PRIOR AUTHORIZATION POLICY

POLICY: Immune Globulin – Atgam Prior Authorization Policy

- Atgam® (lymphocyte immune globulin, anti-thymocyte globulin [equine] intravenous infusion – Pfizer)

REVIEW DATE: 01/03/2024

OVERVIEW

Atgam, an immune globulin, is indicated for the following uses:[1]

- **Allograft rejection**, 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.
- **Aplastic anemia**, 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.

Guidelines

The use of Atgam is supported in a number of clinical guidelines.[2-9]

- **Acute cellular rejection**: The Kidney Disease Improving Global Outcomes (KDIGO) Clinical Practice Guideline for the Care of Kidney Transplant Recipients (2009), recommend anti-thymocyte globulin (ATG) as a treatment option for induction therapy, given prior to, at the time of, or immediately after transplant.[2] The KDIGO guidelines recommend ATG for the treatment of acute cellular rejection unresponsive to corticosteroids, recurrent acute cellular rejection, and for acute antibody-mediated rejection.
- **Aplastic anemia**: The British Society of Haematology guidelines for the diagnosis and management of aplastic anemia recommends immunosuppressive therapy with Atgam plus cyclosporine for the first-line treatment of patients with non-severe aplastic anemia requiring treatment, severe or very severe aplastic anemia in those who lack a matched sibling donor, and severe or very severe aplastic anemia patients aged > 35 to 50 years of age.[3,4] A second course of Atgam is recommended following a relapse after the first course of therapy, or after failure to respond to the first course if the patient is ineligible for a matched unrelated donor hematopoietic stem cell transplant. In addition, Atgam is included in conditioning regimens for bone marrow transplantation.[5]
- The National Comprehensive Cancer Network (NCCN) guidelines:[6-9]
  - **Graft-vs-host disease:** The NCCN Hematopoietic Cell Transplantation Clinical Practice Guidelines (version 3.2023 – October 9, 2023) recommend ATG as additional therapy in conjunction with corticosteroids for the management of acute steroid-refractory disease.[9]
  - **Immunotherapy-related cardiovascular toxicity:** The NCCN Guidelines for the Management of Immunotherapy-Related Toxicities (version 1.2024 – December 7, 2023), recommend Atgam as additional treatment for life-threatening cardiac immune-related adverse events if there is no improvement within 24 hours of starting pulse-dose methylprednisolone.[6,7] Atgam can also be considered for elevated liver transaminases if there is worsening or no improvement after use with corticosteroids, such as prednisone or methylprednisolone.
  - **Myelodysplastic syndrome:** The NCCN Clinical Practice Guidelines (version 3.2023 – November 10, 2023) recommend Atgam as a treatment option for the management of lower

risk disease.[7,8] Treatment with Atgam alone or in combination with cyclosporine and/or Promacta® (eltrombopag olamine tablets) is recommended for select patients with clinically relevant thrombocytopenia or neutropenia; or for select patients with symptomatic anemia.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Atgam. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Atgam as well as the monitoring required for adverse events and long-term efficacy, approval requires Atgam to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Atgam is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Allograft Rejection in Solid Organ Transplant.** Approve for 1 month if the patient meets the following (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; AND
   - **B)** The medication is prescribed by or in consultation with a transplant specialist physician or a physician associated with a transplant center.

2. **Aplastic Anemia.** Approve for 1 month if the patient meets the following (A and B):
   - **A)** Patient has moderate to severe disease; AND
   - **B)** The medication is prescribed by or in consultation with a hematologist or a physician who specializes in the treatment of aplastic anemia.

Other Uses with Supportive Evidence

3. **Hematopoietic Stem Cell Transplantation or Umbilical Cord Transplantation**. Approve for 1 month if the patient meets the following (A and B):
   - **A)** Atgam is used as part of a conditioning regimen beginning prior to hematopoietic stem cell transplantation or umbilical cord transplantation; AND
   - **B)** The medication is prescribed by or consultation with an oncologist or a physician who specializes in stem cell or umbilical cord transplantation.

4. **Graft-Versus-Host Disease**. Approve for 1 month if the patient meets the following (A, B, and C):
   - **A)** Patient has acute disease; AND
   - **B)** Patient's disease is refractory or resistant to corticosteroid therapy; AND
   - **C)** The medication is prescribed by or consultation with an oncologist or a physician who specializes in transplantation.

5. **Immune Checkpoint Inhibitor-Related Toxicities**. Approve for 1 month if the patient meets the following (A, B, C, and D):
   - **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), Libtayo (cemiplimab intravenous infusion), Jemperli (dostarlimab intravenous infusion).
   - **B)** Patient meets ONE of the following (i or ii):
     - **i.** Patient has cardiac immune-related adverse events; OR
       Note: Examples of cardiac immune-related adverse events are myocarditis, pericarditis, arrhythmias, impaired ventricular function, large vessel vasculitis.
     - **ii.** Patient has elevated liver enzymes or toxic liver disease; AND
   - **C)** Patient has not improved after therapy with corticosteroids; AND
     Note: Examples of corticosteroids include prednisone, dexamethasone, methylprednisolone.
   - **D)** The medication is prescribed by or consultation with a cardiologist, oncologist, gastroenterologist, or a physician who specializes in the treatment of immune checkpoint inhibitor-related toxicity.

6. **Myelodysplastic Syndrome**. Approve for 1 month if the patient meets the following (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; IPSS-Molecular (IPSS-M) risk of very low, low, moderate low. Other risk stratification models may also be used (e.g., the MD Anderson Cancer Center or the World Health Organization Prognostic Scoring System).
   - **B)** The medication is prescribed by or in consultation with an oncologist or a physician who specialized in the treatment of myelodysplastic syndromes.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Atgam is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Atgam® intravenous infusion [prescribing information]. New York, NY: Pfizer; August 2023.
2. Kidney Disease: Improving Global Outcomes (KDIGO) Transplant Work Group. KDIGO clinical practice guidelines for the care of kidney transplant recipients. *Am J Transplant*. 2009;9:S1-S157.
3. 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.
4. Samarasinghe S, Veys P, Vora A, Wynn R. Paediatric amendment to adult BSH guidelines for aplastic anaemia. *Br J Haematol*. 2018;180:201-205.
5. Peslak SA, Olson T, Babushok DV. Diagnosis and treatment of aplastic anemia. *Curr Treat Options Oncol*. 2017;18:70.
6. The NCCN Management of Immunotherapy-Related Toxicities Clinical Practice Guidelines in Oncology (version 1.2024 – December 7, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed December 12, 2023.
7. The NCCN Drugs and Biologics Compendium. © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on December 12, 20232. Search term: Atgam.
8. The NCCN Myelodysplastic Syndromes Clinical Practice Guidelines in Oncology (version 3.2023 – November 19, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed December 12, 2023.

9. The NCCN Hematopoietic Cell Transplantation Clinical Practice Guidelines in Oncology (version 3.2023 – October 9, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed December 12, 2023.