Clinical Policy: Antithymocyte Globulin (Atgam, Thymoglobulin)

Reference Number: CP.PHAR.506
Effective Date: 12.01.20
Last Review Date: 11.26
Line of Business: Commercial, HIM/ICHRA, Medicaid

Coding Implications
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 adult and pediatric patients receiving a kidney transplant 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. For Atgam: Age ≥ 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, all of the following (i, ii, or iii):
      i. 15 mg/kg per day;
      ii. 42 days of total treatment duration;
      iii. 21 doses of Atgam;
   b. For Thymoglobulin, all of the following (i, ii, and iii):
      i. 1.5 mg/kg per day;
      ii. For prophylaxis of acute rejection, both of the following (1 and 2):
         1) 7 days of total treatment duration;
         2) 7 doses of Thymoglobulin;
      iii. For treatment of acute rejection, both of the following (1 and 2):
         1) 14 days of total treatment duration;
         2) 14 doses of Thymoglobulin.

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 ≥ 18 years;
5. Prescribed in combination with cyclosporine;
6. Dose does not exceed all of the following (a, b, or c):
   a. 20 mg/kg per day;
   b. 42 days of total treatment duration;
   c. 21 doses of Atgam.

Approval duration: Up to 42 days (21 doses)

C. NCCN Recommended Uses (off-label) (must meet all):
1. Request is for one of the following (a, b, or c):
   a. Immune checkpoint inhibitor-related toxicity that is one of the following (i, ii, or iii; *see Appendix E*):
      i. Myocarditis;
      ii. Hepatobiliary toxicity;
      iii. Aplastic anemia;
   b. CAR T-cell-related cytokine release syndrome (CRS) that is Grade 4*;
      **Grade 4 CRS: fever with hypotension requiring multiple vasopressors, excluding vasopressin, and/or hypoxia requiring positive pressure*
   c. Request is for Atgam, and one of the following indications (i, ii, iii, or iv):
      i. Graft-verus-host disease (GVHD) prophylaxis after hematopoietic stem cell transplant (HSCT);
      ii. Acute GVHD that is steroid-refractory;
      iii. Conditioning for HSCT;
      iv. Myelodysplastic syndrome that is lower-risk (IPSS-R [very low, low, intermediate]);

2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. For immune checkpoint inhibitor-related hepatobiliary toxicity, one of the following (a, b, c, or d):
   a. G2 elevated ALT/AST, and liver enzymes suggest worsening or no improvement after 3-7 days of prednisone;
   b. G3 or G4 elevated ALT/AST, and no improvement after 1-2 days of prednisone/methylprednisolone;
   c. G2 elevated alkaline phosphatase (predominant), and alkaline phosphatase worsens or does not improve within 3 days after initiating corticosteroids;
   d. G3 or G4 elevated alkaline phosphatase (predominant), and no improvement after 1-2 days of prednisone/methylprednisolone and ursodiol;
5. For CAR T-cell-related CRS, member is refractory to high-dose corticosteroids and anti-IL-6 therapy (e.g., Actemra®);
6. For aplastic anemia, both of the following (a and b):
   a. Severe or very severe;
   b. Not responsive to corticosteroids after 7 days;
7. 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*).*

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration: 1 month

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Member meets one of the following (a, b, or c):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;

   b. Documentation supports that member is currently receiving Atgam or Thymoglobulin for kidney transplant rejection and has received this medication for at least 30 days;
   c. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
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: 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. NCCN Recommended Uses (off-label)

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Atgam or Thymoglobulin for a covered indication that has received this medication for at least 30 days;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
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*).*
   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 1 month

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid.

