Mass General Brigham
Health Plan

Medical Policy
Aucatzyl (Obecabtagene Autoleucel)

Policy Number: 088

	Commercial and Qualified Health Plans	MassHealth	Medicare Advantage
Authorization Required	X	X	X
No Prior Authorization			

Overview
Aucatzyl is a chimeric antigen receptor T cell therapy (CAR-T), designed to harness the power of the patient's immune system to recognize and attack their cancer cells. CAR-T is a type of treatment where white blood cells (T cells) are modified in a laboratory to add a gene that helps the patient's own T cells target their cancer.

FDA-Approved Indication
Indicated for the treatment of adults with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL)

Criteria

1. Criteria for Initial Approval
    a. At least 18 years of age; and
    b. Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 or 1; and
    c. Relapsed or refractory CD19-positive B-ALL defined as one of the following:
        i. Primary refractory disease (not achieving CR after two cycles of induction chemotherapy; or
        ii. First relapse if first remission up to 12 months; or
        iii. Relapsed or refractory disease after two or more lines of systemic therapy, or
        iv. Relapsed or refractory disease after allogeneic transplant provided obe-cel infusion occurs at least 3 months after stem cell transplant; and
    d. If member has CD19-positive Ph+ ALL, is intolerant to or has failed two lines of any tyrosine kinase inhibitor therapy or one line of second-generation tyrosine kinase inhibitor therapy, or if tyrosine kinase inhibitor therapy is contraindicated; and
    e. Presence of at least 5% blasts in BM; and
    f. Adequate renal, hepatic, pulmonary, and cardiac function defined as:
        i. Serum alanine aminotransferase/aspartate aminotransferase up to 2.5×ULN; and
        ii. Creatinine clearance (as estimated by Cockcroft Gault) at least 50 cc/minute; and
        iii. Total bilirubin up to 1.5×ULN, except in patients with Gilbert's syndrome who must have normal direct bilirubin; and
        iv. Left ventricular ejection fraction (LVEF) at least 45% (or at least institute's lower limit of normal) confirmed by ECHO or MUGA in patients with history of coronary artery disease or cardiovascular disease or those with history of low LVEF; and
    g. Baseline oxygen saturation more than 92% on room air
2. Required Documentation

a. CD19 expression on leukemic blasts in the BM, peripheral blood, or cerebrospinal fluid by flow cytometry within 1 month of screening. In patients treated with blinatumomab, testing should be undertaken after blinatumomab therapy has been stopped.

3. Dosage and Administration
    a. 410 × 106 CD19 CAR-positive viable T cells; and
    b. Regimen consists of a split dose infusion to be administered on Day 1 and Day 10 (± 2 days); and
    c. Dose administered is determined by the patient bone marrow blast assessment.

Exclusions

- B-ALL with isolated extramedullary disease
- Diagnosis of Burkitt's leukemia/lymphoma according to WHO classification or chronic myelogenous leukemia lymphoid in blast crisis
- History or presence of clinically relevant central nervous system (CNS) pathology such as epilepsy, paresis, aphasia, stroke within 3 months prior to consent, severe brain injuries, dementia, Parkinson's disease, cerebellar disease, organic brain syndrome, uncontrolled mental illness, or psychosis
- Presence of:
    - CNS 3 disease or CNS 2 disease with neurological changes
    - Active or uncontrolled fungal, bacterial, viral, or other infection requiring systemic antimicrobials for management
    - Active or latent hepatitis B virus or active hepatitis C virus
    - HIV, HTLV-1, HTLV-2, or syphilis positive test
- Received a prior stem cell transplant less than 3 months prior to obe-cel infusion.
- Active significant (overall grade ≥2, Seattle criteria) acute Graft v Host Disease (GVHD) or moderate/severe chronic GVHD (NIH consensus criteria) requiring systemic steroids or other immunosuppressants within 4 weeks
- Received prior anti-CD19 targeted therapy other than blinatumomab. Patients who have experienced Grade of at least 3 neurotoxicity following blinatumomab
- Use of the following medications:
    - Steroids: Therapeutic doses of corticosteroids (greater than 10mg daily of prednisone or its equivalent) within 7 days of leukapheresis or 72 hours prior to obe-cel administration (physiological replacement, topical, and inhaled steroids are permitted)
    - Immunosuppression: Immunosuppressive medication must be stopped at least 2 weeks prior to leukapheresis and obe-cel infusion
    - Allogeneic cellular therapy: any donor lymphocyte infusions must be completed more than 2 weeks prior to leukapheresis and not repeated thereafter
    - GVHD therapies: any drug used for GVHD must be stopped more than 2 weeks prior to leukapheresis and not reinitiated thereafter
    - Chemotherapy (including tyrosine kinase inhibitor therapy for patients with Philadelphia chromosome-positive ALL): should be stopped 1 week prior to leukapheresis or starting pre-conditioning chemotherapy
    - Treatment with any T-cell lytic or toxic antibody (e.g. alemtuzumab) within 6 months prior to leukapheresis, or treatment with clofarabine or cladribine within 3 months prior to leukapheresis
    - Live vaccine up to 4 weeks prior to leukapheresis
    - Intrathecal therapy within 2 weeks prior to starting pre-conditioning chemotherapy

- Use of blinatumomab after leukapheresis

MassHealth Variation
Mass General Brigham Health Plan uses the MassHealth Drug List for coverage determinations for members of the MGB ACO. Criteria for Aucatzyl are found in Table 75: T-Cell Immunotherapies.

