

## Clinical Memorandum

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**DATE:** 24 February 2026

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**SUBJECT:** Changes Being Effected-0 (CBE-0) labeling change recommendation

**PRODUCTS:** AUCATZYL (Autolus Limited)

**RECOMMENDATION:** CBE-0 Labeling Change Approval

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### Executive Summary

#### Background

Obecabtagene autoleucel (AUCATZYL) was approved on November 8, 2024 for treatment of adults with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (B-ALL). The approval of AUCATZYL did not include Risk Evaluation and Mitigation Strategy (REMS).

On June 27, 2025, FDA eliminated REMS requirement for all approved CD19 and BCMA-CAR T cell therapies ([FDA Eliminates Risk Evaluation and Mitigation Strategies \(REMS\) for Autologous Chimeric Antigen Receptor CAR T cell Immunotherapies | FDA](#))

Beside REMS removal, additional labeling changes were approved for these products including reduction in driving avoidance from 8 weeks to 2 weeks, and staying in close proximity to hospital from 4 weeks to 2 weeks. These changes were approved based on cumulative data from currently FDA approved CAR T cell products, and were expected to improve patient access to these therapies particularly in the rural areas.

In order to align changes AUCATZYL USPI with other approved CAR T therapy labels,

On July 18, 2025, FDA sent an email to Autolus Limited (the Applicant) and requested to submit CBE-0 supplement including changes as below:

#### **Information Request:**

FDA is requesting submission of a changes being effected (CBE-0) supplement for Aucatzyl for the following label changes; please submit a CBE-0 with tracked change and clean versions of your USPI.

Given the inclusion of the risk of neurologic toxicities/ICANS under Warnings and Precautions (W&P) and other sections of the USPI, improved understanding and the well-established management guidelines for both CRS and ICANS, please remove the subsection “Effect on Ability to Drive and Use Machines” under section 5.2 Neurologic Toxicities. FDA also proposes additional edits throughout USPI to streamline monitoring for product class. To align with these changes, please make the following related edits:

1. **Recent Major Changes:**

- Please add: “Warnings and Precautions, Neurologic Toxicities (5.2)\_\_\_\_\_07/2025”
- Please add “Dosage and Administration (2.4)-----07/2025”

2. **Highlights, W&P:** Remove “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 8 weeks after receiving AUCATZYL (5.2).”

3. **Dosage and Administration**, subsection Monitoring (2.4) (additions in bold; deletions in strikethrough):

- Monitor patients for signs and symptoms of CRS, neurologic toxicities/ICANS and other acute toxicities daily for at least ~~14~~ **7** days ~~at the healthcare facility~~ following the ~~first~~ **each** infusion.
- Continue to monitor patients for at least ~~4 weeks~~ **2 weeks** following each infusion.
- Instruct patients to remain within proximity of a healthcare facility for at least ~~4 weeks~~ **2 weeks** following the ~~first~~ **each** infusion.
- ~~Instruct patients to refrain from driving or hazardous activities for at least 8 weeks following second infusion.~~
- **Avoid driving for at least 2 weeks after each infusion.**

4. **W&P, 5.1** (additions in bold; deletions in strikethrough):

- During and following treatment with AUCATZYL, closely monitor patients for signs and symptoms of CRS daily for at least ~~7~~ **14** days ~~at the healthcare facility~~ following the ~~first~~ **each** infusion.
- Continue to monitor patients for CRS for at least ~~4 weeks~~ **2 weeks** following each infusion with AUCATZYL.

5. **W&P, 5.2** (additions in bold; deletions in strikethrough):

- Following treatment with AUCATZYL, monitor patients daily for at least ~~14~~ **7** days ~~at the healthcare facility~~.
- Continue to monitor patients for at least ~~4 weeks~~ **2 weeks** following treatment with AUCATZYL.
- ~~Effect on Ability to Drive and Use Machines: Due to the potential for neurologic events, including altered mental status or seizures, patients receiving AUCATZYL are at risk for altered or decreased consciousness or coordination in the eight weeks following AUCATZYL infusion or until resolution of the neurological event by the treating physician. Advise patients to refrain from driving and engaging in hazardous occupations or activities, such as operating heavy or potentially dangerous machinery, during this initial period.~~
- **Avoid driving for at least 2 weeks after each infusion.**

6. **Medication Guide** (additions in bold; deletions in strikethrough):

- After AUCATZYL infusion, you will be monitored daily for at least ~~seven~~ **fourteen** days after the infusion so that your healthcare team can closely monitor your recovery.
- You should plan to stay close to **a healthcare facility** ~~the location where you received your treatment~~ for at least ~~four~~ **two** weeks after getting AUCATZYL.

- ~~○ Do not drive, operate heavy machinery, or do other dangerous activities for eight weeks after you get AUCATZYL because the treatment can cause sleepiness, confusion, weakness, and temporary memory and coordination problems.~~
- **Avoid driving for at least 2 weeks after you get AUCATZYL.**

On August 27, 2025, the Applicant submitted BL125813/64 with USPI changes as requested in FDA's July 18, 2025 email.

**Assessment and Recommendation:**

The Applicant's proposed changes are consistent with FDA's request (July 18, 2025). Additionally, the Applicant has included minor editorial changes to the USPI such as correction of grammatical errors, removal of incorrectly placed border etc. These changes are acceptable.

Additionally, the FDA recommended a standard text in Section 12.6 Immunogenicity "The observed incidence of anti-drug antibodies is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of anti-drug antibodies in the studies described below with the incidence of anti-drug antibodies in other studies, including those of AUCATZYL or of other similar products". The Applicant agreed to including this change in the USPI.