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## Memorandum

**DATE:** July 15, 2025

**TO:** Maria Crowley, RPM  
CBER/OTP/ORMRR/DRMRR2/RRB2  
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CBER/OTP/OCE/DCEGM/GMB3

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**THROUGH:** Lisa L. Stockbridge, Ph.D.  
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**SUBJECT:** Labeling Review  
**WASKYRA (etuvetidigene autotemcel)**  
**BLA: 125846/0**  
Sponsor: Fondazione Telethon ETS

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### 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: January 10, 2025

PDUFA Action Date: September 10, 2025

## APLB Comments/Recommendations

This labeling review is for WASKYRA (etuvetidigene autotemcel), an original Biologics License Application (BLA 125846) submitted by Fondazione Telethon ETS on January 10, 2025. The proposed indication is for treatment of patients aged six (6) months and older with severe Wiskott-Aldrich Syndrome (WAS) who have a mutation in the WAS gene and for whom no suitable human leukocyte antigen (HLA)-matched related hematopoietic stem cell donor is available.

From a comprehension, readability, and promotional perspective, we are providing the following comments on the draft labeling that OTP provided to APLB on July 8, 2025.

### OVERALL

- Use active voice (command language) when providing directives.
- Use U.S. English (not British English) throughout the PI.
- Bullet only when there is more than one bullet in a list.
- Minimize repetition of the proprietary name. While it should be mentioned at least once in every section and subsection, overuse is cumbersome, reducing both readability and comprehension.
- Reserve bolding for regulatory headings/subheadings and wording.

### HIGHLIGHTS

#### **PRODUCT TITLE** (see 21 CFR §201.57(a)(2) and CBER SOPP 8426)

- The proper name in the product title should be lower case letters:  
(etuvetidigene autotemcel)
- The dosage form should read: suspension, for intravenous infusion.
- The proprietary name, proper name, dosage form, and route of administration should be the only items in the Product Title:  
WASKYRA (etuvetidigene autotemcel) suspension, for intravenous infusion

#### **DOSAGE AND ADMINISTRATION**

- Delete the sentence: “WASKYRA must be administered in a qualified treatment centre with experience in Haematopoietic Stem Cell Transplantation (HSCT).” Without a REMS or restricted distribution, this is not enforceable.
- Move the following directives (in bold) to immediately beneath header and consider making this a simpler phrase. For example:  
**For autologous intravenous use only.**
- Reorganize this section for readability. For example:

##### -----DOSAGE AND ADMINISTRATION-----

##### **For autologous use. For intravenous use only.**

- Patients must undergo hematopoietic stem and progenitor cell (HSPC) mobilization followed by apheresis to obtain CD34+ cells for WASKYRA manufacturing.
  - Dosing is based on the number of CD34+ cells in the infusion bag(s) per kg of body weight at the time of infusion. (2.1)
  - The minimum recommended dose is  $7 \times 10^6$  cells per kg.
  - Myeloablative conditioning is required before infusion of WASKYRA. (2.2)
  - Prior to infusion, confirm that the patient's identity matches the essential unique patient information on the infusion bag(s). (2.3)
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## DOSAGE FORMS AND STRENGTHS

- Do not bullet when there only is one bullet.
- Add the dosage form to this section. For example:  
WASKYRA is a single-dose cell suspension of  $2 \times 10^6$  cells/mL to (b) (4)  $\times 10^6$  CD34+ cells/mL, provided in one to eight bags for intravenous infusion.

## CONTRAINDICATIONS

Include a likely allergen to the first bullet: Hypersensitivity to the active substance or to any of the excipients, including DMSO. (See DESCRIPTION (11)).

## WARNINGS AND PRECAUTIONS

- The subsection header of a warning should inform the reader of the specific risk.
- The subsections in the HIGHLIGHTS do not match the subsections in the FULL PRESCRIBING INFORMATION.
- Consider changing the header of 5.1 to: Serious Infection.
- There are two separate subsections combined under Thyroid disease. Edit to separate these risks. For example:
  - Thyroid disease: Transient increases in thyroid stimulating hormone (TSH) and free T3 (FT3, Tri-iodothyronine) were observed during clinical development. Assess thyroid function prior to and post treatment. (5.6)
  - Veno-occlusive Disease (VOD): Monitor patients for signs and symptoms of VOD one month after WASKYRA infusion.
- Starting each warning and precaution with “Risk of” makes it difficult to scan for the actual risk, thus reducing readability. Consider the following edits for readability and comprehension:

