

Clinical Policy: Antithymocyte Globulin (Atgam, Thymoglobulin)

Reference Number: PA.CP.PHAR.506

Effective Date: 10/2020

Last Review Date: 10/2024

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 PA Health & Wellness[®] 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. Prescribed in combination with conventional therapy for transplant rejection (*see Appendix D*);
6. 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. Prescribed in combination with cyclosporine;
5. Dose does not exceed 40 mg/kg per day.

Approval duration: Up to 42 days (21 doses)

C. NCCN Recommended Uses (off-label) (must meet all):

1. One of the following (a-e):
 - a. Immunotherapy-related cardiovascular toxicity;
 - b. CAR T-cell-related toxicity;
 - c. Acute graft-versus-host disease (GVHD);
 - d. Myelodysplastic syndrome;
 - e. Conditioning as part of a reduced-intensity regimen in combination with cladribine and busulfan;
2. Prescribed by or in consultation with an oncologist;
3. Age \geq 18 years;
4. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 1 month

D. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. Kidney Transplant Rejection and Aplastic Anemia (must meet all):

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy;
3. For Thymoglobulin for prophylaxis of acute rejection, member has not received more than both of the following (a and b):
 - a. 7 days of total treatment duration;
 - b. 7 doses of Thymoglobulin;
4. For Thymoglobulin for treatment of acute rejection, member has not received more than both of the following (a and b):
 - a. 14 days of total treatment duration;
 - b. 14 doses of Thymoglobulin;
5. For Atgam, member has not received more than both of the following (a and b):
 - a. 42 days of total treatment duration;

- b. 21 doses of Atgam;
- 6. 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: 40 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. NCCN Recommended Uses (off-label)

- 1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
- 2. Member is responding positively to therapy;
- 3. If request is for a dose increase, new dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 1 month

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

- 1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.

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

- 2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

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 – PA.CP.PMN.53

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration

GVHD: graft-versus-host disease

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: 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).
Conventional therapy for transplant rejection include: calcineurin inhibitors (tacrolimus, cyclosporine), antimetabolite (mycophenolate, azathioprine), corticosteroid (prednisone)

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
	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; March 2023. Available at: <http://products.sanofi.us/Thymoglobulin/Thymoglobulin.pdf>. Accessed July 16, 2024.
2. Atgam Prescribing Information. New York, NY: Pfizer; September 2023. Available at: <http://labeling.pfizer.com/ShowLabeling.aspx?id=525>. Accessed July 16, 2024.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at https://www.nccn.org/professionals/drug_compendium/content/. Accessed August 23, 2024.
4. 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
5. 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.
6. 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.
7. Cooper JE. Evaluation and treatment of acute kidney rejection in kidney allografts. CJASN March 2020;15:430-8.
8. Nelson J, Alvey N, Bowman L, et al. Consensus recommendation for use of maintenance immunosuppression in solid organ transplantation: Endorsed by the American College of Clinical Pharmacy, American Society of Transplantation, and the International Society for Heart and Lung Transplantation. Pharmacotherapy 2022;42:599-633.
9. 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.
10. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2019. Available at: <http://www.clinicalpharmacology-ip.com/>.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J7504	Lymphocyte immune globulin, antithymocyte globulin, equine, parenteral, 250 mg
J7511	Lymphocyte immune globulin, antithymocyte globulin, rabbit, parenteral, 25 mg

Reviews, Revisions, and Approvals	Date
Policy created	10/2020

Reviews, Revisions, and Approvals	Date
4Q 2021 annual review: no significant changes; references reviewed and updated.	10/2021
4Q 2022 annual review: no significant changes; references reviewed and updated.	10/2022
4Q 2023 annual review: for transplant rejection added criterion prescribed in combination with conventional therapy per PI with examples added in Appendix D; continuation of care applied to transplant-related indications in continued therapy section; clarified total duration and doses of Thymoglobulin and Atgam therapy in continued therapy section (7days/doses for Thymoglobulin for prophylaxis of acute rejection, 14 days/doses for Thymoglobulin for treatment of acute treatment, and 42 days/21 doses for Atgam); references reviewed and updated	10/2023
4Q 2024 annual review: added NCCN supported recommended uses (off-label) section to include immunotherapy-related cardiovascular toxicity, CAR t-cell-related toxicity; GVHD, and myelodysplastic syndrome, Conditioning as part of a reduced-intensity regimen in combination with cladribine and busulfan; references reviewed and updated.	10/2024