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Reviewed: 10/09/24

Revised: 04/01/25

Subject: Afamitresgene Autoleucel (Tecelra)

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Synovial sarcoma (SyS) is a rare, aggressive soft tissue sarcoma that can occur in many parts of the body but most commonly develops in the extremities. Each year, SyS affects about 1000 people in the United States. Treatment of SyS typically involves surgery to remove the tumor and may also include radiotherapy or chemotherapy if the tumor is larger, returns after being removed, or has spread beyond its original location.

Afamitresgene autoleucel (Tecelra), a melanoma-associated antigen A4 (MAGE-A4)–directed genetically modified autologous T cell immunotherapy, was approved by the U.S. Food and Drug Administration (FDA) on August 1, 2024 for the treatment of adults with unresectable or metastatic SyS 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. This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

The safety and efficacy of afamitresgene autoleucel were evaluated in a Phase 2, single-arm, open-label clinical trial (SPEARHEAD-1, NCT04044768) in adults with previously treated advanced or metastatic synovial sarcoma or myxoid round cell liposarcoma with HLA-A*02:01, HLA-A*02:02, HLA-A*02:03, HLA-A*02:06, or other HLA-A*02 alleles (excluding HLA-A*02:05) and a tumor sample positive for MAGE-A4. Patients underwent leukapheresis for collection of autologous cells for processing and manufacturing into Tecelra. Patients received lymphodepleting chemotherapy with fludarabine 30 mg/m2/day for 4 days (Day −7 to Day −4) and cyclophosphamide 600 mg/m2/day for 3 days (Day −7 to Day −5). The primary endpoint was overall response rate (ORR), defined as the proportion of patients in the analysis population with a complete or partial response.

A total of 52 patients with SyS were enrolled in Cohort 1 of the trial and underwent leukapheresis, eight of whom did not receive Tecelra due to death (n = 3), loss of eligibility prior to lymphodepleting chemotherapy (n = 3), withdrawal by patient (n = 1), and investigator decision (n = 1); 45 patients received lymphodepletion and one patient withdrew consent before treatment, for a total of 44 patients who received a single infusion of Tecelra. The primary efficacy outcome measure of ORR was 43.2% (95% CI: 28.4, 59.0). A complete response occurred in 2 patients (4.5%) and a partial response occurred in 17 patients (38.6%). The median time to response was 4.9 weeks (95% CI: 4.4, 8). The median duration of response was 11.6 months. Among patients who were responsive to the treatment, 45.6% and 39.0% had a duration of response ≥6 months and ≥12 months, respectively. Median progression free survival was 3.8 months and overall survival was 15.4 months.

All treated patients experienced an adverse event with cytopenias being the most common Grade 3 or greater adverse event; lymphopenia occurred in 96% of patients followed by neutropenia (85%) and leukopenia (81%). Prolonged cytopenias were reported in 19% of patients. Serious events were reported in 10% of patients. Cytokine release syndrome occurred in 71% of patients, but events were usually Grade 1 or 2, with one (2%) Grade 3 event. No treatment-related deaths were reported.

National Comprehensive Cancer Network (NCCN) Guidelines have not yet been updated to include recommendations for afamitresgene autoleucel.

POSITION STATEMENT:

Afamitresgene autoleucel (Tecelra) meets the definition of **medical necessity** when **ALL** of the following are met:

1. Member is diagnosed with unresectable or metastatic (stage IV) synovial sarcoma (SyS)
2. Member's disease is HLA-A*02:01P, -A*02:02P, -A*02:03P, or -A*02:06P positive – laboratory documentation must be provided
3. Member's tumor expresses the melanoma-associated antigen A4 (MAGE-A4) antigen as determined by FDA-approved or cleared companion diagnostic devices – laboratory documentation must be provided
4. Member's disease has progressed following at least one prior systemic chemotherapy – documentation from the medical record must be provided
5. Member will receive a lymphodepleting regimen of cyclophosphamide and fludarabine prior to infusion of afamitresgene autoleucel
6. Member will be 18 years of age or older at the time of the treatment infusion
7. Member has been assessed and has stable and adequate organ function (kidney, liver, pulmonary and cardiac function) and bone marrow function with no significant deterioration expected within 4 weeks as determined by the treating oncologist/hematologist
8. Afamitresgene autoleucel will not be administered if the member has an uncontrolled systemic infection at the time of planned treatment initiation
9. Member has **NOT** previously received tumor-derived autologous T cell immunotherapy (including afamitresgene autoleucel) in their lifetime for the treatment of SyS

