LOUISIANA BLUE

afamitresgene autoleucel (Tecelra®)

Policy # 00911
Original Effective Date: 01/01/2025
Current Effective Date: 01/01/2025

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider the use of afamitresgene autoleucel (Tecelra®)‡ for the treatment of unresectable or metastatic synovial sarcoma to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for afamitresgene autoleucel (Tecelra) will be considered when the following criteria are met:

- Patient has a diagnosis of unresectable or stage IV synovial sarcoma; AND
- Patient is ≥ 18 years of age; AND
- Patient is human leukocyte antigen (HLA) positive for at least ONE of the following: HLA-A*02:01P, HLA-A*02:02P, HLA-A*02:03P, HLA-A*02:06P; AND
- Patient is NOT heterozygous or homozygous for HLA-A*02:05P; AND
- Tumor expresses melanoma-associated antigen A4 (MAGE-A4); AND
- Patient has received and progressed after at least one prior systemic chemotherapy regimen containing either an anthracycline (e.g., daunorubicin, doxorubicin, idarubicin, or mitoxantrone) or ifosfamide; AND
- Patient has not been previously treated with Tecelra or any other genetically modified T cell therapy (for example, CAR-T, CAR-NK); AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient has an Eastern Cooperative Oncology Group (ECOG) performance status score of 0 or 1; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

- Patient does not have symptomatic central nervous system (CNS) metastases including leptomeningeal disease; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Tecelra will be administered intravenously as a single dose between 2.68 x 10^9 and 10 x 10^9 MAGE-A4 TCR-positive T cells.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of afamitresgene autoleucel (Tecelra) in patients previously treated with Tecelra or another genetically modified T cell therapy, who have an ECOG performance status score greater than 1, or who have symptomatic CNS metastases to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of afamitresgene autoleucel (Tecelra) when the patient selection criteria are not met (except those listed above as **not medically necessary****) to be **investigational.***

Background/Overview

Tecelra is a melanoma-associated antigen A4 (MAGE-A4) directed genetically modified autologous T cell immunotherapy indicated for the treatment of adults with unresectable or metastatic synovial sarcoma who have received prior chemotherapy, are HLA-A*02:01P, -A*02:02P, -A*02:03P, or -A*02:06P positive; and whose tumor expresses the MAGE-A4 antigen as determined by FDA-approved or -cleared companion diagnostic devices. It is the first FDA-approved T-cell receptor (TCR) gene therapy and the second cell therapy for a solid tumor cancer. It targets MAGE-A4, which is highly expressed in HLA-A*02-positive synovial sarcoma.

Treatment with Tecelra involves removing some of the patient's T cells via leukapheresis and modifying them to express a TCR that targets MAGE-A4. Prior to administration of the drug, patients must receive lymphodepleting chemotherapy with fludarabine and cyclophosphamide beginning 7 days prior to infusion of Tecelra. After treatment, patients must be monitored for at least 4 weeks for adverse effects including severe cytokine release syndrome (CRS) or immune effector cell-associated neurotoxicity syndrome (ICANS).

Synovial sarcoma is a rare, aggressive soft tissue sarcoma that can occur in many parts of the body but most commonly develops in the extremities. It is estimated to affect around 1000 people in the United States each year, most of whom are adult males in their 30s or younger. Of these patients, it is estimated that 400 will be eligible to receive Tecelra. Initial treatment of synovial sarcoma

involves surgery to remove the tumor and may also include radiotherapy and/or chemotherapy if the tumor is larger, returns after being removed, or has spread beyond its original location. Prior to the availability of Tecelra, subsequent treatment options were limited to additional chemotherapy.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Tecelra was approved via the accelerated approval pathway in August 2024 for the treatment of adults with unresectable or metastatic synovial sarcoma who have received prior chemotherapy; are HLA-A*02:01P, -A*02:02P, -A*02:04P, or -A*02:06P positive; and whose tumor expresses the MAGE-A4 antigen as determined by FDA-approved or -cleared companion diagnostic devices.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Tecelra was evaluated in a multicenter, single-arm, open-label clinical trial (SPEARHEAD-1, Cohort 1). The study enrolled HLA-A*02:01P, HLA-A*02:02P, HLA-A*02:03P, and HLA-A*02:06P allele positive patients with inoperable or metastatic synovial sarcoma who had received prior systemic therapy with either doxorubicin and/or ifosfamide and whose tumor expressed the MAGE-A4 tumor antigen. The study included patients with measurable disease according to RECIST v1.1, Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1, and glomerular filtration rate (GFR) $\geq$ 60 mL/min. The study excluded patients with HLA-A*02:05P in either allele, patients on systemic corticosteroids for at least 14 days prior to leukapheresis and lymphodepletion, and recipients of allogeneic hematopoietic stem cell transplants.

Patients underwent high resolution HLA typing at a centralized testing site and had tumor samples tested for MAGE-A4 expression by an immunohistochemistry (IHC) clinical trial assay at a centralized testing site. Patients underwent leukapheresis for collection of autologous cells for processing and manufacture into Tecelra. Risk of manufacturing or delivery failure was 8% in clinical trial patients.

Patients received lymphodepleting chemotherapy with fludarabine 30 mg/m^2 for 4 days (Day -7 to Day -4) and cyclophosphamide 600 mg/m^2/day for 3 days (Day -7 to Day -5). Patients with GFR 60-79 mL/min received an adjusted fludarabine dose of 20 mg/m^2/day. Tecelra was administered as a single intravenous infusion on Day 1.

Of the 52 patients enrolled in the trial, 44 received an infusion of Tecelra. In this group, the median number of prior lines of systemic therapies was three (range: 1 to 12 lines). Between leukapheresis and the initiation of lymphodepletion, 16 (36%) of the 44 patients received bridging therapy. The most commonly used bridging therapy was pazopanib (69%). The median dose of Tecelra was 8 $x10^9$ MAGE-A4 TCR positive T cells (range: 2.68 x 10^9 to 9.99 x 10^9).

The major efficacy outcome measure was overall response rate (ORR) according to RECIST v1.1 evaluated by independent review committee. Duration of response (DoR) was an additional outcome measure. In the Tecelra-treated population, the ORR was 43.2% (95% CI: 28.4, 59.0) with a complete response rate of 4.5% and a partial response rate of 38.6%. The median DoR was 6 months (95% CI 4.6, NR) with a minimum of 1.9 and maximum of 36.1+ months. Thirty-nine percent of responders had a DoR of $\geq$ 12 months.

References

1. Tecelra [package insert]. Adaptimmune LLC. Philadelphia, PA. Updated August 2024.
2. Tecelra (afamitresgene autoleucel) New Drug Review. IPD Analytics. Updated August 2024.

Policy History

Original Effective Date: 01/01/2025
Current Effective Date: 01/01/2025
12/05/2024 Medical Policy Committee review
12/11/2024 Medical Policy Implementation Committee approval. New policy.
03/25/2024 Coding Update
Next Scheduled Review Date: 12/2025

Coding

The five character codes included in the Louisiana Blue Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2023 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	C9399, J9999 Add code effective 04/01/2025: Q2057
ICD-10 Diagnosis	All related Diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.
‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.