Mass General Brigham
Health Plan

Amtagvi
(lifileucel)

Policy Number: 077

	Commercial and Qualified Health Plans	MassHealth	Medicare Advantage
Authorization Required	X	X	X
No Prior Authorization			
Not covered			

Amtagvi is a tumor-derived autologous T cell immunotherapy, or tumor-infiltrating lymphocyte therapy, for the treatment of certain patients with advanced melanoma.

FDA-Approved Indication

Amtagvi is indicated for the treatment of:

- Adult patients with unresectable or metastatic melanoma previously treated with a PD-1 blocking antibody, and if BRAF V600 positive, a BRAF inhibitor with or without a MEK inhibitor.

Criteria

1. Criteria for Initial Approval

   Authorization may be granted for treatment of when ALL of the following criteria are met:

   A. Age 18 or older
   B. Diagnosis of unresectable or metastatic melanoma (Stage IIIC or Stage IV) with BRAF mutation testing
   C. The patient has had progression of disease following treatment with anti-PD-1 based therapy (eg, nivolumab, pembrolizumab)
   D. If BRAF V600 mutation is present, the patient has had progression of disease following treatment with BRAF inhibition (eg, vemurafenib, dabrafenib, encorafenib)
   E. At least one metastasis with diameter ≥1.5cm is resectable
   F. Eastern Cooperative Oncology Group performance status (ECOG PS) of 0 or 1
   G. Evidence of adequate hematologic parameters, liver and renal function within the past 3 months:
      1. Absolute neutrophil count >1,000/mm3
      2. Hemoglobin >9 g/dL
      3. Platelets >100,000/mm3
      4. Alanine transaminase (ALT) and aspartate transaminase <5 times the upper limit of normal
      5. Estimated GFR >40 mL/min
   H. Negative testing for HIV within the past 6 months
   I. Negative antibody testing for hepatitis B or C, or evidence of undetectable viral load within the past 6 months
   J. If the patient has known or suspected heart disease, an echocardiogram within the past 6 months shows left ventricular ejection fraction (LVEF) ≥45%
   K. If the patient has known or suspected lung disease, pulmonary function testing within the past 6 months shows forced expiratory volume in 1 second (FEV-1) >60% of predicted
   L. The treatment will be administered in an Amtagvi Authorized Treatment Center

2. Duration of Therapy
    - Single treatment course
    - Additional courses of therapy are considered experimental/investigational.

Exclusions

1. Organ allograft
2. Prior cell transfer therapy
3. Uveal/ocular melanoma
4. Hypersensitivity to lifileucel
5. Symptomatic and/or untreated brain metastases
6. Chronic systemic steroid therapy
7. Active systemic infections
8. Evidence of liver or kidney dysfunction
9. Administration of live or attenuated vaccine within 28 days of non-myeloablative lymphodepletion (NMA-LD),
10. LVEF <45%
11. FEV-1 ≤60% of predicted
12. Other primary malignancies, unless in remission for at least 3 years
13. Primary immunodeficiency

MassHealth Variation
Prior authorization requests for Amtagvi for Mass General Brigham ACO members should be submitted to the MassHealth Drug Utilization Review Program. Criteria for Amtagvi are found in Table 75: T-Cell Immunotherapies.

Medicare Variation
Mass General Brigham Health Plan uses guidance from the Centers for Medicare and Medicaid Services (CMS) for coverage determinations for its Medicare Advantage plan members. National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), Local Coverage Articles (LCAs) and documentation included in the Medicare manuals are the basis for coverage determinations. When there is no guidance from CMS for the requested service, Mass General Brigham Health Plan's medical policies are used for coverage determinations. At the time of Mass General Brigham Health Plan's most recent policy review, Medicare has **no NCD or LCD for tumor-infiltrating lymphocyte therapy.**

Codes

The following codes are included below for informational purposes only; inclusion of a code does not constitute or imply coverage.

This list of codes applies to commercial and MassHealth plans only.

Authorized CPT/HCPCS Codes	Code Description
J3490	Unclassified drugs
J3590	Unclassified biologics

Summary of Evidence
The pivotal study for lifileucel is C-144-01, a phase 2 study that included patients with advanced unresectable or metastatic melanoma who progressed despite treatment with immune checkpoint inhibitors and targeted therapies. In one cohort of this single-arm study, Sarnaik et al. (2021) reported an overall response rate (ORR) of

36% and median overall survival (OS) of 17.4 months. In a larger cohort of patients (including longer-term follow-up of the cohort reported by Sarnaik), Chesney et al. (2022) reported an ORR of 31.4%, median progression-free survival of 4.1 months, and median OS of 13.9 months.

Lifileucel is also being studied, in combination with pembrolizumab, for first-line treatment of advanced (unresectable or metastatic) melanoma. Preliminary results with this combination from a single-arm phase 2 study, IOV-COM-202, include ORR 63.6%; median duration of response was not reached at a follow-up of 17.8 months, and median OS was not reported (Thomas 2024). A phase 3 trial, IOV-MEL-301 (also known as Tilvance-301), is enrolling patients with treatment-naïve advanced melanoma who will be randomized to lifileucel+pembrolizumab vs pembrolizumab alone, but no results from this study have yet been published (Olson et al. 2023).

FDA approval was granted in February 2024 on the accelerated approval pathway, and required completion of the postmarketing IOV-MEL-301 trial with a final study report due date of March 31, 2031. NCCN Guidelines (Version 1.2025) state "for patients with good performance status who have been previously treated with anti-PD-1 based therapy and BRAF/MEK inhibition (if BRAF V600 mutation present), TIL therapy should be considered, based on durable response rates in anti-PD-1 refractory melanoma. 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." MGB Health Plan considers lifileucel to be medically necessary for members who meet criteria based on those NCCN guidelines and based on inclusion criteria for the pivotal studies described above.

Effective Date
April 2025: Ad hoc review. MassHealth variation updated to include new prior authorization process.
March 2025: Ad hoc review. Summary of evidence added. References updated.
February 2025: Annual Review. Added MassHealth Variation.
May 2024: Effective Date.

References
Amtagvi [package insert]. Philadelphia: Iovance, 2024.

Chesney J, Lewis KD, Kluger H, et al. Efficacy and safety of lifileucel, a onetime 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. J Immunother Cancer. 2022 Dec;10(12):e005755.

Olson DJ, Larkin J, Hong Y, et al. Tilvance-301, a phase 3 study of lifileucel tumor-infiltrating lymphocyte (TUL) cell therapy combined with pembrolizumab (pembro) vs pembro alone in treatment-naïve unresectable or metastatic melanoma. *J Immunother Cancer* 2023;11(Suppl 1):A1-A1731.

NCCN Clinical Practice Guidelines in Oncology- Cutaneous Melanoma Version 1.2025, December 20, 204. https://www.nccn.org/professionals/physician_gls/pdf/cutaneous_melanoma.pdf, accessed January 9, 2025.

Sarnaik AA, Hamid O, Khushalani NI, et al. Lifileucel, a tumor-infiltrating lymphocyte therapy, in metastatic melanoma. 2021. J Clin Oncol 39:2656-2666.

Thomas S, Gogas H, Hong YK. Efficacy and safety of lifileucel, an autologous tumor-infiltrating lymphocyte cell therapy, and pembrolizumab in patients with immune checkpoint inhibitor-naïve unresectable or metastatic melanoma: Updated results from IOV-COM-202 cohort 1A. *J Clinical Oncol* 2024:42(16 suppl), 9505.