



# CIGNA MEDICAL COVERAGE POLICY

The following Coverage Policy applies to all health benefit plans administered by CIGNA Companies including plans formerly administered by Great-West Healthcare, which is now a part of CIGNA.

**Subject Lymphocyte Immune Globulin,  
Anti-Thymocyte Globulin  
[Equine] (Atgam®)**

**Effective Date ..... 8/15/2011  
Next Review Date..... 7/15/2012  
Coverage Policy Number ..... 5004**

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## Hyperlink to Related Coverage Policies

### INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations. Proprietary information of CIGNA. Copyright ©2011 CIGNA

## Coverage Policy

**CIGNA covers lymphocyte immune globulin, anti-thymocyte globulin [equine] (Atgam®) as medically necessary for EITHER of the following indications:**

- management of allograft rejection in renal transplantation
- treatment of moderate-to-severe aplastic anemia in individuals who are unsuitable for bone marrow transplantation

**The dosage, frequency, site of administration, and duration of therapy are reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to Lymphocyte Immune Globulin, Anti-Thymocyte Globulin [Equine] (Atgam®) therapy.**

## FDA Approved Indications

### Renal Transplantation

Atgam sterile solution is indicated for the management of allograft rejection in renal transplant patients. When administered with conventional therapy at the time of rejection, it increases the frequency of resolution of the acute rejection episode. The drug has also been administered as an adjunct to other immunosuppressive therapy to delay the onset of the first rejection episode.

## **Aplastic Anemia**

Atgam is indicated for the treatment of moderate to severe aplastic anemia in patients who are unsuitable for bone marrow transplantation.

## **FDA Recommended Dosing**

### **Renal Allograft Recipients**

Adult renal allograft patients have received Atgam Sterile Solution at the dosage of 10 - 30 mg/kg of body weight daily. The few children studied received 5 to 25 mg/kg daily. Atgam has been used to delay the onset of the first rejection episode and at the time of the first rejection episode. Most patients who received Atgam for the treatment of acute rejection had not received it starting at the time of transplantation. Usually, Atgam is used concomitantly with azathioprine and corticosteroids, which are commonly used to suppress the immune response. Exercise caution during repeat courses of Atgam; carefully observe patients for signs of allergic reactions. To delay the onset of allograft rejection, give a fixed dose of 15 mg/kg daily for 14 days, then every other day for 14 days for a total of 21 doses in 28 days. Administer the first dose within 24 hours before or after the transplant. For treatment of rejection, the first dose can be delayed until the diagnosis of the first rejection episode. The recommended dose is 10 to 15 mg/kg daily for 14 days. Additional alternate-day therapy up to a total of 21 doses can be given.

### **Aplastic Anemia**

The recommended dosage regimen is 10 to 20 mg/kg daily for 8 to 14 days. Additional alternate-day therapy up to a total of 21 doses can be administered. Because thrombocytopenia can be associated with the administration of Atgam, patients receiving it for the treatment of aplastic anemia may need prophylactic platelet transfusions to maintain platelets at clinically acceptable levels.

## **Drug Availability**

Atgam sterile solution, containing 50 mg of horse gamma globulin/mL, is supplied as follows in 5 – 5 mL ampules.

## **General Background**

### **Pharmacology/Disease Overview**

Lymphocyte immune globulin, Anti-thymocyte globulin (ATG [equine]) is an immunoglobulin-containing immunosuppressive agent used in both the management of transplant rejection and the treatment of aplastic anemia. ATG [equine] is a sterile solution of primarily monomeric Immunoglobulin G (IgG) derived from equine sources immunized with human thymus lymphocytes.

ATG [equine] mainly exhibits immunosuppressive activity inhibiting cell-mediated immune responses such as allograft rejection and delayed hypersensitivity reactions. Antilymphocyte preparations may also have activity inhibiting humoral immune responses. The exact mechanism(s) of immunosuppressive action of ATG [equine], though not fully elucidated, may involve elimination of antigen-reactive T cells (T-lymphocytes) in peripheral blood and/or alteration of T-cell function. The effects of antilymphocyte preparations, including ATG [equine], on T-cells are variable and complex, and may depend on the condition being treated such as allograft rejection or aplastic anemia.

Prophylactic immunosuppressive therapy that includes ATG [equine] may reduce the incidence and delay the onset of initial episodes of acute rejection, but improved renal allograft survival with such therapy has not been consistently demonstrated. Further study is needed to determine the optimum dosage and duration of prophylactic ATG [equine] therapy. Many factors, including variability among individual lots of ATG [equine], the number of patients studied and type of allograft received, and low dosage regimens used in early studies have made evaluation difficult, and the effect of prophylactic ATG [equine] on long-term graft survival remains to be clearly determined. Prophylactic immunosuppressive therapy that includes ATG [equine] does not appear to increase long-term patient survival rates compared to immunosuppressive therapy that does not include ATG [equine].

