Molina Clinical Policy
Aucatzyl (obecabtagene autoleucel): Policy No. 462

Last Approval: 12/11/2024
Next Review Due By: December 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 reviews the use of Aucatzyl for the treatment of adult patients with acute, relapsed / refractory (r/r), B-cell precursor, lymphoblastic leukemia (B-ALL).

The incidence of ALL is 1-5 / 100,000 worldwide with two thirds of ALL being of B cell type. While it is most common in children under 6, there is a bimodal distribution with another peak in adults greater than 60 years old. B-ALL cancer almost always has CD-19 antigens and is why CAR-Ts are directed at this protein. Approximately 25% of adults with ALL have the Philadelphia chromosome subtype (Advani et al. 2024). The pathophysiology of B-ALL begins with poorly differentiated lymphoid blast cells that proliferate excessively leading to suppression of normal hematopoiesis. These abnormal cells are present in bone marrow, peripheral blood and other extramedullary sites. Symptomatology at disease onset, including fatigue, easy bruising, and frequent infections, are related to the induced cytopenias (anemia, thrombocytopenia and neutropenia). Occasionally very elevated white blood cells can be found in the peripheral blood. Diagnosis is based on the identification of excessive circulating lymphoblasts. Constitutional symptoms as well as painless lymphadenopathy, organomegaly and neuropathies may occur. B-cell lymphoblastic lymphoma and B-cell lymphoblastic leukemia are the same disease with overlapping manifestations.

Aucatzyl (obecabtagene autoleucel, obe-cel) is a genetically modified, autologous T cell immunotherapy directed at the CD19 antigen found on B- cells. Approval of Aucatzyl is based on the FELIX trial which showed improved overall survival rates in adult patients with acute, relapsed / refractory, B-cell precursor, lymphoblastic leukemia (B-ALL). Manufacture involves apheresis of CD4+ and CD8+ T cells from the peripheral blood which are then transduced ex vivo with a lentiviral vector encoding a chimeric antigen receptor directed at the surface CD19 protein found on B cells (Autolus 2024). Aucatzyl CAR-T therapy is dosed based on disease burden and the dose is split into two parts. The manufacturer has suggested their CAR-T therapy has a lower toxicity profile and less T-cell exhaustion leading to more persistent durable remissions. The FDA approved Aucatzyl without a requirement for a Risk Evaluation Mitigation Strategy (REMS) program. REMS is a program mandated by the FDA for other CAR-T therapies to ensure the safe administrations and management of adverse events. While REMS requirement was not stated in the Aucatzyl label (FDA 2024), there is still a boxed warning for cytokine release syndrome, neurotoxicity, and secondary hematologic malignancy. Malignancy risk was based on this class of therapies, no malignancies have been reported in the early experiences with obe-cel.

RELATED POLICIES

MCP-184: Experimental and Investigational Services

COVERAGE POLICY

Aucatzyl (obecabtagene autoleucel, obe-cel) may be **considered medically necessary** when ALL the following criteria are met:

1. Diagnosed with acute, relapsed / refractory (r/r), B-cell precursor, lymphoblastic leukemia (B-ALL)

2. Member is age 18 years or older

3. ECOG performance status of 0 or 1

4. Patients with Ph+ ALL are eligible if intolerant to tyrosine kinase inhibitors (TKI), failed two lines of any TKI, or failed one line of second-generation TKI, or if TKI is contraindicated

5. Documented CD19 positivity on leukemic blasts within 1 month of screening

6. Presence of ≥ 5% blasts in bone marrow assessment or a positive result for minimal residual disease (MRD) after a second CR/CRi (complete remission /complete remission with incomplete hematologic recovery. MRD-positive defined as ≥ 1 x 10^{-3} by central ClonoSEQ® NGS testing and <5% blasts in bone marrow assessment)

7. Adequate renal, hepatic, pulmonary, and cardiac function as defined by the following:
    a. Serum alanine aminotransferase / aspartate aminotransferase (ALT/AST) ≤ 2.5 x upper limit of normal (ULN)
    b. Creatinine clearance (as estimated by Cockcroft Gault) ≥ 50 cc/minute
    c. Total bilirubin ≤ 1.5 x ULN, except for patients with Gilbert's syndrome
    d. Left ventricular ejection fraction (LVEF) ≥ 45% (or ≥ institutes lower limit of normal) confirmed by echocardiogram (ECHO) or multigated acquisition (MUGA) in patients with history of coronary artery disease or cardiovascular disease or those with a history of low LVEF
    e. Baseline oxygen saturation ≥ 92% on room air

