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.

Other Uses:
NCCN has the following uses of Atgam listed as 2A recommendations:

- Graft-vs-Host Disease: According to the NCCN Hematopoietic Cell Transplantation Clinical Practice Guidelines (version 2.2024 – August 30, 2024), ATG is recommended as an adjunct to corticosteroids for managing acute steroid-refractory graft-vs-host disease.
- Immunotherapy-Related Cardiovascular Toxicity**:** The NCCN Guidelines for the Management of Immunotherapy-Related Toxicities (version 2.2024 –October 25, 2024).) recommend Atgam as an

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additional therapy for life-threatening cardiac immune-related adverse events if no improvement is observed within 24 hours of initiating pulse-dose methylprednisolone. Atgam is also an option for patients with elevated liver transaminases that worsen or fail to improve with corticosteroids, such as prednisone or methylprednisolone. Furthermore, Atgam may be used for severe cytokine release syndrome (CRS) after CAR T-cell therapy in patients unresponsive to high-dose steroids and tocilizumab. In these cases, anakinra is the preferred first-line option, while other agents like siltuximab, ruxolitinib, cyclophosphamide, IVIG, ATG, intrathecal chemotherapy, or extracorporeal cytokine adsorption with continuous renal replacement therapy (CRRT) may also be considered, though evidence for these therapies remains limited.

- Myelodysplastic Syndrome: The NCCN Clinical Practice Guidelines (version 1.2025 – November 15, 2024) include Atgam as a treatment option for managing lower-risk disease. Treatment with Atgam, either alone or in combination with cyclosporine and/or Promacta® (eltrombopag), is recommended for select patients experiencing clinically relevant thrombocytopenia, neutropenia, or symptomatic anemia.

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.

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

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ICD-10	Description
T86.11	Kidney Transplant Rejection
Z94.81	Bone marrow transplant status
D61.9	Aplastic anemia
Z94.89	Other transplanted organ and tissue status
Z94.9	Transplanted organ and tissue status, unspecified
I30.8	Other forms of acute pericarditis
I30.9	Acute pericarditis, unspecified
I40.8	Other acute myocarditis
I40.9	I40.9
K71.1-K71.11	Toxic Liver Disease
K71.0	Toxic liver disease with cholestasis
K71.50	Toxic liver disease with chronic active hepatitis without ascites
K71.51	Toxic liver disease with chronic active hepatitis with ascites
R74.01	Elevation of levels of liver transaminase levels
T80.82XA	Complication of immune effector cellular therapy, initial encounter
T80.82XS	Complication of immune effector cellular therapy, sequela
T80.89XA	Other complications following infusion, transfusion and therapeutic injection, initial encounter
D89.834	Cytokine release syndrome, grade 4
D89.839	Cytokine release syndrome, grade unspecified
C93.10	Chronic myelomonocytic leukemia not having achieved remission
D46.0	Refractory anemia without ring sideroblasts, so stated
D46.1	Refractory anemia with ring sideroblasts
D46.20	Refractory anemia with excess of blasts, unspecified
D46.21	Refractory anemia with excess of blasts 1
D46.4	Refractory anemia, unspecified
D46.9	Myelodysplastic syndrome, unspecified
D46.A	Myelodysplastic syndromes
D46.B	Refractory cytopenia with multilineage dysplasia and ring sideroblasts
D46.Z	Other myelodysplastic syndromes
D89.810	Acute graft-versus-host disease
D89.812	Acute on chronic graft-versus-host disease
D89.813	Graft-versus-host disease, unspecified

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 (*Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met **all** approval criteria.)*

i. For the management of Allograft Rejection in Solid Organ Transplant; **AND**
   a. Atgam is used for induction therapy, prior to, at the time of, or immediately following transplantation; **OR**
   b. Atgam is used for the treatment of acute rejection.

OR

ii. For the management of Aplastic Anemia; **AND**
   a. Individual has moderate to severe disease; **AND**
   b. Individual is unsuitable for bone marrow transplantation.

OR

iii. For Allogeneic Hematopoietic Stem Cell Transplantation (NCCN 2A); **AND**
   a. Atgam is used as part of a conditioning regimen beginning prior to allogeneic hematopoietic stem cell transplantation; **AND**
   b. Atgam is being used in combination with cladribine and busulfan; **AND**
   c. Atgam will be used in a compendia (NCCN) recommended regimen.

OR

iv. Graft-Versus-Host Disease (NCCN 2A); **AND**
   a. Individual has acute disease; **AND**
   b. Individual's disease is refractory or resistant to corticosteroid therapy; **AND**
   c. Atgam will be used as additional therapy in conjunction with systemic corticosteroids; **AND**
   d. Atgam will be used in a compendia (NCCN) recommended regimen.

