** of the following:
 - Interstitial pneumonia (e.g., infectious or idiopathic)
 - Infections (e.g., varicella-zoster virus infection, recurrent bacterial infection)

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

Tennessee State law requires coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is relative to life-threatening illnesses, such as cancer, AIDS, and coronary heart disease and recognized in one of the standard reference compendia (As defined in the statute: The United States Pharmacopoeia Drug Information, The American Medical Association Drug Evaluations, & The American Hospital Formulary Service Drug Information) or in the medical literature. This law is applicable to all fully insured members. The law is not applicable to self-funded accounts, but coverage for off-label uses may be provided based on the contractual agreement.

- Drugdex and the BlueCross BlueShield Association Medical Policy Manual recognize the use of IVIG in the treatment of:
 - Myasthenic crisis (i.e., an acute episode of respiratory muscle weakness) in patients with contraindications to plasma exchange
 - Myasthenia gravis in patients with chronic debilitating disease in spite of treatment with cholinesterase inhibitors, or complications from or failure of steroids and/or azathioprine
- The American Hospital Formulary Service Drug Information (AHFS-DI) recognizes the use of IVIG in the treatment of varicella prophylaxis in the event that varicella zoster immune globulin (VZIG) is unavailable.
- A multicenter, randomized, placebo-controlled, double-blind clinical trial recognizes the use of IVIG in the treatment of biopsy-proven autoimmune mucocutaneous blistering diseases (e.g., pemphigus vulgaris, pemphigus foliaceus).

ADDITIONAL INFORMATION

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For appropriate dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., The American Hospital Formulary Service Drug Information).

No controlled studies were found in the published literature that validate the use of intravenous immune globulins in the treatment or prevention of other conditions/diseases.

SOURCES

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EFFECTIVE DATE 12/12/2009

ID_BT



Pharmaceutical Decision Support Tree

Intravenous Immune Globulins (Trade Name[®])

1. Is the requested medication being used to treat **ANY ONE** of the following conditions?

- Alopecia universalis
- Anemia
- Antenatal and neonatal thrombocytopenia
- Antiphospholipid antibody syndrome (APS)
- Aplasia, pure red cell
- Asthma
- Autoimmune neutropenia
- Behçet's syndrome
- Bullous Pemphigoid
- Burns
- Chronic fatigue syndrome
- Clostridium induced colitis
- Crohn's disease
- Cutaneous polyarteritis nodosa
- Cystic fibrosis
- Diabetic amyotrophy
- Encephalomyelitis - acute, disseminated
- Epidermolysis bullosa acquisita
- Epilepsy
- Epstein-Barr induced cerebellar ataxia
- Hematopoietic stem cell recipients
- Hemolytic uremic syndrome
- Hemophagocytic syndrome
- Hemophilia
- Hopkins' syndrome
- In vitro fertilization
- Isaac's syndrome
- Juvenile rheumatoid arthritis
- Leukocytoclastic vasculitis
- Linear immunoglobulin - A disease
- Lysinuric protein intolerance
- Malaria
- Multiple Myeloma
- Myasthenia gravis
- Myocarditis
- Myositis
- Neonatal jaundice
- Neuropathy
- Nodular pemphigoid
- Ocular cicatricial pemphigoid
- Otitis media
- Paraneoplastic pemphigus
- Paraneoplastic visual loss
- Pemphigus foliaceus
- Pemphigus gestationis
- Pemphigus vulgaris



Pharmaceutical Decision Support Tree

- Polymyositis
- Post transplant lymphoproliferative disorder
- Posttransfusion purpura
- Pyoderma gangrenous
- Recurrent fetal loss
- Respiratory syncytial virus
- Rheumatoid arthritis
- Stevens-Johnson syndrome
- Stiff person syndrome
- Still's disease
- Systemic lupus erythematosus (SLE)
- Systemic vasculitis
- Nonimmune thrombocytopenia
- Quinine-induced thrombocytopenia
- Refractory to platelet transfusion
- Septic thrombocytopenia
- Thrombotic thrombocytopenic purpura
- Toxic shock syndrome
- Uveitis
- Von Willebrand's syndrome
- Wegener's granulomatosis

If yes, this does not meet medical necessity and/or medical appropriateness criteria

