Amtagvi® (lifileucel)
(Intravenous)

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Document Number: IC-0786

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I. Length of Authorization

Coverage will be provided for one treatment course (1 dose) and may not be renewed.

II. Dosing Limits

Max Units (per dose and over time) [HCPCS Unit]:

- A single dose of Amtagvi containing a minimum of 7.5×10^9 of viable cells suspended in one or more patient-specific infusion bags

III. Initial Approval Criteria [1]

Submission of medical records (chart notes) related to the medical necessity criteria is REQUIRED on all requests for authorizations. Records will be reviewed at the time of submission. Please provide documentation related to diagnosis, step therapy, and clinical markers (i.e. genetic and mutational testing) supporting initiation when applicable. Please provide documentation via direct upload through the PA web portal or by fax.

Coverage is provided for the following conditions:

- Patient is at least 18 years of age; **AND**
- Patient does not have uncontrolled brain metastases; **AND**
- Patient does not have signs and symptoms of acute renal failure prior to treatment; **AND**
- Patient does not have hemorrhage (grade 2 or higher) within 14 days prior to therapy; **AND**
- Patient does not have a left ventricular ejection fraction (LVEF) less than 45% or New York Heart Association (NYHA) functional classification greater than Class 1; **AND**
- Patient does not have forced expiratory volume in one second (FEV1) of less than or equal to 60%; **AND**
- Patient does not have a clinically significant active systemic infection; **AND**
- Patient is deemed eligible for IL-2 (aldesleukin) therapy *(refer to manufacturer's prescribing label for more information)*; **AND**

- Patient will not receive concomitant prophylactic systemic corticosteroid therapy; **AND**

Cutaneous Melanoma † Φ [1-5]

- Patient has a diagnosis of unresectable or metastatic melanoma; **AND**
- Patient does not have uveal melanoma; **AND**
- Used as subsequent therapy after the following:
    - Programmed cell death protein-1 (PD-1) blocking antibody; **AND**
    - If BRAF V600 mutation-positive, a BRAF inhibitor with or without a MEK inhibitor

Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria

- Coverage cannot be renewed.

V. Dosage/Administration

Indication	Dose
Cutaneous Melanoma	• Amtagvi is provided as a single dose for infusion containing a suspension of tumor-derived T cells. The dose is supplied in 1 to 4 patient specific IV infusion bag(s) in individual protective metal cassettes. Each dose contains 7.5 x 10^9 to 72 x 10^9 viable cells. • Confirm availability of Amtagvi and IL-2 (aldesleukin) prior to starting the lymphodepleting regimen. Administer a lymphodepleting chemotherapy regimen of cyclophosphamide 60 mg/kg IV with mesna daily for 2 days followed by fludarabine 25 mg/m2 IV daily for 5 days before infusion of Amtagvi. • Infuse Amtagvi after 24 hours have elapsed following the last dose of fludarabine, but no later than 4 days. • Beginning 3 to 24 hours after Amtagvi infusion, administer intravenous IL-2 (aldesleukin) at 600,000 IU/kg every 8 to 12 hours for up to a maximum of 6 doses to support cell expansion in vivo. IL-2 (aldesleukin) should be administered in an inpatient setting under the supervision of a physician experienced in the use of anticancer agents.
– *Administer in an inpatient hospital setting under the supervision of a physician experienced in the use of anticancer agents. An intensive care facility and specialists skilled in cardiopulmonary or intensive care medicine must be available.* – *Amtagvi is for autologous use only. The patient's identity must match the patient identifiers on the drug cassette(s) and infusion bag(s).* – *Avoid prophylactic use of systemic corticosteroids which may interfere with the activity of Amtagvi.*	

VI. Billing Code/Availability Information

HCPCS Code:

- J9999 – Not otherwise classified, antineoplastic drug

NDC(s):

- Amtagvi contains 7.5 x 10^9 to 72 x 10^9 viable cells suspended in 1 to 4 patient-specific infusion bag(s): 73776-0001-xx

