Drug Coverage Policy

Effective Date.....5/1/2026
Coverage Policy Number.....IP0625
Policy Title.....Amtagvi

Oncology (Injectable) – Amtagvi

- Amtagvi™ (lifileucel intravenous infusion – Iovance Biotherapeutics)

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

OVERVIEW

Amtagvi, a tumor-derived autologous T cell immunotherapy, is indicated for the treatment of unresectable or metastatic melanoma in adults who have been previously treated with a

programmed death receptor-1 (PD-1) blocking antibody, and if BRAF V600 mutation positive, a BRAF inhibitor with or without a MEK inhibitor.[1] This indication is approved under accelerated approval based on objective response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trials.

Dosing Information
Amtagvi is provided as a single dose for intravenous infusion containing a suspension of tumor-derived T cells in 5% dimethyl sulfoxide.[1] The dose contains between 7.5 x 10^9 to 72 x 10^9 viable cells and is supplied in one or more frozen infusion bags. The bags are stored in the vapor phase of liquid nitrogen (less than or equal to minus 150°C). Amtagvi is for autologous use only.

Prior to receiving Amtagvi, patients are pretreated with lymphodepleting chemotherapy consisting of cyclophosphamide 60 mg/kg intravenously with mesna for 2 days followed by fludarabine 25 mg/m^2 intravenously daily for 5 days. Amtagvi is administered as soon as possible, 24 hours after the last dose of fludarabine but no later than 4 days after the last dose of fludarabine.

Guidelines
The National Comprehensive Cancer Network (NCCN) melanoma: cutaneous (version 2.2025 – January 28, 2025) treatment guidelines recommend Amtagvi as a "Preferred" high-dose therapy as second-line or subsequent treatment for metastatic or unresectable disease following progression on anti-PD-1 therapy and BRAF/MEK inhibitor therapy if BRAF V600 mutation positive (category 2A).[2,3]

Safety
Amtagvi has a Boxed Warning for treatment-related mortality, prolonged severe cytopenia, severe infection, and cardiopulmonary and renal impairment.[1]

Coverage Policy

POLICY STATEMENT
Prior Authorization is required for medical benefit coverage of Amtagvi. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Because of the specialized skills required for evaluation and diagnosis of patients treated with Amtagvi as well as the monitoring required for adverse events and long-term efficacy, approval requires Amtagvi to be prescribed by or in consultation with a physician who specializes in the condition being treated. The approval duration is 6 months to allow an adequate time frame to prepare and administer 1 dose of therapy.

Amtagvi is considered medically necessary when the following is met:

1. **Melanoma.** Approve a single dose if the patient meets ALL of the following (A, B, C, D, E, F, and G):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient has unresectable or metastatic disease; AND
   - **C)** Patient has been treated with a programmed death receptor-1 (PD-1) blocking antibody or a programmed death-ligand 1 (PD-L1) blocking antibody; AND
     Note: Examples of PD-1/PD-L1 blocking antibodies includes Keytruda (pembrolizumab intravenous infusion), Opdivo (nivolumab intravenous infusion), and Tecentriq (atezolizumab intravenous infusion).
   - **D)** If the patient is BRAF V600 mutation positive, the patient has been treated with a BRAF inhibitor with or without a MEK inhibitor; AND
     Note: Examples of BRAF inhibitors includes Braftovi (encorafenib capsules), Zelboraf (vemurafenib tablets), and Tafinlar (dabrafenib capsules).

E) Patient has received or is planning to receive lymphodepleting chemotherapy prior to infusion of Amtagvi; AND
F) Patient has NOT been previously treated with Amtagvi; AND
G) The medication is prescribed by or in consultation with an oncologist.

Dosing. The dose of Amtagvi is between 7.5 x 10^9 and 72 x 10^9 viable cells administered intravenously as a single dose.

Conditions Not Covered

Amtagvi for any other use is considered not medically necessary. Criteria will be updated as new published data are available.

Coding Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
C9399	Unclassified drugs or biologicals
J3590	Unclassified biologics

References

1. Amtagvi™ intravenous infusion [prescribing information]. Philadelphia, PA: Iovance Biotherapeutics; February 2024.
2. The NCCN Drugs & Biologics Compendium. © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 10, 2025. Search term: lifileucel.
3. The NCCN Melanoma: Cutaneous Clinical Practice Guidelines in Oncology (version 2.2025 – January 28, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 10, 2025.

Revision Details

Type of Revision	Summary of Changes	Date
New	New policy	6/15/2024
Annual Revision	No criteria changes	5/1/2025
Annual Revision	No criteria changes	5/1/2026

The policy effective date is in force until updated or retired.