

Clinical Policy: Antithymocyte Globulin (Thymoglobulin, Atgam)

Reference Number: HIM.PA.16

Effective Date: 09.04.18

Last Review Date: 11.19

Line of Business: HIM

[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.

It is the policy of health plans affiliated with Centene Corporation[®] 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 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 the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): HIM.PHAR.21 for health insurance marketplace.

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit 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 Centene benefit and documentation supports positive response to therapy.

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

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): HIM.PHAR.21 for health insurance marketplace.

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 policies – HIM.PHAR.21 for health insurance marketplace 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 for all relevant lines of business 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 Thymoglobulin 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

Drug Name	Indication	Dosing Regimen	Maximum 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: 50 mg/mL

VII. References

1. Thymoglobulin Prescribing Information. West Chester, PA: Therakos, Inc.; September 2018. Available at: <https://www.thymoglobulin.com>. Accessed August 13, 2019.
2. Atgam Prescribing Information. New York, NY: Pfizer; May 2018. Available at: <http://labeling.pfizer.com/ShowLabeling.aspx?id=525>. Accessed August 13, 2019.
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): S1-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. 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.
6. 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; 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

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

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Note:

For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the non-formulary policy; HIM.PA.103.

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