VII. References (STANDARD)

1. Amtagvi [package insert]. Philadelphia, PA; Iovance Biotherapeutics Manufacturing, LLC; February 2024. Accessed February 2025.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) lifileucel. National Comprehensive Cancer Network, 2025. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed February 2025.
3. Referenced with permission from the NCCN Clinical Practice Guidelines (NCCN Guidelines®) Melanoma: Cutaneous. Version 2.2025. National Comprehensive Cancer Network, 2025. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed February 2025.
4. ClinicalTrials.gov. A Phase 2, Multicenter Study to Assess the Efficacy and Safety of Autologous Tumor Infiltrating Lymphocytes (LN-144) for Treatment of Patients With Metastatic Melanoma. https://clinicaltrials.gov/study/NCT02360579?intr=NCT02360579&rank=1.
5. Sarnaik A, Khushalani NI, Chesney JA, et al. Safety and efficacy of cryopreserved autologous tumor infiltrating lymphocyte therapy (LN-144, lifileucel) in advanced metastatic melanoma patients who progressed on multiple prior therapies including anti-PD-1. Journal of Clinical Oncology 2019 37:15_suppl, 2518-2518

VIII. References (ENHANCED)

1e. Sarnaik AA, Hamid O, Khushalani NI, et al. Lifileucel, a Tumor-Infiltrating Lymphocyte Therapy, in Metastatic Melanoma. J Clin Oncol. 2021 Aug 20;39(24):2656-2666.

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4e. Arance AM, de la Cruz-Merino L, Petrella TM, et al. Lenvatinib (len) plus pembrolizumab (pembro) for patients (pts) with advanced melanoma and confirmed progression on a PD-1 or PD-L1 inhibitor: Updated findings of LEAP-004. Journal of Clinical Oncology 2021 39:15_suppl, 9504-9504.

5e. Hodi FS, O'Day SJ, McDermott DF, et al. Improved survival with ipilimumab in patients with metastatic melanoma [published correction appears in N Engl J Med. 2010 Sep 23;363(13):1290]. N Engl J Med. 2010;363(8):711–723.

6e. Larkin J, Minor D, D'Angelo S, et al. Overall Survival in Patients With Advanced Melanoma Who Received Nivolumab Versus Investigator's Choice Chemotherapy in CheckMate 037: A Randomized, Controlled, Open-Label Phase III Trial. J Clin Oncol. 2018;36(4):383–390.

7e. Pires da Silva I, Ahmed T, Reijers ILM, et al. Ipilimumab alone or ipilimumab plus anti-PD-1 therapy in patients with metastatic melanoma resistant to anti-PD-(L)1 monotherapy: a multicentre, retrospective, cohort study. Lancet Oncol. 2021 Jun;22(6):836-847.

8e. Ascierto PA, Lipson EJ, Dummer R, et al. Nivolumab and Relatlimab in Patients With Advanced Melanoma That Had Progressed on Anti-Programmed Death-1/Programmed Death Ligand 1 Therapy: Results From the Phase I/IIa RELATIVITY-020 Trial. J Clin Oncol. 2023 Feb 13:JCo2202072.

9e. Hersh EM, O'Day SJ, Ribas A, et al. A phase 2 clinical trial of nab-paclitaxel in previously treated and chemotherapy-naive patients with metastatic melanoma. Cancer. 2010 Jan 1;116(1):155-63.

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14e. Einzig AI, et al. A phase II study of taxol in patients with malignant melanoma. Invest New Drugs. 1991 Feb;9(1):59-64.

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18e. Prime Therapeutics Management. Amtagvi Clinical Literature Review Analysis. Last updated February 2025. Accessed February 2025.

IX. Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C43.0	Malignant melanoma of lip
C43.111	Malignant melanoma of right upper eyelid, including canthus
C43.112	Malignant melanoma of right lower eyelid, including canthus
C43.121	Malignant melanoma of left upper eyelid, including canthus
C43.122	Malignant melanoma of left lower eyelid, including canthus
C43.20	Malignant melanoma of unspecified ear and external auricular canal
C43.21	Malignant melanoma of right ear and external auricular canal
C43.22	Malignant melanoma of left ear and external auricular canal
C43.30	Malignant melanoma of unspecified part of face
C43.31	Malignant melanoma of nose
C43.39	Malignant melanoma of other parts of face
C43.4	Malignant melanoma of scalp and neck
C43.51	Malignant melanoma of anal skin
C43.52	Malignant melanoma of skin of breast
C43.59	Malignant melanoma of other part of trunk
C43.60	Malignant melanoma of unspecified upper limb, including shoulder
C43.61	Malignant melanoma of right upper limb, including shoulder
C43.62	Malignant melanoma of left upper limb, including shoulder
C43.70	Malignant melanoma of unspecified lower limb, including hip
C43.71	Malignant melanoma of right lower limb, including hip
C43.72	Malignant melanoma of left lower limb, including hip
C43.8	Malignant melanoma of overlapping sites of skin
C43.9	Malignant melanoma of skin, unspecified

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC