Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Antithymocyte Globulin Equine, (Atgam)	MP-RX-FP-08-24	☒ MMM MA ☐ MMM Multihealth

Service Category

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Part B Drugs

Service Description

This document addresses the use of Antithymocyte Globulin Equine, (Atgam) , a drug approved by the Food and Drug Administration (FDA) for the treatment of management of allograft rejection in renal transplant patients and for the treatment of moderate to severe aplastic anemia in patients unsuitable for bone marrow transplantation.

Background Information

ATGAM Sterile Solution contains lymphocyte immune globulin, anti-thymocyte globulin [equine]. It is the purified, concentrated, and sterile gamma globulin, primarily monomeric IgG, from hyperimmune serum of horses immunized with human thymus lymphocytes. ATGAM is a transparent to slightly opalescent aqueous protein solution. It may appear colorless to faintly pink or faintly brown and is nearly odorless. It may develop a slight granular or flaky deposit.

ATGAM is composed of antibodies that bind a wide variety of proteins on the surface of lymphocytes. In addition, ATGAM binds to granulocytes, platelets, bone marrow cells, and other cell types. The mechanism of ATGAM-induced immunosuppression has not been determined. Published data indicate that the primary mechanism is the depletion of circulating lymphocytes, with greatest effect on T lymphocytes. Lymphocyte depletion may be caused by complement dependent lysis and/or activation-induced apoptosis. In addition, immunosuppression may be mediated by the binding of antibodies to lymphocytes which results in partial activation and induction of T lymphocyte anergy.

The mechanism of ATGAM therapy for aplastic anemia is attributed to its immunosuppressive actions. In addition, ATGAM directly stimulates the growth of hematopoietic stem cells and release of hematopoietic growth factors such as interleukin-3 and granulocyte/macrophage colony stimulating factor.

Approved Indications

A. Renal Allograft Rejection
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.

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B. Aplastic Anemia
ATGAM is indicated for the treatment of moderate to severe aplastic anemia in patients unsuitable for bone marrow transplantation.

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.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS	Description
J7504	Antithymocyte globulin equine, parenteral, 250 mg

ICD-10	Description
T86.11	Kidney transplant rejection
D61.9	Aplastic anemia

Medical Necessity Guidelines

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Antithymocyte Globulin Equine, (Atgam)

A. Criteria For Initial Approval

1.Allograft Rejection in Solid Organ Transplant. Approve for 1 month if the patient meets the following criteria (A and B): A) Patient meets one of the following (i or ii): i. Atgam is used for induction therapy, prior to, at the time of, or immediately following transplantation; OR ii. Atgam is used for the treatment of acute rejection. Dosing. Approve the following dosing regimen (A and B): A) Up to 15 mg/kg administered intravenously daily for up to 14 days; AND B) Up to seven additional doses can be administered intravenously every other day for a maximum total of 21 doses in 28 days.

2. Aplastic Anemia. Approve for 1 month if the patient meets the following criteria (A and B): A) Patient has moderate to severe disease; AND B) Patient is unsuitable for bone marrow transplantation. Dosing. Approve the following dosing regimen (A and B): A) Up to 20 mg/kg administered intravenously daily for up to 14 days; AND B) Additional alternate-day therapy up to a total of 21 doses may be given.

Other Uses with Supportive Evidence:

3. Allogeneic Hematopoietic Stem Cell Transplantation. Approve for 1 month if the patient meets the following criteria: Atgam is used as part of a conditioning regimen beginning prior to allogeneic hematopoietic stem cell transplantation. Dosing. Approve the following dosing regimens (A and B): A) Up to 40 mg/kg administered intravenously daily as a single dose, or divided and given twice daily; AND B) Atgam is given for up to 4 days.

4. Graft-Versus-Host Disease. Approve for 1 month if the patient meets the following criteria (A and B): A) Patient has acute disease; AND B) Patient's disease is refractory or resistant to corticosteroid therapy. Dosing. Approve the following dosing regimens (A and B): A) Up to 40 mg/kg/day administered intravenously; AND B) Up to 10 doses can be administered in a course of therapy.

5. Immune Checkpoint Inhibitor-Related Toxicities. Approve for 1 month if the patient meets the following criteria (A, B and C): A) Patient has received at least one immune checkpoint inhibitor; AND Note: Immune checkpoint inhibitors include Opdivo (nivolumab intravenous infusion), Keytruda (pembrolizumab intravenous infusion), Tecentriq (atezolizumab intravenous infusion), Bavencio (avelumab intravenous infusion), Imfinzi (durvalumab intravenous infusion), Yervoy (ipilimumab intravenous infusion). B) Patient has life-threatening myocarditis, pericarditis, arrhythmias, or impaired ventricular function, according to the prescriber; AND C) Patient has not improved within 24 hours of starting pulse-dose methylprednisolone. Dosing. Approve the following dosing regimens (A and B): A) Up

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to 15 mg/kg administered intravenously daily for 14 days; AND B) Up to seven additional doses can be administered intravenously every other day for a maximum total of 21 doses in 28 days.

6. Myelodysplastic Syndrome. Approve for 1 month if the patient meets the following criteria (A and B): A) Patient has lower risk disease; AND Note: Lower risk disease is defined as International Prognostic Scoring System (IPSS) risk of low or intermediate-1; IPSS-Revised (IPSS-R) risk of very low, low, or intermediate; World Health Organization Prognostic Scoring System (WPSS) risk of very low, low, or intermediate. B) Patient has one of the following according to the prescriber (i, ii, iii, or iv): i. Clinically relevant thrombocytopenia; OR ii. Clinically relevant neutropenia; OR iii. Increased marrow blasts; OR iv. Symptomatic anemia. Dosing. Approve up to 40 mg/kg/day administered intravenously for up to 4 days.

B. Authorization Duration

i. Approval

a. Initial Approval Duration: 1 month

For details regarding National Coverage Determination (NCD-260.7) including service description, indications and limitations of coverage, please visit NCD - Lymphocyte Immune Globulin, Anti-Thymocyte Globulin (Equine) (260.7) (cms.gov)

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Reference Information

1. DailyMed - atgam- equine thymocyte immune globulin injection, solution. U.S. National Library of Medicine. Accessed July 11, 2023. Available at https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=bd545ba1-2366-4df1-bd67-10dfd7632b54.
2. Micromedex products: Please Login. Accessed July 11, 2023. Available at https://www.micromedexsolutions.com/micromedex2/librarian/CS/F4509B/ND_PR/evidencexpert/ND_P/evidencexpert/DUPLICATIONSHIELDSYNC/E3DE8C/ND_PG/evidencexpert/ND_B/evidencexpert/ND_AppProduct/evidencexpert/ND_T/evidencexpert/PFActionId/evidencexpert.GoToDashboard?docId=928697&contentSetId=100&title=Antithymocyte%2BGlobulin%2BEquine&servicesTitle=Antithymocyte%2BGlobulin%2BEquine&brandName=Atgam&UserMdxSearchTerm=atgam&=null#.
3. National Coverage Determination (NCD). Manual Section Number: 260.7.(1966) Title: Lymphocyte Immune Globulin, Anti-Thymocyte Globulin (Equine). Available at NCD - Lymphocyte Immune Globulin, Anti-Thymocyte Globulin (Equine) (260.7) (cms.gov)

Policy History

Revision Type	Summary of Changes	P&T Approval Date	MPCC Approval Date
Policy Inception	Policy reviewed and approved by P&T Committee.	10/30/2023	11/30/2023

Rev. 9/27/2023