8. Member does not have isolated extramedullary disease

9. Member does not have a diagnosis of Burkitt leukemia/lymphoma or chronic myelogenous leukemia lymphoid in blast crisis

10. Member does not have a history or presence of clinically relevant central nervous system (CNS) pathology such as epilepsy, paresis, aphasia, or strokes 3 months prior to obe-cel administration or other severe brain injuries, dementia, Parkinson's disease, cerebellar disease, organic brain syndrome, or uncontrolled mental illness or psychosis

11. CNS staging does not reveal the presence of CNS-3 disease or CNS-2 disease with neurological changes (CNS staging table in supplemental information section)

12. Member does not have active or uncontrolled fungal, bacterial, viral, or other infection requiring systemic antimicrobials for management

13. Member does not have active or latent Hepatitis B virus or active Hepatitis C virus

14. Member does not have Human Immunodeficiency Virus (HIV), HTLV-1 (Human T-Lymphotropic Virus Type 1), HTLV-2 (Human T-Lymphotropic Virus Type 2), or is syphilis positive

15. Member does not have prior CD19 targeted therapy other than blinatumomab. Member has not experienced Grade 3 or higher neurotoxicity following blinatumomab

LIMITATIONS AND EXCLUSIONS:

QUANTITY LIMITATIONS: FDA approved split dosed therapy once per lifetime. Additional infusions of Aucatzyl will not be authorized.

CONTINUATION OF THERAPY

Aucatzyl (Obe-cel) is indicated as a split dosed infusion only. Repeat treatment is not supported by labeling or compendia and is not considered medically necessary.

Continued Aucatzyl therapy is considered **experimental, investigational, and unproven** due to insufficient evidence in the peer-reviewed medical literature to establish long-term safety, efficacy, and effect on net health outcomes.

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

Approval was based on the FELIX trial (NCT04404660) an open label, multicenter, global, single arm, phase 1b / 2 study. 153 participants were enrolled, 127 received at least one of the two required infusions of obe-cel. Participants were split into the two phases, phase 1 and phase 2. Data for approval were focused on phase 2, cohort 2A. The phase 1 aim was just to evaluate the feasibility of manufacturing and administering obe-cel per protocol. A bone marrow burden-guided split dose regimen was used. Before lymphodepletion all patients underwent bone marrow assessment and initial dosing was based on the amount of bone marrow blasts. The second dose was given in the absence of cytokine release syndrome and ICANS (Roddie et al. 2024).

Phase 2A had 94 participants of which 88 of 94 received both doses of obe-cel. Data cut off was February 7, 2024. The median age was 47 years, and this group had between 2-6 previous lines of therapy. Key inclusion criteria were relapsed/refractory adult B-ALL with five percent or more bone marrow blasts or minimal residual disease (greater than or equal to 0.1% blasts but less than 5% blasts). Bridging therapy was allowed. Lymphodepletion was required prior to dosing (Roddie et al. 2024). Key exclusions were those with isolated extra medullary disease, active or serious infections requiring systemic antimicrobials, active graft versus host disease, history or presence of CNS disorders (FDA package insert 2024).

The primary endpoint was overall remission. Overall remission was 77% in cohort 2A. The secondary endpoint was complete remission. 55% met the secondary endpoint and 21% had complete remission with incomplete hematologic recovery. Both outcomes, overall remission and complete remission, exceeded the threshold for positive effect. The median duration of response was 14.1 months The median event free survival was 9 months.

There was a high incidence of overall remission across all patient groups, but a lower incidence of remission observed in patients with high bone marrow burden (>75% bone marrow blasts before lymphodepletion). The authors suggested low to intermediate bone marrow burden is optimal for CAR-T therapy and optimizing bridging therapies prior to CAR-T therapy may optimize outcomes. In comparison to reported adverse events from Tecartus therapy, Obe-cel had much lower rates of cytokine release syndrome at grade 3 or higher, 2.4% with obe-cel, compared to 24 -26% for Tecartus. Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) higher than grade 3 was also higher in Tecartus at 25-35% compared to obe-cel at 2.4%. The toxic effects of obe-cel were mostly limited to those with high bone marrow burden.

There were two patient deaths attributable to obe-cel: one due to acute respiratory distress syndrome and ICANS and another due to neutropenic sepsis. No REMS requirement was noted in the FDA label but there is still a boxed warning for cytokine release syndrome CRS, neurotoxicity, and secondary hematological malignancy. The most common (non-laboratory) adverse reactions (incidence ≥ 20%) were: CRS, infections - pathogen unspecified, musculoskeletal pain, viral infections, fever, nausea, bacterial infectious disorders, diarrhea, febrile neutropenia, ICANS, hypotension, pain, fatigue, headache, encephalopathy, and hemorrhage.

