# Up Close with Tebentafusp

This section provides an overview of tebentafusp-tebn (KIMMTRAK®).

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💊 Dosing and Administration

⚠️ CRS

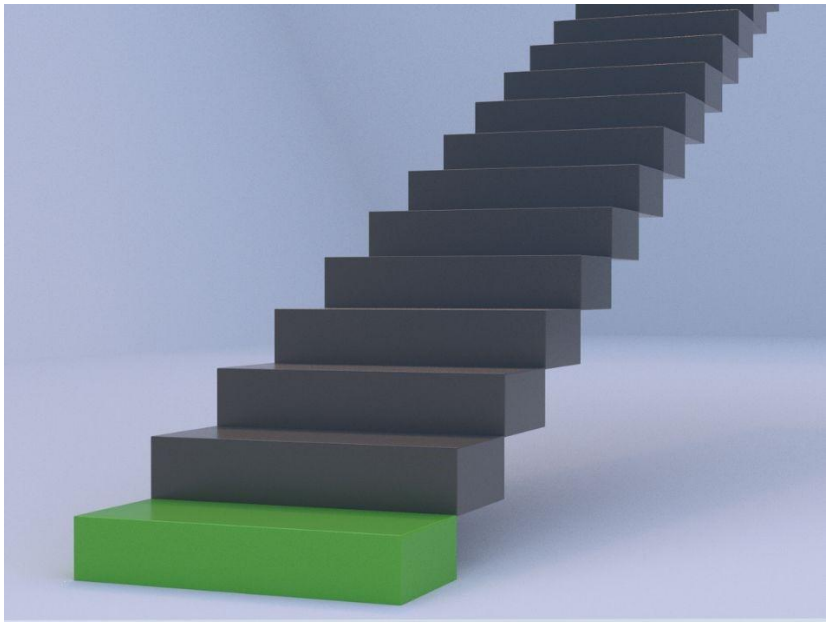
🚨 Other Toxicities

## 🏷️ Indications

Tebentafusp is a **bispecific glycoprotein 100 (gp100) peptide human leukocyte antigen (HLA)-directed CD3 T cell engager** indicated for the treatment of:

- **HLA-A*02:01-positive** adult patients with **unresectable or metastatic uveal melanoma**

# 💊 Dosing and Administration



Tebentafusp is administered **intravenously (IV)** as part of a weekly cycle, with unique **step-up dosing** requirements during Cycle 1 to reduce the risk of cytokine release syndrome (CRS).

| Dosing Schedule | Day of Treatment | Tebentafusp Dose / Route |
|---|---|---|
| **Cycle 1**[a] | Day 1 | 20 mcg IV |
| | Day 8 | 30 mcg IV |
| | Day 15[b] | 68 mcg IV |
| **Cycle 2+** | Once weekly thereafter | 68 mcg IV |

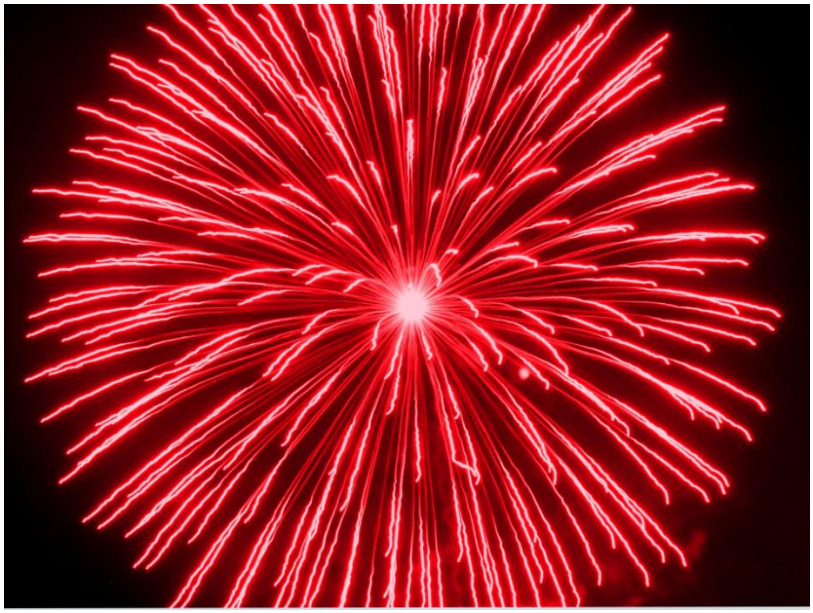
[a]The first three doses (Cycle 1) of tebentafusp should be administered in an appropriate healthcare setting via IV infusion over 15-20 minutes. All patients should be monitored for at least 16 hours following completion of each infusion.

[b]If patients do not experience Grade 2 ≤ hypotension (requiring medical attention) during or after third infusion (Cycle 1 Day 15), subsequent doses may be administered in an appropriate ambulatory care setting. All patients should be monitored for a minimum of 30 minutes or longer following each infusion.

