

Medical Necessity Guidelines Amtagvi (lifileucel)

Policy Number: 077

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Overview

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.

Medicare Advantage

Prior Authorization Required	Yes ☒ No ☐
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Mass General Brigham Health Plan uses guidance from the Centers for Medicare and Medicaid Services (CMS) for medical necessity 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 medical necessity determinations. When there is no guidance from CMS for the requested service, Mass General Brigham Health Plan's medical policies are used for medical necessity determinations. **At the time of Mass General Brigham Health Plan's most recent policy review, CMS offered the following guidance:**

- [Medicare Benefit Policy Manual Chapter 15: Covered Medical and Other Health Services](#)

When CMS documentation references FDA labeling, Mass General Brigham Health Plan develops coverage criteria to clarify medical necessity of the requested services. Mass General Brigham Health Plan coverage criteria align with FDA labeling without contradicting existing determinations and enhance the clarity of medical necessity requirements, documentation requirements, and clinical indications.

Criteria

- Criteria for Initial Approval

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

1. The member is aged 18 years or older; and
2. The member has a diagnosis of unresectable or metastatic melanoma (Stage IIIC or Stage IV) with BRAF mutation testing; and
3. The member experienced disease progression following treatment with anti-PD-1 based therapy (eg, nivolumab, pembrolizumab); and
4. If the BRAF V600 mutation is present, the member experienced disease progression following treatment with BRAF inhibition (eg, vemurafenib, dabrafenib, encorafenib)
5. Evidence of adequate hematologic parameters, liver, and renal function within the past 3 months:
 - a. Absolute neutrophil count greater than 1,000/mm³; and
 - b. Hemoglobin greater than 9 g/dL; and
 - c. Platelets greater than 100,000/mm³; and
 - d. Alanine transaminase (ALT) and aspartate transaminase greater than 5 times the upper limit of normal; and
 - e. Estimated GFR greater than 40 mL/min; and
6. Within the past six months, the member:
 - a. Tested negative for HIV; and
 - b. Tested negative for HBV or HCV antibodies, or their viral load was undetectable; and
7. The treatment will be administered in an Amtagvi Authorized Treatment Center

B. Duration of Therapy

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

Exclusions

1. The member is deemed ineligible for IL-2 (aldesleukin) infusion.
2. The member has evidence of liver or kidney dysfunction.
3. The member's left ventricle ejection fraction (LVEF) is less than 45%.
4. The member's forced expiratory volume in one second (FEV-1) is less than or equal to 60% of predicted value.
5. The member is pregnant or plans to become pregnant during the treatment course.

Mass General Brigham ACO

Prior Authorization Required	Yes ☒ No ☐
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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](#).



One Care and Senior Care Options (SCO)

Prior Authorization Required	Yes ☐ No ☐
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Mass General Brigham Health Plan uses guidance from CMS for medical necessity determinations for its One Care and SCO plan members. NCDs, LCDs, LCAs, and documentation included in the Medicare manuals are the basis for medical necessity determinations. When there is no guidance from CMS for the requested service, or the member does not meet all of the medical necessity criteria for the requested service, Mass General Brigham Health Plan uses medical necessity guidelines from MassHealth. **See Medicare Advantage criteria and exclusions above. If Medicare Advantage criteria are not met, then MassHealth criteria are applied.**

Commercial and Qualified Health Plans

Prior Authorization Required	Yes ☒ No ☐
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Prior authorization for Amtagvi for Commercial and Qualified Health Plan members is managed by Prime Therapeutics. See [Prime Therapeutics policy for Amtagvi](#) for medical necessity information.

Codes

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

Authorized Code	Code Description
C9399	Unclassified drugs or biologicals
J3490	Unclassified drugs
J3590	Unclassified biologics
J9999	Not otherwise classified, antineoplastic drugs

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 Dates

January 1, 2027: Annual review. Reformatted policy. Streamlined criteria based on FDA label. Added exclusion for members who are pregnant or planning to become pregnant during course of treatment. References updated.

January 2026: Ad hoc review. Updated prior authorization table and added variation for One Care and SCO members.

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: Jovance, Sep 2025.

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. Tivance-301, a phase 3 study of lifileucel tumor-infiltrating lymphocyte (TIL) 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, 2024. 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.

