Molina Clinical Policy
Tecelra (afamitresgene autoleucel) Policy No. 460

Last Approval: 08/14/2024
Next Review Due By: August 2025

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment, and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a Member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

OVERVIEW

This policy covers Tecelra (afamitresgene autoleucel or ADP-A2M4), an autologous T-cell therapy with an engineered T-cell receptor for the treatment of advanced synovial sarcoma.

Sarcomas are solid tumors of mesenchymal origin (embryonic tissue that gives rise to connective tissue and bone). Sarcomas are broadly divided into soft tissue sarcomas and bone sarcomas. Soft tissue sarcomas can originate from tendons, synovium, muscle, fat, vasculature, fibrous tissue, and other connective tissues.

Synovial sarcomas histologically resemble synovial cells, but the specific cell of origin is unknown. Most synovial sarcomas share a common chromosomal translocation between the X chromosome and chromosome 18. The resulting fusion protein from the translocation likely plays a role in tumorigenesis and its detection can aid in diagnosis and prognosis.

Patients with synovial sarcoma originating from the extremities present with a gradual growth of a deep seated, painless mass. When the mass is large enough, compression may cause symptoms such as edema, paresthesias, or pain from organ or nerve compression. Synovial sarcomas have a high potential for metastasis. Treatment is dependent on the location, grade, and stage. Local tumors are treated with local resection and are potentially curable. However, approximately 50% of patients thought to have local disease progress to metastatic synovial sarcoma which has been incurable to date. Treatments for aggressive synovial sarcoma include chemotherapy and targeted therapy such as pazopanib.

In August 2024, the FDA approved Tecelra under the accelerated approval pathway. “TECELRA is a genetically modified autologous T cell immunotherapy indicated for the treatment of adults with unresectable or metastatic synovial sarcoma who have received prior chemotherapy, and 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” (FDA package insert 2024). The companion MAGE-A4 diagnostic tool is called, “MAGE-A4 IHC 1F9 pharmDx.” MAGE-A4 (melanoma-associated antigen A4) is a cancer-testis antigen overexpressed in various cancers, including synovial sarcoma.

The genetic instructions to make a T cell receptor are introduced into CD4+ and CD8+ T cells ex vivo via a lentiviral vector. It takes about 1 month from cell collection, T cell isolation, genetic modification and expansion before the therapy is ready to infuse back into patients. Once infused into the patient, the engineered T cell recognizes MAGE-A4 tumor specific antigen bound to certain HLA complexes. This antigen-specific activation of modified T-cells via TCR-peptide-HLA-A*02 complex results in T cell proliferation, cytokine secretion, and killing of MAGE-A4/HLA-A*02 expressing synovial sarcoma cells (FDA prescribing information 2024).

RELATED POLICIES

MCP-184: Experimental and Investigational Services

COVERAGE POLICY

Tecelra (afamitresgene autoleucel) **may be considered medically necessary** when **ALL** the following criteria are met:

