Clinical Policy: Antithymocyte Globulin (Atgam, Thymoglobulin)

Reference Number: LA.PHAR.506
Effective Date: 10.25.23
Last Review Date: 04.22.24 ~~07.24.23~~ Coding Implications
Line of Business: Medicaid Revision Log

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

Please note: This policy is for medical benefit

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 Louisiana Healthcare Connections® 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 ≥ 18 years;

5. Prescribed in combination with conventional therapy for transplant rejection (*see Appendix D*);
~~5.~~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. Age ≥ 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 (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 LA.PMN.255
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: LA.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Louisiana Healthcare Connections 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;

~~**A. All Indications in Section I** (must meet all)**:**~~
~~1. Currently receiving medication via Louisiana Healthcare Connections benefit or member has previously met initial approval criteria;~~
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;

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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;

~~3.~~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)

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B. 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 LA.PMN.255
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: LA.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 – LA.PMN.53 for Medicaid, 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 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 (Thymogobulin)	Prophylaxis of acute renal transplant rejection	1.5 mg/kg IV QD for 4 to 7 days	1.5 mg/kg/dose

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Drug Name	Indication	Dosing Regimen	Maximum Dose
~~Antithymocyte globulin (Thymogobulin)~~	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.~~http://products.sanofi.us/Thymoglobulin/Thymoglobulin.pdf. Accessed July ~~24~~6, 2023.
2. Atgam Prescribing Information. New York, NY: Pfizer; May 2023. Available at: ~~http://labeling.pfizer.com/ShowLabeling.aspx?id=525.~~http://labeling.pfizer.com/ShowLabeling.aspx?id=525. Accessed July ~~24~~6, 2023.
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. 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.
~~7.~~8. 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.~~9. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2019. ~~Available at: http://www.clinicalpharmacology-ip.com/.~~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	LDH Approval Date
Policy created	05.01.23	09.25.23
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.	04.22.24	

Important Reminder

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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. LHCC 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.

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 LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. 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. LHCC 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 LHCC has no control or right of control. Providers are not agents or employees of LHCC.

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