### Recommendations for Restarting Therapy with Tebentafusp After Dosage Delay

There are **no dose modifications** recommended for tebentafusp following a dose delay.

# ⚠️ CRS



**What is it? Cytokine release syndrome (CRS)** is a systemic inflammatory response that can occur when the immune system is activated and releases large amounts of cytokines—proteins that help regulate immune responses.

- **Signs and symptoms:** pyrexia, hypotension, hypoxia, dyspnea, chills, and tachycardia.
- CRS is frequently graded using the American Society for Transplantation and Cellular Therapy (ASTCT) consensus criteria.

**Why it matters.** CRS occurred in **77%** of patients who received tebentafusp in the study IMCg100-202. Most patients **(60%)** experienced **≥ Grade 2 CRS** events **after receiving more than 1 infusion**, with the median number of events found to be 2 (range: 1-12).

- Among the majority of cases, **(84%)** CRS episodes:
  - **Began:** On the day of infusion
  - **Resolved:** Within 2 days
- Care teams should **withhold or discontinue** tebentafusp **based on the persistence and severity CRS.**

**The bottom line.** CRS occurred in a large number of patients within the clinical trial, however the duration remained low and resolved relatively quickly.

# 🚨 Other Toxicities


Tebentafusp may cause other adverse reactions such as **skin reactions, elevated liver enzymes, and embryo-fetal toxicity**.

**Why it matters.** In addition to the risks of CRS, care teams need to be on the lookout for other **tebentafusp**-associated toxicities.

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**Skin Reactions.** Tebentafusp may cause **skin reactions**, which include rash, pruritis, and cutaneous edema.

- In the study IMCg100-202 **skin reactions** occurred in **91%** of patients treated with tebentafusp including **Grade 2 (44%)** and **Grade 3 (21%)**.
    - Specific incidence of reactions were as followed:
        - Rash (83%)
        - Cutaneous edema (27%)
        - Erythema (25%)
        - Pruritus (69%)
- Skin reactions typically had an **onset of 1 day following infusion** (range: 1-55) and **resolved to ≤ Grade 1 or baseline** over approximately **6 days**.

**The bottom line.** Skin reactions will likely occur within 24 hours of receiving an infusion, however resolved relatively quickly.

- Care teams should **treat patients with antihistamine and topical/systemic steroids** based on the persistence and severity of the skin reaction.
- Additionally, tebentafusp **should be withheld or permanently discontinued depending** on the **severity** of the reaction.

**Elevated Liver Enzymes.** Tebentafusp may cause elevations in liver enzymes, including alanine aminotransferase (ALT) or aspartate aminotransferase (AST).

- In the study, **liver enzyme elevations** were observed in approximately **65%** of patients treated with tebentafusp and led to **0.4% of permanent discontinuation**.
    - The majority (**73%**) of these elevations initially occurred within the **first three infusions**, and most **patients who experienced Grade 3 or 4** ALT/AST elevations **resolved to ≤ Grade 1 or baseline** over approximately 7 **days**
    - Events reported **outside of the setting of CRS**, typically had liver enzyme **elevations** with an **onset of 129 days.**
        - Grade 3 ≤ elevations occurred in 8% of patients.

**The bottom line.** Liver enzyme elevations were reported predominantly in the first cycle and may be associated with incidence of CRS.

- Care teams should **monitor ALT/AST and total bilirubin** prior to tebentafusp treatment and during the course of treatment and withhold according to severity.

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**Embryo-Fetal Toxicity.** Tebentafusp may cause fetal harm when administered to a pregnant woman.

- Advise **females of reproductive potential** to use effective contraception **during treatment** and **for at least 1 week after** the last dose.
- Verify pregnancy status before initiating tebentafusp.

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**Use in Specific Populations**

- **Lactation:** Advise women not to breastfeed during treatment and for 4 months after the last dose.
- **Geriatric Use:** 47% of the population studied in IMCgp100-202 were 65 years of age or older and 9% were 75 years of age or older. No overall difference in safety and efficacy were observed when comparing patients 65 years of age or older to younger adult patients.
- **Pediatric Use:** Safety and efficacy of tebentafusp has not yet been established in the pediatric population.

Updated: 5/16/2025

References:


1. Lee DW, Santomasso BD, Locke FL, et al. ASTCT Consensus grading for cytokine release syndrome and neurologic toxicity associated with immune effector cells. *Biol Blood Marrow Transplant*. 2019;25(4):625-638. doi:10.1016/j.bbmt.2018.12.758.
2. Nathan P, Hassel JC, Rutkowski P, et al. Overall survival benefit with tebentafusp in metastatic uveal melanoma. *N Engl J Med*. 2021;385(13):1196-1206. doi:10.1056/NEJMoa2103485
3. KIMMTRAK® (tebentafusp-tebn) [package insert]. Immunocore Limited. Oxfordshire, United Kingdom. 2022.