1. Age of member is ≥ 18 and ≤ 75
2. Diagnosis of advanced synovial sarcoma (metastatic or inoperable) & cytogenetics consistent with synovial sarcoma:
   a. Translocation t(X;18) between SYT on the X chromosome and SSX1, SSX2 or SSx4 on Chromosome 18
3. Prior treatment with anthracycline or ifosfamide containing regimen. Members intolerant of both anthracycline and ifosfamide must have had prior treatment with at least one other type of chemotherapy
4. Disease is measurable according to RECIST v1.1 (Response Evaluation Criteria in Solid Tumors v1.1)
5. The tumor is positive for HLA-A*02:01, HLA-A*02:03 or HLA-A*02:06 allele. HLA-A*02 alleles with the same protein sequence as these alleles in the peptide binding domains (P group) are also permitted. (Note: HLA-A*02:05 in either allele or having the same protein sequence as HLA-A*02:05) in the peptide binding domains is not permitted)
6. Tumor sample shows MAGE-A4 expression of ≥ 2+ staining in ≥ 30% of the cells by immunohistochemistry (P-score) per the companion diagnostic MAGE-A4 diagnostic tool, MAGE-A4 IHC 1F9 pharmDx.
7. Member has an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
8. Member has a left ventricular ejection fraction > 50%
9. Female members of childbearing potential must have a negative urine or serum pregnancy test and must agree to effective contraception starting at the first dose of chemotherapy and continuing for at least 12 months or 4 months after the gene modified cells are no longer detected in the blood
10. Male members must be either surgically sterile or agree to use double barrier contraception methods or abstain from heterosexual activity with a female of childbearing potential starting at the first dose of chemotherapy and continuing for 4 months thereafter
11. Members must have adequate organ function as indicated by the following laboratory values:
    a. Absolute neutrophil count ≥ 1.5 x 10^9/L (without G-CSF) within 7 days prior to lymphodepletion and leukapheresis
    b. Platelets ≥ 100 x 10^9/L (without transfusion support within 7 days prior to lymphodepletion and leukapheresis)
    c. Hemoglobin ≥ 80 g/L (without transfusion support within 7 days prior to lymphodepletion and leukapheresis)
    d. Prothrombin time or INR ≤ 1.5 x upper limit of normal unless receiving therapeutic anticoagulation
    e. Partial thromboplastin time (PTT) ≤ 1.5x upper limit of normal unless receiving therapeutic anticoagulation
    f. Glomerular filtration rate ≥ 60 ml/min
    g. Serum total bilirubin ≤ 1.5 x ULN (unless subject has documented Gilbert's Syndrome with direct bilirubin < 35% of total bilirubin)
    h. Alanine aminotransferase (ALT)/Serum Glutamic Pyruvic Transaminase ≤ 2.5x ULN
12. The member is not receiving or planning to receive the following therapies prior to leukapheresis or lymphodepleting chemotherapy:
    a. Cytotoxic chemotherapy (3 weeks washout period prior to either leukapheresis or lymphodepletion)
    b. Tyrosine kinase inhibitor (i.e., pazopanib; 1 week washout period prior to either leukapheresis or lymphodepletion)

c. Immune therapy (including monoclonal antibody therapy or checkpoint inhibitors. Four-week washout period is required prior to either leukapheresis or lymphodepletion)
d. Anti-cancer Vaccine (8 weeks washout period prior to either leukapheresis or lymphodepletion)
e. Gene therapy using an integrating vector other than a lentivirus is not permitted. If lentivirus has been used lentiviral quantification assay results must be consistently below the lower limit of quantification for at least 2 samples taken at least 1 month apart
f. Corticosteroids or any other immunosuppressive therapy (not including topical steroids). Two-week washout period is required prior to either leukapheresis or lymphodepletion)
g. Investigational or interventional clinical trial (Four-week washout period is required prior to either leukapheresis or lymphodepletion)
h. Allogeneic hematopoietic stem cell transplant is not permitted at all.
i. Targeted radiotherapy (three-month washout period prior to lymphodepletion; no washout required for palliative radiotherapy to non-target organs)
j. Major surgery (Four weeks post-surgery to allow for full recovery of surgical related toxicities)

13. Member must have recovered from previous anti-cancer therapy related toxicities to ≤ Grade 1 (except non-clinically significant toxicities such as alopecia or vitiligo). Irreversible or stable Grade 2 toxicities (for example peripheral neuropathy) are permitted

14. No history of allergic reactions attributed to compounds of similar chemical or biologic composition to fludarabine, cyclophosphamide

15. No history of autoimmune or immune mediated disease
    a. *Exceptions*
        i. Members with hypothyroidism, diabetes, adrenal insufficiency, or pituitary insufficiency that are stable on replacement therapy
        ii. Members with disorders such asthma, psoriasis or atopic dermatitis that are well controlled without requiring systemic immunosuppression

16. No history of active, symptomatic CNS metastases including leptomeningeal disease
    a. Members with a prior history of symptomatic CNS metastasis including leptomeningeal disease must have received treatment (i.e., stereotactic radiosurgery (SRS), whole brain radiation (WBRT) and/or surgery) and be neurologically stable for at least 1 month, not requiring anti-seizure medications and off steroids for at least 14 days prior to leukapheresis and lymphodepletion. Anti-seizure prophylaxis is permitted
    b. Members who have asymptomatic CNS metastases without associated edema, shift, requirement for steroids or anti-seizure medications for the treatment of seizures are permitted

17. No history of any other prior malignancy that is not in complete remission
    a. *Exceptions*:
        i. Resectable squamous or basal cell carcinoma of the skin
        ii. Prior malignancies that have been surgically resected and show no evidence of disease