10. The healthcare facility where afamitresgene autoleucel will be administered is a Tecelra Authorized Treatment Center
11. Dose does not exceed 10 x 10^9 MAGE-A4 T cell receptor (TCR) positive T cells
12. The administration of afamitresgene autoleucel will not exceed one single IV infusion

    NOTE: One of more infusion bags may be required to complete the single infusion

Approval duration: 3 months to allow for one-time infusion of therapy

DOSAGE/ADMINISTRATION:

FDA-approved

- The recommended dose is between 2.68 x 109 to 10 x 109 MAGE-A4 T cell receptor (TCR) positive T cells

Dose Adjustments

- None

Drug Availability

- A cell suspension for intravenous infusion.
- Provided in one or more infusion bag(s) containing 2.68 x 109 to 10 x 109 MAGE-A4 TCR positive T cells

PRECAUTIONS:

Boxed Warning

- Cytokine Release Syndrome (CRS), which may be severe or life-threatening, occurred in patients receiving TECELRA. At the first sign of CRS, immediately evaluate patient for hospitalization and institute treatment with supportive care. Ensure that healthcare providers administering TECELRA have immediate access to medications and resuscitative equipment to manage CRS

Contraindications

- DO NOT use TECELRA in adults who are heterozygous or homozygous for HLA-A*02:05P

Precautions/Warnings

- Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS): Monitor for ICANS events for at least 4 weeks after treatment with TECELRA
- Prolonged Severe Cytopenia: Patients may exhibit cytopenia (hemoglobin < 8.0 g/dL, neutrophils < 1,000/mm3, platelets < 50,000/mm3) for several weeks following lymphodepleting chemotherapy and TECELRA infusion. Monitor blood counts prior to and after TECELRA infusion
- Infections: Monitor patients for signs and symptoms of infection; treat appropriately
- Secondary Malignancies: In the event that a secondary malignancy occurs after treatment with TECELRA, contact Adaptimmune at 1-855-24MYADAP (1-855-246-9232)

- Hypersensitivity Reactions: Monitor for hypersensitivity reactions during infusion
- Effects on Ability to Drive and Use Machines: Advise patients to refrain from driving and engaging in hazardous occupations or activities, such as operating heavy or potentially dangerous machinery, for at least 4 weeks after receiving TECELRA

BILLING/CODING INFORMATION:

HCPCS Coding

Q2057	Afamitresgene autoleucel, including leukapheresis and dose preparation procedures, per therapeutic dose

ICD-10 Diagnosis Codes That Support Medical Necessity

C38.0-38.8	Malignant neoplasm of heart, mediastinum and pleura
C48.1-48.8	Malignant neoplasm of retroperitoneum and peritoneum
C49.0-49.9	Malignant neoplasm of connective and soft tissue

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

DEFINITIONS:

None

RELATED GUIDELINES:

None

OTHER:

None

REFERENCES:

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2. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 2024 [cited 9/1/24]. Available from: http://www.clinicalpharmacology.com/.
3. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine; 2000 Feb 29 - [cited 9/1/24]. Available from: http://clinicaltrials.gov/.
4. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 9/1/24].
5. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2024 [cited 9/1/24]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 10/09/24.

GUIDELINE UPDATE INFORMATION:

11/15/24	New Medical Coverage Guideline.
04/01/25	Revision: Added HCPCS code Q2057 and deleted code J9999.