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 – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ALT: alanine aminotransferase
AST: aspartate aminotransferase
CRS: cytokine release syndrome
FDA: Food and Drug Administration
GVHD: graft-versus-host disease
HSCT: hematopoietic stem cell transplant
IPSS-R: Revised International Prognostic Scoring System
ULN: upper limit of normal

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: 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)
- Myelodysplastic syndrome prognostic scoring system online calculator for IPSS-R: https://qxmd.com/calculate/calculator_109/mds-revised-international-prognostic-scoringsystem-ipss-r

Appendix E: Immune Checkpoint Inhibitor-Related Toxicity

- Immune checkpoint inhibitors comprise a class of agents that target immune cell checkpoints, such as programmed cell death-1 (PD-1; e.g., Opdivo®, Keytruda®) and PD-1 ligand (PD-L1; e.g., Tecentriq®, Bavencio®, Imfinzi®), as well as cytotoxic T-lymphocyte–associated antigen 4 (e.g., Yervoy®, Imjudo®).
- NCCN grading of hepatobiliary toxicity by elevated alanine aminotransferase (ALT)/ aspartate aminotransferase (AST)
  - G1: ALT/AST elevation of < 3x upper limit of normal (ULN)
  - G2: ALT/AST elevation of 3-5x ULN
  - G3: ALT/AST elevation of > 5 to 20x ULN
  - G4: ALT/AST elevation of > 20x ULN
- NCCN grading of hepatobiliary toxicity by elevated alkaline phosphatase (predominant) with or without ALT/AST elevation
  - G1: alkaline phosphatase elevation of < 2.5x ULN (or baseline)
  - G2: alkaline phosphatase elevation of 2.5-5x ULN (or baseline)
  - G3: alkaline phosphatase elevation of > 5 to 20x ULN (or baseline)
  - G4: alkaline phosphatase elevation of > 20x ULN (or baseline)

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	20 mg/kg/dose

Drug Name	Indication	Dosing Regimen	Maximum Dose
		a total of 21 doses may be given	
	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 (Thymogobulin)	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; June 2026. Available at: http://products.sanofi.us/Thymoglobulin/Thymoglobulin.pdf. Accessed July 10, 2026.
2. Atgam Prescribing Information. New York, NY: Pfizer; September 2023. Available at: http://labeling.pfizer.com/ShowLabeling.aspx?id=525. Accessed July 10, 2026.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at https://www.nccn.org/professionals/drug_compendium/content/. Accessed July 21, 2026.
4. National Comprehensive Cancer Network. Management of Immune Checkpoint Inhibitor-Related Toxicities Version 1.2026. Available at https://www.nccn.org/professionals/physician_gls/pdf/ici_tox.pdf. Accessed July 21, 2026.
5. National Comprehensive Cancer Network. Hematopoietic Cell Transplantation Version 3.2026. Available at https://www.nccn.org/professionals/physician_gls/pdf/hct.pdf. Accessed August 24, 2026.
6. National Comprehensive Cancer Network. Myelodysplastic Syndromes Version 3.2026. Available at https://www.nccn.org/professionals/physician_gls/pdf/mds.pdf. Accessed August 24, 2026.
7. 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
8. 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.
9. 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.

10. Cooper JE. Evaluation and treatment of acute kidney rejection in kidney allografts. CJASN March 2020;15:430-8.
11. 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.
12. 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.
13. Clinical Pharmacology [database online]. Philadelphia, PA: Elsevier. Updated periodically. Available at: http://www.clinicalkey.com/pharmacology.

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	P&T Approval Date
4Q 2022 annual review: no significant changes; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section.	08.26.22	11.22
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.	07.06.23	11.23
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; references reviewed and updated.	07.16.24	11.24
4Q 2025 annual review: no significant changes; references reviewed and updated.	07.16.25	11.25
RT4: updated Thymoglobulin indication to include pediatric and adult patients; per NCCN: updated “immunotherapy-related” to “immune checkpoint inhibitor-related” toxicity, specified cardiovascular toxicity as myocarditis, added indications of	02.16.26	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
immune checkpoint inhibitor-related hepatobiliary toxicity and aplastic anemia, specified that myelodysplastic syndrome and acute GVHD are specific to Atgam requests, specified that acute GVHD is steroid-refractory, specified that myelodysplastic syndrome is lower-risk, added conditioning regimen as an option for Atgam use, and clarified that CAR T-cell-related toxicity is specific to grade 4 CRS.		
4Q 2026 annual review: added ICHRA line of business; for Atgam, added option to be prescribed for GVHD prophylaxis per NCCN; references reviewed and updated.	07.10.26	11.26

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.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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