Clinical Policy: Antithymocyte Globulin (Thymoglobulin, Atgam)

Reference Number: ERX.SPA.286
Effective Date: 09.04.18
Last Review Date: 11.18

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 anaplastic anemia in patients unsuitable for bone marrow transplantation

Limitation(s) of use: The usefulness of Atgam has not been demonstrated in patients with anaplastic 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 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, or transplant specialist;
      4. Age ≥ 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)
   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 ≥ 18 years;
      5. Prescribed in combination with cyclosporine;
      6. Dose does not exceed 20 mg/kg per day.
   Approval duration: 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 prophylaxis of acute rejection: 15 mg/kg per day;
            ii. For aplastic anemia: 20 mg/kg per day;
         b. For Thymoglobulin: 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.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>cyclosporine</td>
<td>Aplastic Anemia</td>
<td>See dosing regimen</td>
</tr>
<tr>
<td></td>
<td>Adults: 12 mg/kg PO QD</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Children: 15 mg/kg PO QD</td>
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</tbody>
</table>

   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):
     o 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
     o 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

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antithymocyte globulin (Thymogobulin)</td>
<td>Prophylaxis of acute renal transplant rejection</td>
<td>1.5 mg/kg IV QD for 4 to 7 days</td>
<td>1.5 mg/kg/dose</td>
</tr>
<tr>
<td>Antithymocyte globulin (Thymogobulin)</td>
<td>Treatment of acute renal transplant rejection</td>
<td>1.5 mg/kg IV QD for 7 to 14 days</td>
<td>1.5 mg/kg/dose</td>
</tr>
</tbody>
</table>

### VI. Product Availability

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Availability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antithymocyte globulin (Thymogobulin)</td>
<td>Vial, powder for solution: 25 mg</td>
</tr>
<tr>
<td>Antithymocyte globulin (Atgam)</td>
<td>Ampule: 50 mg/mL</td>
</tr>
</tbody>
</table>

### VII. References

medical judgment in providing the most appropriate care, and are solely responsible for the medical
advice and treatment of members.

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