Clinical Policy: Lifileucel (Amtagvi)

Reference Number: CP.PHAR.598
Effective Date: 02.16.24
Last Review Date: 05.24
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Lifileucel (Amtagvi®) is an autologous tumor infiltrating lymphocyte (TIL) cell therapy.

FDA Approved Indication(s)

Amtagvi is indicated for the treatment of adult patients with unresectable or metastatic melanoma previously treated with a programmed death receptor-1 (PD-1) blocking antibody, and if BRAF V600 mutation positive, a BRAF inhibitor with or without MEK inhibitor*.

**This indication is approved under accelerated approval based on objective response rate (ORR). Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).*

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.

All requests reviewed under this policy **require medical director review.**

It is the policy of health plans affiliated with Centene Corporation® that Amtagvi is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Melanoma (must meet all)**:**

1. Diagnosis of unresectable or metastatic melanoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Documentation of disease progression, inadequate response, or intolerance while on the following regimens (a and b) (*see Appendix B*):
   a. Anti-PD-1 or PD-L1 therapy;
   b. If BRAF V600 mutation positive: BRAF inhibitor therapy with or without a MEK inhibitor;
5. Amtagvi is prescribed in combination with IL-2* therapy (e.g., aldesleukin);
   **Prior authorization may be required for IL-2 therapy*
6. Documentation that member has at least one resectable lesion (or aggregate of lesions resected) of a minimum 1.5 cm in diameter (*see Appendix D)*;
7. Documentation that the member's melanoma is not of known uveal/ocular origin *(see Appendix D)*;

8. Member has not received an organ allograft or treatment with prior TIL therapy or prior chimeric antigen receptor T-cell (CAR-T) therapy (e.g., Breyanzi®, Kymriah®, Tecartus®, Yescarta®, Carvykti®) *(see Appendix D)*;
9. Request meets both of the following (a and b):
   a. Dose contains a minimum of 7.5×10^9 viable T cells;
   b. Dose does not exceed a single administration of 72×10^9 viable T cells.

Approval duration: 3 months *(1 dose only, with up to 6 doses of IL-2 therapy [aldesleukin])*

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Melanoma

1. Continued therapy will not be authorized as Amtagvi is indicated to be dosed one time only.

Approval duration: Not applicable

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

BRAF: B-Raf proto-oncogene, serine/threonine kinase
CAR: chimeric antigen receptor
FDA: Food and Drug Administration
IL-2: interleukin-2
MEK: mitogen-activated extracellular signal-regulated kinase
PD-1: programmed death receptor-1
PD-L1: programmed death-ligand 1
TIL: tumor infiltrating lymphocytes

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 for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
PD-1/PDL-1 targeted combination therapy (Opdivo® with Yervoy®, Opdualag®)	Varies	Varies
PD-1/PDL-1 targeted monotherapy (Opdivo, Keytruda®)	Varies	Varies
PD-1/PDL-1 and BRAF-MEK combintation targeted therapy (Tecentriq®/Cotellic®/ Zelboraf®)	Varies	Varies
BRAF-MEK combination targeted therapy (Cotellic®/ Zelboraf®, Tafinlar®/ Mekinist®, Mektovi®/Braftovi®)	Varies	Varies

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): none reported
- Boxed warning(s): treatment-related mortality, prolonged severe cytopenia, severe infection, cardiopulmonary and renal impairment

Appendix D: General Information

- Amtagvi requires the administration of IL-2 (e.g., aldesleukin) to stimulate TIL cells after infusion.

- One resectable lesion (or aggregate of lesions resected) of a minimum 1.5 cm in diameter is required because TIL therapy involves resectioning a tumor and amplifying the T-cells within the resectioned tumor. If a smaller tumor/aggregate tumor size was used, then there may not be adequate volume of T-cells after amplification, resulting in a less efficacious product.
- The safety and efficacy of Amtagvi is unknown in patients with melanoma of uveal/ocular origin and patients with previous organ allograft or prior cell transfer therapy.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Melanoma	Single dose IV infusion of 7.5×10^9 to 72×10^9 viable T cells	72×10^9 viable T cells

VI. Product Availability

Infusion bag(s): frozen suspension of tumor-derived T-cells labeled for specific recipient

VII. References

1. Amtagvi Prescribing Information. Philadelphia, PA, NJ: Iovance Biotherapeutics Manufacturing LLC; February 2023. Available at: https://www.fda.gov/media/176417/download?attachment. Accessed February 21, 2023.
2. Sarnaik AA, Hamid O, Khushalani NI, et al. Lifileucel, a tumor-infiltrating lymphocytes therapy, in metastatic melanoma. *J Clin Oncol* 2021 39:2656-2666. DOI: 10.1200/JCO.21.00612.
3. National Comprehensive Cancer Network. Melanoma: Cutaneous v1.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cutaneous_melanoma.pdf. Accessed March 13, 2024.
4. ClinicalTrials.gov. Study of Lifileucel (LN-144), Autologous tumor infiltrating lymphocytes, in the treatment of patients with metastatic melanoma (LN-144). Available at: https://clinicaltrials.gov/ct2/show/NCT02360579. Accessed March 13, 2024.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
C9399	Unclassified drugs or biologicals
J9999	Not otherwise classified, antineoplastic drugs

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	10.11.22	11.22

Reviews, Revisions, and Approvals	Date	P&T Approval Date
RT1: Drug is now FDA approved - criteria updated per FDA labeling: added requirement for Amtagvi to be prescribed in combination with IL-2 therapy; added documentation of at least one resectable lesion; added documentation that the member's melanoma is not of known uveal/ocular origin, added restriction in prior organ allograft, prior TIL therapy, or prior CAR-T therapy; references reviewed and updated.	04.09.24	05.24

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.