

Clinical Policy: Antithymocyte Globulin (Atgam, Thymoglobulin)

Reference Number: ERX.SPA.286

Effective Date: 12.01.18

Last Review Date: 11.21

Line of Business: Commercial, Medicaid

[Revision Log](#)

See **Important Reminder** at the end of this policy for important regulatory and legal information.

Description

Antithymocyte globulin (Thymoglobulin[®], Atgam[®]) is an immunoglobulin G.

FDA Approved Indication(s)

Atgam is indicated for:

- The management of allograft rejection in renal transplant patients; when administered with conventional therapy at the time of rejection, Atgam increases the frequency of resolution of the acute rejection episode
- The treatment of moderate-to-severe aplastic anemia in patients unsuitable for bone marrow transplantation

Limitation(s) of use: The usefulness of Atgam has not been demonstrated in patients with aplastic anemia who are suitable candidates for bone marrow transplantation or in patients with aplastic anemia secondary to neoplastic disease, storage disease, myelofibrosis, Fanconi's syndrome, or in patients known to have been exposed to myelotoxic agents or radiation.

Thymoglobulin is indicated for the prophylaxis and treatment of acute rejection in patients receiving a kidney transplant. Thymoglobulin is used in conjunction with concomitant immunosuppression.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions[™] that Atgam and Thymoglobulin are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Kidney Transplant Rejection (must meet all):

1. Member has received or is scheduled for a kidney transplant;
2. If request is for prophylaxis of acute rejection, request is for Thymoglobulin;
3. Prescribed by or in consultation with a nephrologist, transplant specialist, or hematologist/oncologist;
4. Age \geq 18 years;
5. Dose does not exceed one of the following (a or b):
 - a. For Atgam: 15 mg/kg per day;
 - b. For Thymoglobulin: 1.5 mg/kg per day.

Approval duration:

7 days for Thymoglobulin for prophylaxis of acute rejection (7 doses)

14 days for Thymoglobulin for treatment of acute rejection (14 doses)

Up to 42 days for Atgam (21 doses)

B. Aplastic Anemia (must meet all):

1. Diagnosis of moderate to severe aplastic anemia;

2. Request is for Atgam;
3. Prescribed by or in consultation with a hematologist;
4. Age \geq 18 years;
5. Prescribed in combination with cyclosporine;
6. Dose does not exceed 20 mg/kg per day.

Approval duration: Up to 42 days (21 doses)

C. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all):

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed (a or b):
 - a. For Atgam (i or ii):
 - i. For treatment of acute rejection: 15 mg/kg per day;
 - ii. For aplastic anemia: 20 mg/kg per day;
 - b. For Thymoglobulin for treatment or prophylaxis of acute rejection: 1.5 mg/kg per day.

Approval duration: Up to a total treatment duration of:

7 days for Thymoglobulin for prophylaxis of acute rejection (7 doses)

14 days for Thymoglobulin for treatment of acute rejection (14 doses)

42 days for Atgam (21 doses)

B. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.**

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria.

The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
cyclosporine	Aplastic Anemia Adults: 12 mg/kg PO QD Children: 15 mg/kg PO QD	See dosing regimen

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
 - Atgam: patients with a history of a systemic reaction (e.g., anaphylactic reaction) during prior administration of Atgam or any other equine gamma globulin preparation
 - Thymoglobulin:
 - Patients with history of allergy or anaphylactic reaction to rabbit proteins or to any product excipients
 - Patients who have active acute or chronic infections that contraindicate any additional immunosuppression
- Boxed warning(s):
 - Atgam: anaphylaxis
 - Thymoglobulin: immunosuppression

Appendix D: General Information

- The current standard first-line treatment for aplastic anemia is equine antithymocyte globulin (Atgam) combined with cyclosporine (off-label use).

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Antithymocyte globulin (Atgam)	Aplastic anemia	10 to 20 mg/kg IV QD for 8 to 14 days. Additional alternate-day therapy up to a total of 21 doses may be given	20 mg/kg/dose
Antithymocyte globulin (Atgam)	Treatment of acute renal transplant rejection	10 to 15 mg/kg IV QD for 14 days. Additional alternate-day therapy up to a total of 21 doses may be given.	15 mg/kg/dose
Antithymocyte globulin (Thymoglobulin)	Prophylaxis of acute renal transplant rejection	1.5 mg/kg IV QD for 4 to 7 days	1.5 mg/kg/dose
Antithymocyte globulin (Thymoglobulin)	Treatment of acute renal transplant rejection	1.5 mg/kg IV QD for 7 to 14 days	1.5 mg/kg/dose

VI. Product Availability

Drug Name	Availability
Antithymocyte globulin (Thymoglobulin)	Vial, powder for solution: 25 mg
Antithymocyte globulin (Atgam)	Ampule: 250 mg/5 mL

VII. References

1. Thymoglobulin Prescribing Information. Cambridge, MA: Genzyme Corporation; April 2020. Available at <http://products.sanofi.us/Thymoglobulin/Thymoglobulin.pdf>. Accessed August 19, 2021.
2. Atgam Prescribing Information. New York, NY: Pfizer; August 2021. Available at: <http://labeling.pfizer.com/ShowLabeling.aspx?id=525>. Accessed August 19, 2021.
3. Kidney Disease Improving Global Outcomes. KDIGO clinical practice guideline for the care of kidney transplant recipients. American Journal of Transplantation 2009; 9 (Suppl 3): Si-S155. doi: 10.1111/j.1600-6143.2009.02834.x
4. Bia M, Adey DB, Bloon RD, Chan L, Kulkarni S, and Tomlanovich S. KDOQI US Commentary on the 2009 KDIGO clinical practice guideline for the care of kidney transplant recipients. Am J Kidneys Dis 2010;56:189-218.
5. Schinstock CA, Mannon RB, Budde K, et al. Recommended treatment for antibody-mediated rejection after kidney transplantation: the 2019 expert consensus from the Transplantation Society Working Group. Transplantation May 2020;104(5):911-22.
6. Cooper JE. Evaluation and treatment of acute kidney rejection in kidney allografts. CJASN March 2020;15:430-8.

7. Killick SB, Bown N, Cavenagh J, et al. Guidelines for the diagnosis and management of adult aplastic anaemia. Br J Haematol. 2016; 172:187-207.
8. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2019. Available at: <http://www.clinicalpharmacology-ip.com/>.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	09.04.18	11.18
4Q 2019 annual review: no significant changes; added hematologist/ oncologist prescriber option; revised initial approval duration for Atgam to allow “up to” 42 days since labeling recommends a minimum of 14 days of therapy, with the option to go to alternate-day therapy up to 21 doses; corrected dosing in continued therapy for Atgam from “prophylaxis” to “treatment”; added clarification that Thymoglobulin dosing in continued therapy applies to both prophylaxis and treatment of acute rejection; references reviewed and updated.	08.13.19	11.19
4Q 2020 annual review: no significant changes; for aplastic anemia, clarified that only FDA-approved moderate-to-severe disease is covered; references reviewed and updated.	07.20.20	11.20
4Q 2021 annual review: no significant changes; references reviewed and updated.	08.19.21	11.21

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

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