CLINICAL GUIDELINES FOR MEDICAL NECESSITY

MEDICAL POLICY

Obecabtagene Autoleucel (Aucatzyl®)

Version: 1.0

EFFECTIVE DATE: 2/1/2025

NantHealth® | Eviti®

Please note the following:

Obecabtagene Autoleucel (Aucatzyl®)

Note: For Medicare members/enrollees, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Please refer to the CMS website at http://www.cms.gov for additional information.

Note: For Medicaid members/enrollees, circumstances when state Medicaid coverage provisions conflict with the coverage provisions within this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Obecabtagene Autoleucel (Aucatzyl): Discussion

Acute lymphoblastic leukemia (ALL) is a heterogeneous hematologic disease characterized by the proliferation of immature lymphoid cells in the bone marrow, peripheral blood, and other organs. The age-adjusted incidence rate of ALL in the US is 1.8 per 100,000 individuals per year, with approximately 6550 new cases and 1330 deaths estimated in 2024. The median age at diagnosis for ALL is 17 years with 53.5% of patients diagnosed at younger than 20 years of age. In contrast, 29.6% of cases are diagnosed at 45 years or older and only approximately 13.7% of patients are diagnosed at 65 years or older. ALL represents 75% to 80% of acute leukemias among children, making it the most common form of childhood leukemia; by contrast**,** acute lymphoblastic leukemia represents approximately 20% of all leukemias among adults.[1]

Obecabtagene autoleucel is a CD19-directed genetically modified autologous T cell immunotherapy consisting of the patient's own T cells expressing an anti-CD19 CAR. Engagement of anti-CD19 CAR-positive T cells with CD19 expressed on target cells, such as cancer cells and normal B cells, leads to activation of the anti-CD19 CAR-positive T cells and downstream signaling through the CD3-zeta domain. Proliferation and persistence by the anti-CD19 CAR-positive T cells following activation are enhanced by the presence of the 4-1BB co-stimulatory domain. This binding to CD19 results in anti-tumor activity and killing of CD19-expressing target cells.

Available CAR-T therapies are customized for each individual patient. They are made by collecting T cells from the patient and re-engineering them in the laboratory to produce proteins on their surface called chimeric antigen receptors, or CARs. The CARs recognize and bind to specific proteins, or antigens, on the surface of the cancer cells. After the revamped T cells are expanded into the millions in the laboratory, they are infused back into the patient. The CAR-T cells will continue to multiply in the patient's body and, with guidance from their engineered receptor, recognize and kill any cancer cells that harbor the target antigen on their surfaces.

A life-threatening complication of CAR-T therapy called cytokine release syndrome (CRS) occurred in 75% of patients receiving obecabtagene autoleucel. The prescribing information has a box warning for cytokine release syndrome (CRS), immune effector cell-associated

neurotoxicity syndrome (ICANS) and T cell malignancies. CRS occurred in 75% (Grade 3, 3%) and neurologic toxicities occurred in 64% (Grade ≥3, 12%), including ICANS in 24% (Grade ≥3, 7%).The most common non-laboratory adverse reactions (incidence ≥ 20%) included CRS, infections-pathogen unspecified, musculoskeletal pain, viral infections, fever, nausea, bacterial infectious disorders, diarrhea, febrile neutropenia, ICANS, hypotension, pain, fatigue, headache, encephalopathy, and hemorrhage.

The National Comprehensive Cancer Network (NCCN) and Food and Drug Administration (FDA) approved obecabtagene autoleucel for acute lymphoblastic leukemia (ALL).[1,2]