Medicare Variation
Mass General Brigham Health Plan uses guidance from the Centers for Medicare and Medicaid Services (CMS) for coverage determinations for its Medicare Advantage plan members. National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), Local Coverage Articles (LCAs) and documentation included in the Medicare manuals are the basis for coverage determinations. When there is no guidance from CMS for the requested service, Mass General Brigham Health Plan's medical policies are used for coverage determinations. At the time of Mass General Brigham Health Plan's most recent policy review, Medicare has an **NCD for Chimeric Antigen Receptor (CAR) T-cell Therapy (110.24).**

Codes

The following codes are included below for informational purposes only; inclusion of a code does not constitute or imply coverage or reimbursement.

This list of codes applies to commercial and MassHealth only.

Authorized Code	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 (eg, 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
C9301	Obecabtagene autoleucel, up to 410 million cd19 car-positive viable t cells, including leukapheresis and dose preparation procedures, per therapeutic dose

Summary of Evidence
Immunotherapy-based therapy, including CAR-T therapies directed at CD19, constitutes the primary method of inducing remission in patients with relapsed or refractory B-cell acute lymphoblastic leukemia (R/R B-ALL). Aucatzyl (obecabtagene autoleucel, obe-cel), a CD19-directed chimeric antigen receptor T-cell (CAR-T) therapy developed by Autolus, Inc., has been approved for the treatment of R/R B-ALL in adults. It is the first CAR-T administered in a split-dosing schedule designed to lower toxicity, and the first to be approved without a requirement for a risk evaluation and mitigation strategy (REMS) program. The combined phase 1b-2 FELIX study, published in the New England Journal of Medicine by Roddie et al. (2024), enrolled 153 patients, with 127 receiving at least one obe-cel infusion. Within this study, the pivotal cohort (designated as 2A) of 94 patients demonstrated significant clinical efficacy with an overall remission rate of 77%. The study reported a median event-free survival of 11.9 months, with 6-month and 12-month event-free survival rates of 65.4% and 49.5% respectively, and 12-month overall survival of 61.1%.

Notably, obe-cel demonstrated a favorable safety profile compared to existing CAR-T therapies, with markedly lower rates of severe adverse events. Only 2.4% of patients experienced grade 3 or higher cytokine release syndrome, and 7.1% developed grade 3 or higher immune effector cell-associated neurotoxicity syndrome (ICANS). The study identified that patients with low (<5% blasts) or intermediate (5-75% blasts) bone marrow burden achieved better outcomes, suggesting potential for outpatient administration in select patients. Additionally, some patients achieved durable responses without requiring consolidative allogeneic stem-cell transplantation.

In a pooled analysis including both patients from the trial study and also patients ≥16 years with R/R B-ALL, B-cell chronic lymphocytic leukemia (B-CLL), or R/R B-cell non-Hodgkin lymphoma (B-NHL) enrolled in the phase I extended ALLCAR19 study, sustained remission was observed in 36% of patients with B-ALL after a median 43 months of follow-up, and progression-free survival was observed in 54% of patients with B-CLL or B-NHL after a median of 24 months of follow-up (Roddie et al. 2023).

The FELIX trial has established obe-cel as a reasonable option for relapsed/refractory B-ALL (NCCN 2024). Compared with other CAR-T therapies including tisagenleucel and brexucabtagene autoleucel, it appears to offer a more manageable safety profile. Head-to-head comparisons have yet to demonstrate whether any one of these CAR-T therapies, or other immunotherapies such as blinatumomab and inotuzumab ozogamicin, provide superior safety and/or efficacy.

Effective
May 12, 2025: Effective Date.

References
Aucatzyl [package insert]. Gaithersburg, MD: Autolus, Inc.; 2024.

IPD Analytics. IPD Analytics Market Forecast Update: Autolus' Aucatzyl Approved for Relapsed/Refractory B-Cell ALL. November 20, 2024.

NCCN Clinical Practice Guidelines in Oncology. Acute lymphoblastic leukemia. Version 3.2024. Accessed 2/24/2025 at https://www.nccn.org/professionals/physician_gls/pdf/all.pdf

Roddie C, Sandhu KS, Tholouli E, et al. Obecabtagene Autoleucel in Adults with B-Cell Acute Lymphoblastic Leukemia. N Engl J Med. 2024 Dec 12;391(23):2219-2230. doi: 10.1056/NEJMoa2406526. Epub 2024 Nov 27. PMID: 39602653.

Roddie C, Tholouli E, Shaughnessy P, et al. Long-term efficacy of obecabtagene autoleucel (obe-cel) in adult patients (pts) with relapsed/refractory B-cell acute lymphoblastic leukemia ([R/R B-ALL]; Pooled analysis from ALLCAR19 and Felix Phase !b studies) or other B-cell malignancies (ALLCAR19 extension study). Abstract. *Blood* 2023;142:2114-5.