Blue Cross Blue Shield Blue Care Network of Michigan

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Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

Effective Date: 04/11/2024

Amtagvi™ (lifileucel)

HCPCS: J3590

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved indication
   b. FDA approved age
   c. Must have progressive disease following at least one prior systemic therapy including a programmed cell death protein ligand-1 (PD-1) inhibitor and if BRAF V600 mutation-positive, a BRAF inhibitor or BRAF inhibitor in combination with a MEK inhibitor
   d. Must have at least one measurable, resectable lesion that is a minimum of 1.5 cm in diameter post-resection
   e. Must not have any of the following:
      i. ECOG performance status > 1
      ii. Absolute neutrophil count (ANC) ≤ 1,000/mm^3
      iii. Hemoglobin < 9.0 g/dL
      iv. Platelets ≤ 100,000/mm^3
      v. Alanine transaminase (ALT) and aspartate transaminase (AST) ≥ 5 time the upper limit of normal (ULN)
      vi. Creatinine clearance < 40 mL/min
      vii. Left ventricular ejection fraction (LVEF) < 45%
      viii. Symptomatic and/or untreated brain metastases
      ix. History of another primary malignancy that has not been in remission for at least 3 years prior to consideration of Amtagvi
      x. Infection that is uncontrolled or requires IV or long-term oral antimicrobial therapy
      xi. HIV infection; hepatitis B or C virus infection permitted only if viral load undetectable
      xii. Any primary immunodeficiency
   f. Have not received prior treatment with any tumor infiltrating lymphocyte (TIL) therapy despite indication or any other genetically-modified TIL therapy or are being considered for treatment with any other genetically-modified TIL therapy
   g. Only to be administered at a certified TIL treatment center
   h. Trial and failure, contraindication, or intolerance to the preferred drugs as listed in BCBSM/BCN's utilization management medical drug list

B. Quantity Limitations, Authorization Period and Renewal Criteria
    a. Quantity Limit: Align with FDA recommended dosing
    b. Authorization Period: 3 months with the allowance of only one dose per lifetime
    c. Renewal Criteria: Not applicable as no further authorization will be provided

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Tumor infiltrating lymphocyte (TIL) therapy is a type of treatment the utilizes the body's own immune system to fight cancer. The immune system naturally creates TIL cells that can recognize distinctive markers on the surface of cancer cells and launch an attack. To make TIL therapy, a patient's TIL cells are collected from a portion of their resected tumor and then expanded outside the body before being infused back into the patient. Once the body is resupplied with TIL cancer-fighting immune cells, tumor cells are attacked and killed.

- TIL therapy has not been studied when given following prior treatment with any TIL therapy or following any other genetically-modified TIL therapy.

- Due to the risk of treatment-related deaths, prolonged severe cytopenia, severe infection, cardiopulmonary impairment, and kidney impairment, TIL therapy is only allowed to be given at certified inpatient treatment centers. The labeling requires patients be monitored for side effects in an intensive care facility and that specialists be available.

- Amtagvi is a tumor-derived autologous T cell immunotherapy indicated for the treatment of adult patients with unresectable or metastatic melanoma previously treated with a PD-1 blocking antibody, and if BRAF V600 mutation positive, a BRAF inhibitor with or without a MEK inhibitor.

- Safety and efficacy were established in the C-144-01 trial, a phase II, open-label, single-arm, multicenter study in patients with advanced melanoma who had progressed following a PD-1 inhibitor and BRAF ± MEK targeted agents if indicated. The primary efficacy analysis set included 82 patients who received Amtagvi, among these, 9 patients received Amtagvi at a dose less than 7.5×10^9 viable cells and did not achieve an objective response. Amtgavi was produced from harvested tumor specimens with an average manufacturing time of 23 days and median time to infusion of 34 days. Patients received a non-myeloablative lymphodepletion regimen, a single infusion of Amtagvi, and up to six doses of high-dose interleukin-2. The study excluded patients with an ECOG score of greater than 1, a creatinine clearance of less than or equal to 40 mL/minute, hemoglobin less than 9.0 g/dL, and left ventricular ejection fraction less than 45%. Patients were also excluded if they had an absolute neutrophil count less than 1000 cells/mm^3, platelet count less than 100,000/mm^3, symptomatic and/or untreated brain metastases, history of another primary malignancy that has not been in remission for at least 3 years prior to consideration of Amtagvi, infection that is uncontrolled or requires IV or long-term oral antimicrobial therapy, a detectable HIV, hepatitis B or C viral load, or any primary immunodeficiency. Patients were required to have at least one measurable, resectable lesion that is a minimum of 1.5 cm in diameter post-resection. The primary endpoints included objective response rate (ORR) and duration of response (DoR). The ORR was 31.5% (95% CI: 21.1, 43.4) with 3 complete responses (CR) and 20 partial responses (PR). The median time to initial response was 1.5 months with the median DoR not reached after 18.6 months.

References:

1. Amtagvi [prescribing information]. Philadelphia, PA: Iovance Biotherapeutics Manufacturing LLC; February 2024.
2. Liu A. FDA approves Iovance's Amtagvi as first T-cell therapy for a solid tumor. 2024 Feb 17. Available at: https://www.fiercepharma.com/pharma/fda-approves-iovances-amtagvi-first-cell-therapy-solid-tumor. Accessed on February 19, 2024.
3. Chesney J, Lewis KD, Kluger H, 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. J ImmunoTher Cancer. 2022; 10: e005755.
4. National Comprehensive Cancer Network. Melanoma: cutaneous (Version 1.2024). 2024 Feb 12. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cutaneous_melanoma.pdf. Accessed on February 19, 2024.

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<tr><td>1.2</td><td>Effective Date: 04/01/2024</td><td>UM medical management system update for MAPPO and BCNA
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** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*