Obecabtagene Autoleucel: Definitions

- **Food and Drug Administration (FDA)** - The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation.
- **National Comprehensive Cancer Network (NCCN)** - An alliance of more than 30 leading cancer centers devoted to patient care, research, and education. The NCCN guidelines are utilized for Radiation Therapy and Medical Oncology standards. NCCN consensus clinical standards are periodically updated and Nanthealth, Inc. reviews these and updates its policies within a timely manner.
- **Risk Evaluation and Mitigation Strategy (REMS)** - A drug safety program to manage known or potential risks associated with a drug(s) and is required by the US Food and Drug Administration (FDA) to ensure that the benefits of a drug outweigh its risks. These therapies are only available through this restricted program. The program ensures that hospitals and their associated clinic(s) that dispense these drugs are specially certified and have on-site, immediate access to a minimum of two doses of tocilizumab. The program also ensures that those who prescribe, dispense, or administer these drugs are aware of how to manage the risks of CRS and neurologic toxicities. Currently, obecabtagene autoleucel is not a part of the REM program.[4]

Obecabtagene Autoleucel: Policy

Note: Coverage of obecabtagene autoleucel will be provided for FDA-approved indications or National Comprehensive Cancer Network (NCCN) guidelines when it is a Category 1, 2A, or 2B recommendation OR when all criteria are met.

Obecabtagene Autoleucel will be considered for coverage when the following criteria are met:

Acute Lymphoblastic Leukemia

1. At least 18 years of age; AND

2. Prescribed by or in consultation with an oncologist; AND

For **FDA** required criteria coverage:

3. Relapsed/refractory disease with one of the following:
   a) 2 or more prior lines of systemic therapy
   b) 3 or more months after allogeneic stem cell transplantation[1]; OR

For **NCCN** required criteria coverage:

4. Single-agent CD19 antigen-directed therapy for relapsed or refractory (R/R) disease for one of the following:
   a) Philadelphia chromosome-positive B-ALL following therapy that has included TKIs
   b) Philadelphia chromosome-negative disease.[2]

   Note:

   1. Patients will receive a lymphodepleting chemotherapy regimen. This regimen of cyclophosphamide and fludarabine is per the physician's discretion.
   2. Patients must have an ECOG performance of 0 to 1.
   3. Patients must be screened for hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV).[1,2]

Dosage:

The dose of obecabtagene autoleucel is 410 X 106 CD19 chimeric antigen receptor (CAR)-positive viable T cells to be administered as a split dose infusion on Day 1 and Day 10 (±2 days) based on bone marrow blast assessment and preceded by fludarabine and cyclophosphamide lymphodepleting chemotherapy.[1]

For reauthorization:

Obecabtagene autoleucel is a one-time dose and will not be renewed.

Obecabtagene Autoleucel: References

1. Obecabtagene autoleucel (Aucatzyl) Package Insert. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-obecabtagene-autoleucel-adults-relapsed-or-refractory-b-cell-precursor-acute. Accessed February 21, 2025.
2. National Comprehensive Cancer Network Guidelines. Acute Lymphoblastic Leukemia. https://www.nccn.org/professionals/physician_gls/pdf/all.pdf. Accessed February 21, 2025.

3. CAR T Cells: Engineering Patients' Immune Cells to Treat Their Cancers. https://www.cancer.gov/about-cancer/treatment/research/car-t-cells/. Accessed February 21, 2025.
4. Risk Evaluation and Mitigation Strategy (REMS). https://www.fda.gov/drugs/drug-safety-and-availability/risk-evaluation-and-mitigation-strategies-rems. Accessed February 21, 2025.

Obecabtagene Autoleucel: Coding (CPT®, ICD 10 and HCPCS) *

*Procedure codes appearing in medical policy documents are only included as a general reference. This list may not be all-inclusive and is subject to updates. In addition, the codes listed are not a guarantee of payment. CPT codes are available through the AMA.

Code	Description
C91.0, C91.02	Acute lymphoblastic leukemia
J999	Obecabtagene autoleucel
0537T	Chimeric antigen receptor T-cell (CAR-T) therapy; harvesting of blood-derived T lymphocytes for development of genetically modified autologous CAR-T cells

Obecabtagene Autoleucel: Revision and Review History

No.	Description	Date(s)
1	Original Effective Date:	2/1/2025
2	Policy Review Dates:	
3	Policy Revision Dates:	
4	Department Owner:	Medical Affairs
5	NH Advisory Committee Approval Dates:	2/25/2025
6	Revision Changes:	