### -----WARNINGS AND PRECAUTIONS-----

- Serious Infection: Monitor for serious infections after myeloablative conditioning and WASKYRA infusion.(5.1).
- Hypersensitivity and infusion-related reactions: Monitor for hypersensitivity reactions during infusion. (5.2)
- Engraftment failure: Engraftment failure may occur. In case of failure, the non-transduced back-up haematopoietic stem cells may be infused according to local standards. (5.3)
- Prolonged cytopenia: Severe cytopenias, including severe neutropenia (defined as Absolute Neutrophil Count (ANC) <500/ $\mu$ L), have occurred for several weeks following reduced intensity conditioning and WASKYRA infusion. (5.4)
- Transmission of an infectious agent: Although WASKYRA is tested for sterility and mycoplasma at release, a small risk of transmission of infectious agents exists. Healthcare professionals administering WASKYRA should therefore monitor patients for signs and symptoms of infections after treatment and treat appropriately. (5.5)
- Thyroid disease: Transient increases in thyroid stimulating hormone (TSH) and free T3 (FT3, Tri-iodothyronine) were observed in some patients during clinical development. Assess thyroid function and structure prior to treatment with WASKYRA, and during the follow up after treatment. (5.6)
- Veno-occlusive Disease (VOD): Monitor patients for signs and symptoms of VOD, including liver function tests one month after WASKYRA infusion.
- Insertional oncogenesis: There is a theoretical risk of leukaemia or lymphoma after treatment with WASKYRA. (5.7)

## **CONTENTS**

Ensure that the CONTENTS aligns with the FULL PRESCRIBING INFORMATION.

## **FULL PRESCRIBING INFORMATION**

### **2 DOSAGE AND ADMINISTRATION**

- Change the subheading of **2.1** from **Recommended Dose** to **Dose**.
- Remove the underlining of **2.2** subheading and change it to **2.2 Patient Preparation**

### **3 DOSAGE FORMS AND STRENGTHS**

See comment for this section in the HIGHLIGHTS.

### **4 CONTRAINDICATIONS**

List DMSO as a potential allergen for a hypersensitivity reaction. Cross reference this contraindication the DESCRIPTION section: *[See Description 11]*

### **5 WARNINGS AND PRECAUTIONS**

- The subsections in the FULL PRESCRIBING INFORMATION do not match the subsections in the HIGHLIGHTS.
- Revise **5.1 Serious Infections** to include necessary monitoring.
- The first two sentences in subsection **5.2** are redundant. Remove the first sentence, *There is a potential risk of allergic reaction in patients treated with WASKYRA*, and revise the second sentence to remove the limitation of a hypersensitivity reaction to only involve DMSO: *Hypersensitivity and infusion related reactions, including anaphylaxis, may occur with WASKYRA infusion.*
- Revise subsection **5.2** to remove statements that are practice of medicine (e.g., listing vital signs to monitor).
- Under **5.4 Prolonged cytopenia**, revise to command language to improve readability. For example, change the sentence: *Patients should, therefore, be monitored for signs and symptoms of cytopenia for at least 6 weeks after infusion.* to *Monitor patients for signs and symptoms of cytopenia for at least 6 weeks following infusion.*

### **6 ADVERSE REACTIONS**

- Remove the header: “**Adverse reactions attributed to WASKYRA**”. By definition, an adverse reaction is attributable to WASKYRA. (See 21 CFR §201.57(c)(7) and (c)(7)(i)).
- Subsection 6.1 must list adverse reactions identified in the clinical trials that occurred at or above a pre-specified rate. (See 21 CFR §201.57(c)(7)(A)).

### **7 DRUG INTERACTIONS**

The first two sentences, about expectations in the absence of a formal drug interaction study, are not informative and should be deleted. However, the subsections regarding the expected impact on vaccines or the effects of anti-retrovirals following treatment are class expectations and important for inclusion.

### **8 USE IN SPECIFIC POPULATIONS**

Cross-reference the description in subsection **8.4 Pediatric Use** to section 14.

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**12 CLINICAL PHARMACOLOGY**

Under **12.1 Mechanism of Action**, ensure the information described in this section is factual and not theoretical.

**15 REFERENCES**

All references used in the USPI are listed here in numerical order. Only use references when labeling must summarize or otherwise rely on a recommendation by an authoritative scientific body, or on a standardized methodology, scale, or technique, because the information is important to prescribing decisions. (See 21 CFR §201.57(c)(16))

**CONTAINER AND PACKAGE LABELS**

There are no comments on the container and package labels as of July 15, 2025.

If you have any questions regarding this review, please contact CAPT Teresa Vu, PharmD, at [Teresa.Vu@fda.hhs.gov](mailto:Teresa.Vu@fda.hhs.gov).

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