

Up Close with Tebentafusp

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

-  Indications
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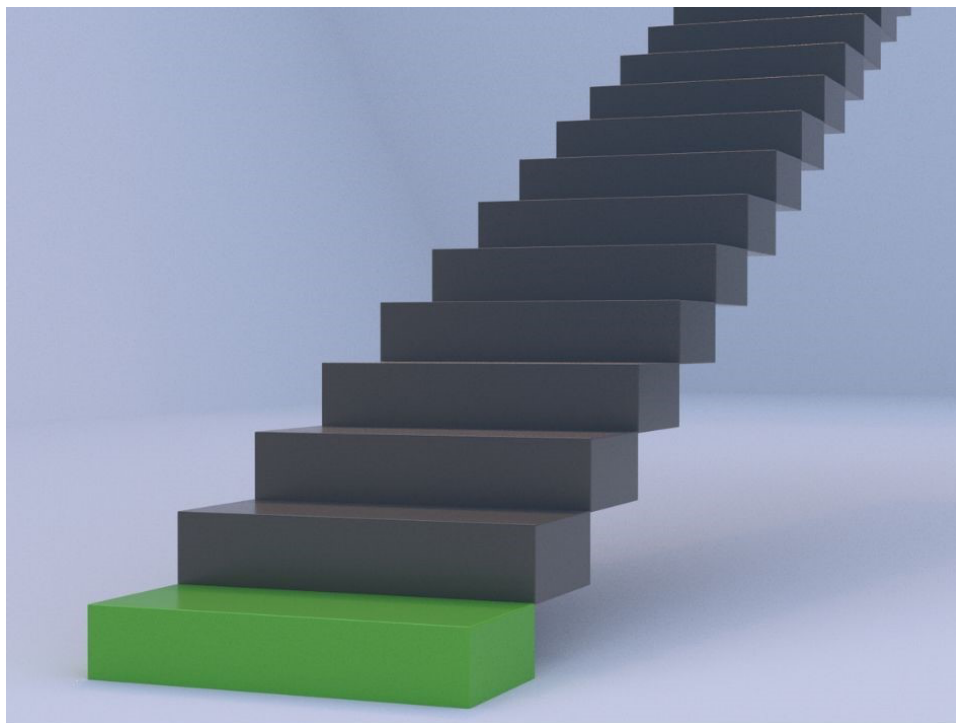
Indications



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.

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.
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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.

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References:

1. [Lee DW, Santomaso 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.](#)