CLINICAL GUIDELINES FOR MEDICAL NECESSITY

MEDICAL POLICY

Lifileucel (Amtagvi®)

Version: 1.0

EFFECTIVE DATE: 5/1/2024

NantHealth® | Eviti®

Please note the following:

Lifileucel (Amtagvi®)

Note: For Medicare members/enrollees, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Please refer to the CMS website at http://www.cms.gov for additional information.

Note: For Medicaid members/enrollees, circumstances when state Medicaid coverage provisions conflict with the coverage provisions within 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.

Lifileucel (Amtagvi): Discussion

Lifileucel is the first tumor-derived autologous T cell immunotherapy therapy to be approved by the US Food and Drug Administration (FDA) for certain adults with stage 3 unresectable or metastatic melanoma previously treated with a PD-1 blocking antibody second line or greater, and if BRAF V600 positive, a BRAF inhibitor with or without a MEK inhibitor. It is also the first non-CAR-T adoptive cell therapy to reach the market.[1,2,3,4]

The National Comprehensive Cancer Network (NCCN) endorses lifileucel in metastatic or unresectable cutaneous melanoma.[5]

Lifileucel is designed to deploy patient-specific T cells called tumor infiltrating lymphocyte (TIL) cells to locate and attack cancer cells. For the approved CAR-T cell therapies, the T cells are collected from a patient's circulating blood. For TIL therapy, by contrast, the T cells are collected from the patient's tumor.[4]

The therapy's mechanism involves deploying patient-specific T cells called tumor-infiltrating lymphocytes (TIL cells) to recognize and fight cancer. Lifileucel has a boxed warning for treatment-related mortality and other potential risks like prolonged severe cytopenia, severe infections, cardiopulmonary impairment, and renal impairment. Among the 73 patients, the objective response rate was 31.5% (95% CI, 21.1-43.4), with 3 complete responses and 20 partial responses.[3,4]

The primary efficacy analysis set included 73 patients from Cohort 4 who received the recommended lifileucel dose from an approved manufacturing facility. Among the 73 patients, 31.5% achieved an objective response by Response Evaluation Criteria in Solid Tumors (RECIST 1.1) with a median duration of response not reached at 18.6 months follow-up2 (43.5% of responses had a duration greater than 12 months). Additionally, the supporting pooled efficacy set included a total of 153 patients from Cohort 4 and Cohort 2. Among the 153 patients, 31.4% achieved an objective response by RECIST 1.1 with a median duration of response not reached at 21.5 months follow-up2 (54.2% of responses had a duration greater than 12 months). The detailed results of clinical trial C-144-01 are published in The Journal for ImmunoTherapy of Cancer.[3] About 40% of those whose cancer responded to lifileucel still had no progression of their cancer a year after receiving the one-time infusion treatment.[4] Lifileucel

is also well along in testing and showing promise as a treatment for other cancers, including advanced lung cancer, ovarian and head and neck cancers.[4]

Neurotoxicity can be a life-threatening side effect. The most common side effects from lifileucel treatment include chills, fever, low white blood cell count (may increase risk of infections), fatigue, low red blood cell count, fast or irregular heartbeat, rash, low blood pressure, and diarrhea. Greater than 10% of adverse effects of any grade are thrombocytopenia (78.2%), chills (75.6%), neutropenia (69.2%), nausea (68.6%), pyrexia (60.9%), anemia (58.3%), fatigue (55.8%), tachycardia (47.4%), febrile neutropenia (46.8%), diarrhea (46.8%), leukopenia (46.8%), vomiting (43.6%), edema (42.3%), and lymphopenia (42.3%). There are other adverse effects that are less than 40%.[2,3]