## Off Label Non-Covered Indications

### Immunosuppressant for Non-Renal Transplantation

Atgam may be used as an immunosuppressant in the course of liver, bone-marrow, heart, and other organ transplants, however the safety and efficacy is not definitively established for Atgam's use for these indications. There are no transplant guidelines or recommendations available to establish an off label indication for the use of Atgam for immunosuppression in any transplant other than renal transplantation.

### Multiple Sclerosis (MS)

Data evaluating the efficacy of Atgam for the treatment of MS are dated. No new research has been published in almost 30 years and lymphocyte immune globulin is not included as a treatment option in the American Academy of Neurology (AAN) practice guidelines for MS. Therefore, its use in patients with MS is not recommended.

### Adverse Reactions

Fever and chills are the most common side effects of ATG [equine], occurring in 51% and 16% of patients, respectively. Febrile reactions will decrease in severity after the first few doses and are managed with antipyretics, antihistamines, corticosteroids, or a combination of these agents. Leukopenia and thrombocytopenia occur in 14 and 30% of patients, respectively, receiving ATG [equine] or potentially more frequently in patients with aplastic anemia. The effects are generally transient and may respond to dosage reduction without platelet transfusion. Anaphylaxis, though rare, could occur at any time during treatment. Serum sickness reactions have been reported in as many as 10% of renal allograft recipients receiving ATG [equine]; however, this may be confounded by the difficulty in diagnosing serum sickness reactions in these patients.

ATG [equine] should not be administered to patients who have had severe systemic reactions (e.g., generalized rash, tachycardia, dyspnea, hypotension, or anaphylaxis) during prior administration of ATG [equine] or any other equine gamma globulin preparation. Before the first dose of ATG [equine], patients should undergo intradermal sensitivity testing to look for a local allergic reaction. However, allergic reactions such as anaphylaxis have occurred even in patients whose skin test is negative. ATG [equine] should only be administered by physicians experienced in immunosuppressive therapy in the treatment of renal transplant or aplastic anemia patients. Additionally, ATG [equine] should only be administered to patients in facilities equipped and staffed with adequate laboratory and supportive medical resources. Immunosuppression with ATG [equine], which may be combined with other immunosuppressive therapy (e.g., corticosteroids, antimetabolites), may result in increased susceptibility to infection (e.g., with cytomegalovirus); patients receiving ATG [equine] should be closely observed for signs of leukopenia, thrombocytopenia, and/or concurrent infection. Treatment with ATG [equine] should be discontinued if any of the following occurs: symptoms of anaphylaxis, severe and unremitting thrombocytopenia in renal transplant patients, or severe and unremitting leukopenia in renal transplant patients. Use of ATG [equine] may carry a risk of transmitting infectious agents such as viruses and the Creutzfeldt-Jakob disease agent because the product is made using equine and human blood components.

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## Coding/Billing Information

**Note:** This list of codes may not be all-inclusive.

### Covered when medically necessary:

HCPCS Codes	Description
J7504	Lymphocyte immune globulin, antithymocyte globulin, equine, parenteral, 250mg

ICD-9-CM Diagnosis Codes	Description
284.01-284.9	Aplastic anemia an other bone marrow failure syndromes
996.81	Complications of transplanted kidney

V42.1	Heart replaced by transplant
V42.3	Skin replaced by transplant
V42.7	Liver replaced by transplant
V42.81	Bone-marrow replaced by transplant
V42.89	Other organs replaced by transplant

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## References

1. Drug Facts and Comparisons St. Louis, MO: Wolters Kluwer Health, Inc. 2011.
2. McEvoy GK, ed. AHFS 2011 Drug Information. Bethesda, MD: American Society of Health-Systems Pharmacists, Inc. 2011.
3. Pfizer. Lymphocyte immune globulin, anti-thymocyte globulin [equine] sterile solution (Atgam<sup>®</sup>) injection package insert. NY, NY: Pfizer, November 2005.

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## Policy History

Pre-Merger Organizations	Last Review Date	Policy Number	Title
CIGNA HealthCare Great-West Healthcare	7/15/2008	5004	Lymphocyte Immune Globulin, Anti-Thymocyte Globulin [Equine] (Atgam <sup>®</sup> )

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