



Memorandum

DATE: March 16, 2026

TO: Linda Le, RPM
CBER/OTP/ORMRR/DRMRR2/RRB2
Afsah Amin
CBER/OTP/OCE/DCEGM/GMB3

FROM: Teresa Vu, Pharm.D., MBA.
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Division of Case Management (DCM)
Office of Compliance and Biologics Quality (OCBQ)

THROUGH: Kristine Khuc, Pharm.D.
Acting Branch Chief
APLB/DCM/OCBQ

SUBJECT: Labeling Review
TREGZI ([REDACTED])
BLA: 125868/0
Sponsor: Orca Biosystems Inc.

Background

The sponsor submitted:

☒ New Approval
☐ Changes Being Effectuated (CBE) supplement
☐ Prior Approval Supplement (PAS)
☐ Major Amendment

Submission contains:

☒ Prescribing Information (PI)
☐ Patient Package Insert (PPI)
☐ Package and/or container labels
☐ Other (Instructions for Use/User Manual)

Submission Date: August 6, 2025

PDUFA Action Date: April 6, 2026

APLB Comments/Recommendations

This labeling review is for TREGZI () an original Biologics License Application (BLA 125868) submitted by Orca Biosystems Inc., on August 6, 2025. The proposed indication is for use in adult patients with hematologic malignancies to improve survival free of Graft-Versus-Host disease (GVHD) in conjunction with an appropriate preparative regimen.

Through March 10, 2026, APLB iteratively reviewed the draft Prescribing Information (PI) with the TREGZI Review Team and provided comments from a comprehension, readability, and promotional perspective. We have the following additional comments on the PI submitted on August 6, 2025:

OVERALL

- Use active voice (command language) when providing directive.
- Replace the term PROPRIETARY NAME with the approved name TREGZI throughout the PI.
- Ensure for proper spacing and alignment throughout the PI.
- Reserve bolding of words for headers and subleaders.

PRODUCT TITLE

Fix Product Title and include the proper name (non-proprietary name) along with the suffix - vldg.

HIGHLIGHTS OF PRESCRIBING INFORMATION

INDICATIONS AND USAGE

Suggest removing “to improve survival free of graft versus host disease (GVHD). This has promotional tone.

DOSAGE AND ADMINISTRATION

- Bold “**For intravenous use only**”.
- Reorganize this section for readability. Move the statement: “Verify patient’s identity prior to infusion” to be the first bullet of this section. For example, see below:

-----DOSAGE AND ADMINISTRATION-----
For intravenous use only. (2.1)
• Verify patient's identity prior to infusion (2.3)
• TREGZI is available as 4 single-dose infusion bags (HSPCs, Tregs, Tcons, and Tcon diluent). (2.2)
• Administer an appropriate myeloablative preparative regimen before infusion of TREGZI. (2.3)
• DO NOT use a leukodepleting filter. (2.3)
-----DOSAGE FORMS AND STRENGTHS-----

FULL PRESCRIBING INFORMATION

INDICATIONS AND USAGE

Suggest removing “to improve survival free of graft versus host disease (GVHD). This has promotional in tone.

DOSAGE AND ADMINISTRATION

- Change 2.2 **Recommended Dosage** subheader to **Dose**.
- Change 2.3 **Dosing and Administration** subheader to **Administration**.
- If there are more subsections needed, add more subsections and name these subheaders appropriately (e.g., Preparation, Administration).

DOSAGE FORMS AND STRENGTH

Edit and add the word “four” to this sentence: “TREGZI is a cell suspension for intravenous infusion. TREGZI is provided in **four** separate infusion bags labeled for the specific patient” to align with the number of product bags described throughout the PI.

WARNINGS AND PRECAUTIONS

Edit this sentence to correct spelling and grammatical errors: “Graft **faiure** has occurred **after TREGZI administration [see Adverse reactions (6.1)]. can cause** graft failure”.

CLINICAL PHARMACOLOGY

- Under **12.1 Mechanism of Action**, ensure the information described in this section is factual and not theoretical.
- Remove the following promotional language: “Tregs are administered prior to Tcons to control GVHD and promote immune reconstitution. Tregs home rapidly to secondary lymphoid organs and recognize alloantigen, proliferate, and disrupt the priming of Tcons by host antigen-presenting cells. The immunoregulatory activity preserves lymphoid architecture and suppress the proliferation of alloreactive Tcons in GVHD target organs.”
 - If opting to this language, edit this sentence as it is not easily understood: “Tregs home rapidly to secondary lymphoid organs and recognize alloantigen, proliferate, and disrupt the priming of Tcons by host antigen-presenting cells.”

HOW SUPPLIED/STORAGE AND HANDLING

Unbold the sentence: “The metal cassettes are NOT to be opened upon receipt, only at the time of thaw”. Ensure this information is also included in the DOSAGE AND ADMINISTRATION section.

CONTAINER AND PACKAGE LABELS

To improve readability and avoid confusion, we recommend the following changes:

HSCP Bag

- Change “Administration Step 1” to “Step 1 of Administration: HSCP Component”.
- Move this “Step 1 of Administration: HSCP Component” all the way to the left.
- Edit/change the following description under Dosage: Infuse HSPC Component (Step 1). Infuse Treg Component (Step 2) following Step1. See Full Prescribing Information for complete description of dosage and administration instructions.

Treg Bag

- Change “Administration Step 2” to “Step 2 of Administration: Treg Component”.
 - Move this “Step 2 of Administration: Treg Component” all the way to the left.
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- Edit/change the following description under Dosage: Infuse Treg Component (Step 2) following infusion of HSCP Component (Step 1). See Full Prescribing Information for complete description of dosage and administration instructions.

TCon Bag:

- Change “Administration Step 3a” to “Step 3a of Administration: TCon Component”.
- Move this “Step 3 of Administration: Tcon Component” all the way to the left.
- Edit/change the following description under Dosage: Infuse after 2+ or 3+ day following infusion of HSCP and Treg components. See Full Prescribing Information for complete description of dosage and administration instructions.

Diluent Bag:

- Change “Administration Step 3b” to “Step 3b of Administration: Diluent”.
- Move this “Step 3b of Administration: Diluent” all the way to the left.
- Edit/change the following description under Dosage: Add Diluent (Step 3b) to Tcon Component (Step 3a). See Full Prescribing Information for complete description of dosage and administration instructions.

If you have any questions regarding this review, please contact CAPT Teresa Vu, PharmD, at Teresa.Vu@fda.hhs.gov.