18. No history of uncontrolled intercurrent illness including, but not limited to:
    a. Ongoing or active infection
    b. Clinically significant cardiac disease defined by congestive heart failure New York Heart Association (NYHA) Class 3 or Class 4
    c. Uncontrolled clinically significant arrhythmia
    d. Acute Coronary Syndrome (ACS) (angina or MI) in last 6 months
    e. Interstitial lung disease (subjects with existing pneumonitis due to radiation are permitted so long as they are not oxygen dependent)
    f. Congenital or family history of long QT syndrome
    g. Current uncontrolled hypertension despite optimal medical therapy
    h. History of stroke or central nervous system bleeding; transient ischemic attack (TIA) or reversible ischemic neurologic deficit (RIND) in last 6 months
    i. Incipient compression/occlusion of a vital structure (e.g. bronchus; superior vena cava; renal outflow tract) which cannot undergo prophylactic stenting
    j. COVID-19 infection or a positive COVID-19 RT-PCR test within 28 days of leukapheresis or

lymphodepleting chemotherapy. If a subject has a positive COVID-19 test, then two subsequent negative tests are required, taken at least 7 days apart

19. No history of active infection with HIV, HBV, HCV or HTLV as defined below:
    a. Positive serology for HIV
    b. Active hepatitis B infection as demonstrated by test for hepatitis B surface antigen
        i. Members who are hepatitis B surface antigen negative but are hepatitis B core antibody positive must have undetectable hepatitis B DNA and receive prophylaxis against viral reactivation. Prophylaxis should be initiated prior to lymphodepleting therapy and continued for 6 months
    c. Active hepatitis C infection as demonstrated by hepatitis C RNA test. Members who are HCV antibody positive will be screened for HCV RNA by any RT PCR and must obtain a negative screening RNA value
    d. Positive serology for HTLV 1 or 2
    e. Re-screening for infectious disease markers is not required at baseline (prior to lymphodepletion) unless > 6 months has elapsed

20. Not Pregnant or breastfeeding

Limitations and Exclusions

QUANTITY LIMITATIONS: FDA approved dosing with one-time dose per lifetime. Additional infusions of Tecelra will not be authorized.

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

CONTINUATION OF THERAPY
Tecelra is indicated as a one-time infusion only. Repeat treatment or re-administration of a dose is not supported by labeling or compendia and is not considered medically necessary.

DOCUMENTATION REQUIREMENTS. Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

SUMMARY OF MEDICAL EVIDENCE

Data from two trials led to the accelerated approval of Tecelra.

The SPEARHEAD-1 trial (NCT04044768) is a phase 2, non-randomized open label international, single arm study evaluating the safety and initial efficacy of Tecelra in advanced synovial sarcoma expressing HLA-A*02 and MAGE-A4. Data from Cohort 1 (the main investigational cohort; n = 44) was recently published (D'Angelo et al 2024). Participants were aged 16-75 years with metastatic, unresectable synovial cancer and had already received 2-4 previous lines of chemotherapy. The mean age was 40.5 years and genders were evenly split 50%.

A single dose of Tecelra was given post lymphodepletion followed by assessment at a median follow-up time of 32.6 months. The primary endpoint was overall response rate in cohort 1 using RECIST criteria version 1.1. Overall response rate was 39% (17 of 44) according to D'Angelo (2024). Additional trial results submitted to the FDA indicated an overall response rate of 43.2%, partial response in 17 (39%) and complete response in 2 (4.5%). The median duration of response for patients with synovial sarcoma was 11.6 months. By comparison to current standard of care, overall response to second line therapies and beyond in synovial sarcoma range from 4.2% to 14.7%.
The null hypothesis was defined by an overall response rate of 18% or less thus Tecelra met its primary endpoint.

No treatment related deaths occurred. No cases of replication-competent lentivirus or secondary malignancies. Adverse events included cytokine release syndrome (33%, all cases but one were below grade 3) and cytopenias. Other clinically important adverse reactions occurring in patients receiving Tecelra include Grade 1 ICANS (Immune Effector Cell-associated Neurotoxicity Syndrome) reported in one patient (2%).