Other clinical trials for Obe-cel include those for systemic lupus erythematosus (NCT06333483) and obe-cel for B-ALL in pediatric patients and aggressive non-Hodgkin B-cell lymphoma (NCT06173518).

National and Specialty Organizations

Obe-cel was just approved in 2024 and guidelines to date have not specifically included obe-cel in their recommendations.

SUPPLEMENTAL INFORMATION

CNS staging status definitions - Table 1 (Thastrup et al. 2022)

CNS staging is a function of white blood cells count in cerebrospinal fluid along with microscopy of a cyto-centrifuged CSF sample to morphologically identify leukemic blasts. CNS status is also given to patients with clinical or radiological evidence of CNS-leukemia, irrespective of CSF findings e.g., cranial nerve palsies, or other neurological symptoms that mostly, but not always, are associated with CNS-imaging findings.

	CSF cytospin findings		
CNS status	**WBCs/µL**	**RBCs/µL**	**Leukemic blasts**
CNS1	≤5	<10	Absent
CNS2	≤5	<10	Present
CNS3	>5	<10	Present
TLP+	N/A	≥10	Present
TLP−	N/A	≥10	Absent

CNS central nervous system, *CSF* cerebrospinal fluid, *N/A* not applicable, *RBCs* red blood cells, *TLP* traumatic lumbar puncture, *WBCs* white blood cells.

CODING & BILLING INFORMATION

CPT (Current Procedural Terminology)

Code	Description
38225	Chimeric antigen receptor T-cell (CAR-T) therapy; harvesting of blood-derived T lymphocytes for development of genetically modified autologous CAR-T cells, per day
38226	Chimeric antigen receptor T-cell (CAR-T) therapy; preparation of blood-derived T lymphocytes for transportation (e.g., cryopreservation, storage)
38227	Chimeric antigen receptor T-cell (CAR-T) therapy; receipt and preparation of CAR-T cells for administration
38228	Chimeric antigen receptor T-cell (CAR-T) therapy; CAR-T cell administration, autologous

HCPCS (Healthcare Common Procedure Coding System)

Code	Description
C9301	Obecabtagene autoleucel, up to 400 million CD19 CAR-positive viable T cells, including

	leukapheresis and dose preparation procedures, per therapeutic dose *[effective until 06/30/2025]*
Q2058	Obecabtagene autoleucel, 10 up to 400 million cd19 CAR-Positive viable T cells, including leukapheresis and dose preparation procedures, per infusion *[effective 07/01/2025]*

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

12/11/2024 New policy. IRO completed December 2024 by practicing physician board certified in hematology / oncology.

REFERENCES

1. Advani A, Larson R, Rosmarin A. Clinical manifestations pathologic features and diagnosis of B-cell acute lymphoblastic leukemia/lymphoma. https://www.uptodate.com. Updated September 27, 2022.
2. ClinicalTrials.gov. National Library of Medicine. NCT04404660. A Study of CD19 Targeted CAR T Cell Therapy in Adult Patients with Relapsed or Refractory B Cell Acute Lymphoblastic Leukaemia (ALL). Last updated September 3, 2024. Accessed November 11, 2024.
3. Roddie C, Sandhu KS, Tholouli E, et al. Obecabtagene Autoleucel in Adults with B-Cell Acute Lymphoblastic Leukemia. N Engl J Med. 2024 Nov 27. doi: 10.1056/NEJMoa2406526. Epub ahead of print. PMID: 39602653.
4. Roddie C, Sandhu KS, Tholouli E, et al. S262: Safety and efficacy of Obecabtagene autoleucel (Obe-cel), A fast Off rate CD19 CAR in r/r Adult B-cell acute lymphoblastic leukemia: Top line results of Pivotal FELIX study. Hemasphere. 2023 Aug 8;7(Suppl):e998506d. doi: 10.1097/01.HS9.0000967960.99850.6d. PMCID: PMC10428320.
5. Thastrup M, Duguid A, Mirian C, et al. Central nervous system involvement in childhood acute lymphoblastic leukemia: challenges and solutions. Leukemia. 2022 Dec;36(12):2751-2768. doi: 10.1038/s41375-022-01714-x. Epub 2022 Oct 20. PMID: 36266325; PMCID: PMC9712093.
6. United States Food and Drug Administration (FDA). Aucatzyl (obecabtagene autoleucel) FDA Prescribing information. November 2024. https://www.fda.gov/media/183463/download?attachment

APPENDIX

Reserved for State specific information. *Information includes, but is not limited to, State contract language, Medicaid criteria and other mandated criteria.*