Lifileucel: Definitions

- **V-raf murine sarcoma viral oncogene homolog B (BRAF) Gene -** A gene that encodes a protein belonging to the RAF family of serine/threonine protein kinases. This protein plays a role in regulating the mitogen-activated protein (MAP) kinase/extracellular signal-regulated (ERK) signaling pathway, which affects cell division, differentiation, and secretion.
- **Food and Drug Administration (FDA) -** The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation.
- **Mitogen-Activated Protein Kinase (MEK) Inhibitor** - A drug that inhibits the mitogen-activated protein kinase enzymes MEK1 and/or MEK2. They can be used to affect the MAPK/ERK pathway which is often overactive in some cancers.
- **National Comprehensive Cancer Network (NCCN) -** An alliance of 33 leading cancer centers devoted to patient care, research, and education. The NCCN guidelines are utilized for Radiation Therapy and Medical Oncology standards. NCCN consensus clinical standards are periodically updated and NantHealth, Inc. reviews these and updates its policies within a timely manner.
- **Programmed cell death protein 1 (PD-1)/Programmed cell death-ligand 1 (PD-L1) –** Checkpoint proteins, such as PD-L1 on tumor cells and PD-1 on T cells, help keep immune responses in check. The binding of PD-L1 to PD-1 keeps T cells from killing tumor cells in the body. Blocking the binding of PD-L1 to PD-1 with an immune checkpoint inhibitor (anti-PD-L1 or anti-PD-1) allows the T cells to kill tumor cells.

Lifileucel: Policy

Note: Coverage of lifileucel will be provided for FDA-approved indications or National Comprehensive Cancer Network (NCCN) guidelines when it is a Category 1, 2A, or 2B recommendation or when all criteria are met.

Lifileucel will be considered for coverage when the following criteria are met:

Unresectable or Metastatic Melanoma

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND
3. Metastatic or unresectable disease; AND
4. A lymphodepleting chemotherapy regimen will be administered before infusion of lifileucel; AND

For FDA required criteria coverage:

5. Previously treated with a PD-1 blocking antibody; AND
6. Previously treated with a BRAF inhibitor with or without a MEK inhibitor, if BRAF V600 mutation positive[2] ; OR

For NCCN required criteria coverage:

7. Progression on anti-PD-1-based therapy; AND
8. Progression on BRAF/MEK inhibitor therapy (if BRAF V600 mutation positive); AND
9. Second-line or subsequent systemic therapy[5]

Note:

TIL therapy should not be considered for patients with inadequate cardiac, pulmonary, and/or renal function, poor performance status, or with untreated or active brain metastases. Referral to a TIL authorized treatment center is recommended.[5]

Dosage:

Each dose contains 7.5 x 10^9 to 72 x 10^9 viable cells.[2]

For reauthorization:

Lifileucel is a one-time dose and will not be renewed.

Lifileucel: References

1. FDA grants accelerated approval to lifileucel for unresectable or metastatic melanoma. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerate-approval-lifileucel-unresectable-or-metastatic-melanoma. Accessed February 23, 2024.
2. Lifileucel (Amtagvi) Package Insert. https://www.fda.gov/media/176417/download?attachment. Accessed February 23, 2024.
3. Chesney et al. Efficacy and safety of lifileucel, a one-time autologous tumor-infiltrating lymphocyte (TIL) cell therapy, in patients with advanced melanoma after progression on

immune checkpoint inhibitors and targeted therapies: pooled analysis of consecutive cohorts of the C-144-01 study. https://pubmed.ncbi.nlm.nih.gov/36600653/. Accessed March 6, 2024.
4. National Cancer Institute. First Cancer TIL Therapy Gets FDA Approval for Advanced Melanoma. https://www.cancer.gov/news-events/cancer-currents-blog/2024/fda-amtagvi-til-therapy-melanoma. Accessed March 6, 2024.
5. National Comprehensive Cancer Network. Melanoma: Cutaneous. https://www.nccn.org/professionals/physician_gls/pdf/cutaneous_melanoma.pdf. Accessed April 23, 2024.

Lifileucel: Coding (CPT®, ICD 10 and HCPCS) *

*Procedure codes appearing in medical policy documents are only included as a general reference. This list may not be all-inclusive and is subject to updates. In addition, the codes listed are not a guarantee of payment. CPT codes are available through the AMA.

CODE	DESCRIPTION
C43	Malignant melanoma of the skin
J9999	Lifileucel- antineoplastic - autologous cellular immunotherapy
M0075	Cellular therapy
XW033L7	Introduction of lifileucel immunotherapy into peripheral vein, percutaneous approach, new technology group 7
XW043L7	Introduction of lifileucel immunotherapy into central vein, percutaneous approach, new technology group 7

Lifileucel: Revision and Review History

No.	Description	Date(s)
1	Original Effective Date:	5/1/2024
2	Policy Review Dates:	
3	Policy Revision Dates:	
4	Department Owner:	Medical Affairs
5	NH Advisory Committee Approval Dates:	6/13/2024
6	Revision Changes:	