The phase 1 study of Tecelra (NCT03132922) was an open label, single arm dose escalation trial looking at safety and tolerability in HLA-eligible patients with relapsed or refractory synovial sarcoma expressing MAGE-A4. This trial enrolled 16 patients with synovial sarcoma. The primary endpoint was the incidence of adverse events. All patients had at least 1 TEAE. Adverse events included anemia, lymphopenia, neutropenia, and thrombocytopenia. One patient died of aplastic anemia which may have been treated related. That patient and another in the highest dose group passed away due to treatment related effects. Cytokine release syndrome occurred in 55% of the patients most of which were below grade 3. Overall response rate was included in the secondary endpoints. The overall response rate was 44% (7 of 16) and a median duration of response was 28.1 weeks. Overall, the trial demonstrated an acceptable risk to benefit ratio in favor of treatment of synovial sarcoma with Tecelra.

National/Specialty Organizations
Currently there are no guidelines that mention Tecelra for synovial sarcoma due to its recent approval.

The **National Institute for Health and Care Excellence (NICE)** has not released guidelines for Tecelra.

CODING & BILLING INFORMATION

CPT (Current Procedural Terminology) Codes

Code	Description
96413	Chemotherapy administration, intravenous infusion technique; up to 1 hour, single or initial substance/drug
96415	Chemotherapy administration, intravenous infusion technique; each additional hour (List separately in addition to code for primary procedure)

HCPCS (Healthcare Common Procedure Coding System) Codes

Code	Description
C9399	Unclassified drugs or biologicals [when specified as Tecelra (afamitresgene autoleucel)]
J3590	Unclassified biologics [when specified as Tecelra (afamitresgene autoleucel)]

CODING DISCLAIMER. Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

08/14/2024 New policy. IRO Peer Review Pending on August 12, 2024, by a practicing physician board-certified in Oncology.

REFERENCES

1. Centers for Medicare and Medicaid Services (CMS). Medicare coverage database. No LCD or NCDs. Accessed August 9, 2024. https://www.cms.gov/medicare-coverage-database/search.aspx
2. ClinicalTrials.gov. NCT03132922. MAGE-A4^{c1032}T for Multi-Tumor. Last updated January 01, 2022. Accessed August 9, 2024. http://clinicaltrials.gov.
3. ClinicalTrials.gov. NCT04044768. Spearhead 1 Study in Subjects With Advanced Synovial Sarcoma or Myxoid/Round Cell Liposarcoma. Last updated February 20, 2024. Accessed August 9, 2024. http://clinicaltrials.gov.
4. D'Angelo SP, Araujo DM, Abdul Razak AR, et al. Afamitresgene autoleucel for advanced synovial sarcoma and myxoid round cell liposarcoma (SPEARHEAD-1): an international, open-label, phase 2 trial. Lancet. 2024 Apr 13;403(10435):1460-1471. doi: 10.1016/S0140-6736(24)00319-2. Epub 2024 Mar 27. PMID: 38554725.
5. Eisenhauer EA, Therasse P, Bogaerts J, et al. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). Eur J Cancer. 2009 Jan;45(2):228-47. doi: 10.1016/j.ejca.2008.10.026. PMID: 19097774.
6. FDA Package insert. TECELRA® (afamitresgene autoleucel) suspension, for intravenous infusion. August 2024. https://www.fda.gov/media/180565/download?attachment
7. Hayes: Afamitresgene Autoleucel (Tecelra; Adaptimmune LLC) for Advanced Synovial Sarcoma. Published August 5, 2024. Accessed August 6, 2024. https://evidence.hayesinc.com/.
8. Hong DS, Van Tine BA, Biswas S, et al. Autologous T cell therapy for MAGE-A4+ solid cancers in HLA-A*02+ patients: a phase 1 trial. Nat

Med. 2023 Jan;29(1):104-114. doi: 10.1038/s41591-022-02128-z. Epub 2023 Jan 9. PMID: 36624315; PMCID: PMC9873554.
9. Pokras S, Tseng WY, Espirito JL, et al. Treatment patterns and outcomes in metastatic synovial sarcoma: a real-world study in the US oncology network. Future Oncol. 2022 Oct;18(32):3637-3650. doi: 10.2217/fon-2022-0477. Epub 2022 Aug 26. PMID: 36018238.
10. UpToDate. Clinical presentation, diagnostic evaluation, and staging of soft tissue sarcoma. Ryan, Christopher Meyer, Janelle. Last updated July 3, 2024. Accessed August 5, 2024. http://www.uptodate.com