OR

v. Immune Checkpoint Inhibitor-Related Toxicities (immunotherapy-related myocarditis) (NCCN 2A); **AND**
   a. Individual has received at least one immune checkpoint inhibitor. 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); **AND**
   b. Individual has life-threatening myocarditis, pericarditis, arrhythmias, or impaired ventricular function, according to the prescriber; **AND**

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c. Individual has not improved within 24 hours of starting pulse-dose methylprednisolone; **AND**

d. Atgam will be used in a compendia (NCCN) recommended regimen.

OR

vi. Immune Checkpoint Inhibitor-Related Toxicities (cytokine release syndrome) (NCCN 2A); **AND**

a. Individual has received Cart-T Cell therapy. Note: CAR T-cell therapies include: Tisagenlecleucel (Kymriah), Axicabtagene ciloleucel (Yescarta), Brexucabtagene autoleucel (Tecartus), Lisocabtagene maraleucel (Breyanzi), Idecabtagene vicleucel (Abecma), and Ciltacabtagene autoleucel (Carvykti); **AND**

b. Individual's condition is refractory to both, high-dose corticosteroids and anti-IL-6 therapy (tocilizumab product); **AND**

c. Atgam will be used in a compendia (NCCN) recommended regimen.

OR

vii. Low Risk Myelodysplastic Syndrome (NCCN 2A)

a. Individual has lower risk disease. 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; **AND**

b. Individual has one of the following according to the prescriber:

1. Clinically relevant thrombocytopenia; **OR**
2. Clinically relevant neutropenia; **OR**
3. Increased marrow blasts; **OR**
4. Symptomatic anemia

AND

c. Atgam will be used in a compendia (NCCN) recommended regimen.

NOTE: *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)]*

B. Continuation Criteria

i. MMM considers continuation of Antithymocyte Globulin Equine (Atgam®) therapy medically necessary in members requesting reauthorization for an indication listed in Section A above (Criteria for Initial Approval) when all initial approval criteria are met.

C. Authorization Duration

i. Click or tap here to enter text.Approval Duration: 1 month

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D. Conditions not covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

I. When the above criteria are not met and for all other indications.

Limits or Restrictions

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Drug	Recommended Dosing Schedule
Antithymocyte Globulin Equine (Atgam®)	Allograft Rejection in Solid Organ Transplant: • Up to 15 mg/kg administered intravenously daily for up to 14 days • Up to seven additional doses can be administered intravenously every other day for a maximum total of 21 doses in 28 days. Aplastic Anemia • Up to 20 mg/kg administered intravenously daily for up to 14 days • Additional alternate-day therapy up to a total of 21 doses may be given. Allogeneic Hematopoietic Stem Cell Transplantation • Up to 40 mg/kg administered intravenously daily as a single dose, or divided and given twice daily for up to 4 days. Acute Graft-Versus-Host Disease • Up to 40 mg/kg/day administered intravenously for up to 10 doses in a course of therapy. Immune Checkpoint Inhibitor-Related Toxicities • Up to 15 mg/kg administered intravenously daily for 14 days. • Up to seven additional doses can be administered intravenously every other day for a maximum total of 21 doses in 28 days. Myelodysplastic Syndrome. • Up to 40 mg/kg/day administered intravenously for up to 4 days; OR

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	• Up to 15 mg/kg administered intravenously daily for 5 days
Exceptions	
None	

Reference Information

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Policy History

Revision Type	Summary of Changes	P&T Approval Date	MPCC Approval Date
Annual Review 09/15/2024	Added NCCN supported uses in the Other Uses section (background section); Added used in combination with cladribine and busulfan when used for Allograft Rejection in Solid Organ Transplant; clarified criteria to use in immune checkpoint inhibitor-related toxicities to make it specific for immunotherapy-related myocarditis, and added Car T Cell related CRS use and criteria as per NCCN compendia guidelines; Added the following statement to the criteria of all NCCN supported uses: Atgam will be used in a compendia (NCCN) recommended regimen; Added Continuation Criteria statement; Added Conditions Not Covered section; Wording and formatting changes; Coding reviewed: Added the following codes: D89.810, D89.812, D89.813, T86.09, Z94.81, Z94.89, Z94.9, I30.8, I30.9, I40.8, I40.9, K71.1-K71.9, K71.0, K71.10, K71.11, K71.50, K71.51, R74.01, T80.82XA, T80.82XS, T80.89XA, D89.834, D89.839, C93.10, D46.0, D46.1, D46.20, D46.21, D46.4, D46.9, D46.A, D46.B, D46.Z.	2/18/2025	3/6/2025
Policy Inception 09/27/2023	Policy reviewed and approved by P&T Committee.	10/30/2023	11/30/2023