If no, go to question #2

2. Does the individual have a diagnosis of **ANY ONE** of the following?
- Chronic inflammatory demyelinating polyneuropathies (CIDP)
 - Hyperimmunoglobulinemia E syndrome
 - Lambert-Eaton myasthenic syndrome
 - Pediatric AIDS-related complex (ARC) (i.e., for serious bacterial infection prevention)
 - Pediatric human immunodeficiency virus (HIV) (i.e., for serious bacterial infection prevention)
 - Primary humoral immunodeficiency, including, but not limited to, **ANY ONE** of the following:
 - Congenital agammaglobulinemia (X-linked agammaglobulinemia)
 - Hypogammaglobulinemia
 - Common variable immunodeficiency
 - X-linked immunodeficiency with hyperimmunoglobulin M
 - Severe combined immunodeficiency (SCID)
 - Wiskott-Aldrich syndrome

If yes, this satisfies medical necessity and medical appropriateness criteria

If no, go to question # 3

3. Is the individual a neonate with bacterial infections or at risk for infections?

If yes, go to question # 4

If no, go to question #5

4. Is the treatment is adjunctive to treat or prevent bacterial infections?

If yes, this satisfies medical necessity and medical appropriateness criteria

If no, this does not meet medical necessity and/or medical appropriateness criteria



Pharmaceutical Decision Support Tree

5. Does the individual have a diagnosis of dermatomyositis?

If yes, go to question # 6

If no, go to question #8

6. Is treatment with IVIG second-line therapy (i.e., after failure of initial treatment of choice)?

If yes, go to question #7

If no, this does not meet medical necessity and/or medical appropriateness criteria

7. Is corticosteroid therapy contraindicated or ineffective due to proven resistance?

If yes, this satisfies medical necessity and medical appropriateness criteria

If no, this does not meet medical necessity and/or medical appropriateness criteria

8. Does the individual have a diagnosis of Guillain-Barré syndrome (GBS) with **ALL** of the following?

- Individual is 18 years of age or older
- Disease is acute
- GBS diagnosis is made within the first two weeks of the illness
- Individual requires assistance to walk due to severity of GBS impairment

If yes, this satisfies medical necessity and medical appropriateness criteria

If no, go to question #9

9. Does the individual have a diagnosis of immune/idiopathic thrombocytic purpura (ITP) and a rise in platelet count is required (e.g., prior to surgery, to control excessive bleeding, to defer or avoid a splenectomy, or to prevent bleeding post-splenectomy)

If yes, this satisfies medical necessity and medical appropriateness criteria

If no, go to question #10

10. Does the individual have a diagnosis of Kawasaki disease and will take aspirin with therapy if tolerated?

If yes, this satisfies medical necessity and medical appropriateness criteria

If no, go to question #11

11. Does the individual have a diagnosis of multifocal motor neuropathy and treatment is second line?

If yes, this satisfies medical necessity and medical appropriateness criteria

If no, go to question #12

12. Does the individual have a diagnosis of multiple sclerosis with **ALL** of the following?

- Disease is relapsing-remitting
- Treatment is second-line treatment therapy

If yes, this satisfies medical necessity and medical appropriateness criteria

If no, go to question #13

13. Is the individual a solid organ transplant recipient with **ANY ONE** of the following?

- Pre-transplant, individual is at high risk for antibody-mediated rejection, (e.g., highly sensitized individuals or those receiving an ABO/blood type incompatible organ)
- Post-transplant, for treatment of an antibody-mediated rejection



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of Tennessee**

Pharmaceutical Decision Support Tree

If yes, this satisfies medical necessity and medical appropriateness criteria

If no, go to question #14

14. Does the individual have a diagnosis of chronic parvovirus B19 with severe anemia secondary to bone marrow suppression?

If yes, this satisfies medical necessity and medical appropriateness criteria

If no, go to question #15

15. Is the individual at risk for bacterial infections associated with chronic lymphocytic leukemia with **ALL** of the following?

- Recurrent infections
- Treatment is adjunctive

If yes, this satisfies medical necessity and medical appropriateness criteria

If no, go to question #16

16. Is the individual at risk for graft-versus-host disease (GVHF) associated with interstitial pneumonia (infectious or idiopathic) or infections such as varicella-zoster infection or recurrent bacterial infections with **ALL** of the following:

- Treatment is adjunctive
- Individual is 20 years of age or older
- GVHF is acute
- IVIG is administered in the first 100 days after bone marrow transplantation

If yes, this satisfies medical necessity and medical appropriateness criteria

If no, this does not meet medical necessity and/or medical appropriateness criteria