Up Close with Tebentafusp

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

Indications

Dosing & Administration

Cytokine Release Syndrome (CRS)

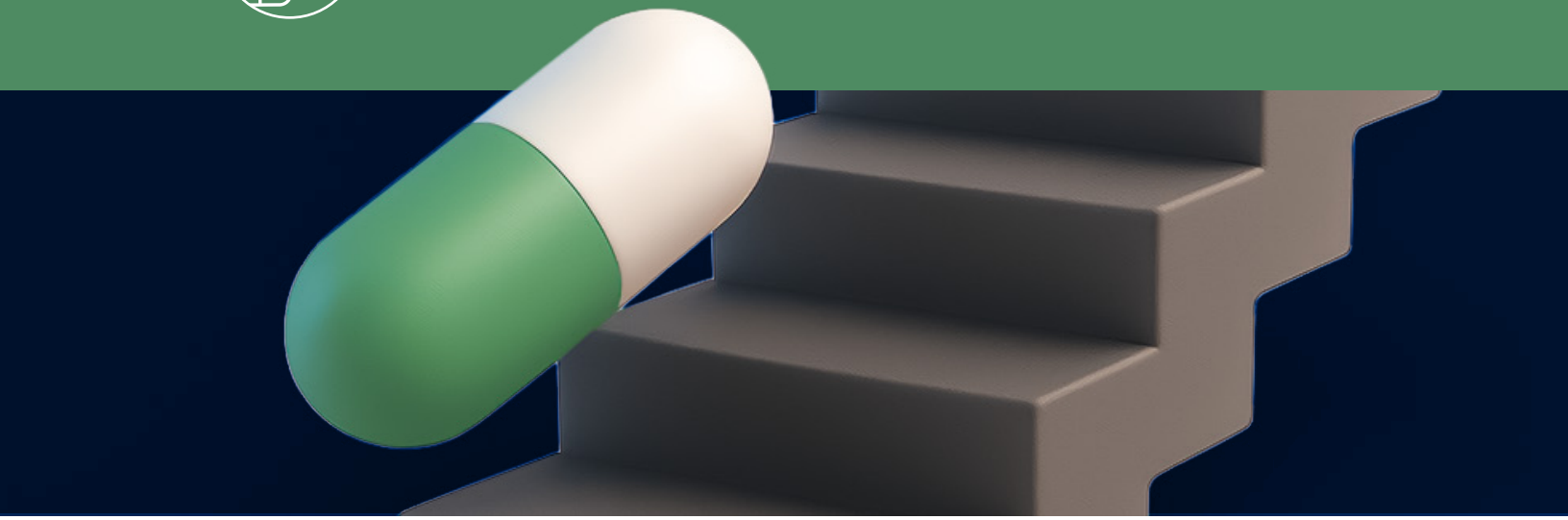
Other Toxicities

Indications

Tebentafusp is a **bispecific gp100 peptide-HLA-directed T-cell receptor-CD3 T-cell engager** indicated for HLA-A*02:01-positive adults with unresectable or metastatic uveal melanoma.

- Select patients for treatment based on a positive HLA-A*02:01 genotyping test using a whole-blood sample.

Dosing & Administration



Tebentafusp is administered by **intravenous (IV)** infusion once weekly. Treatment begins with **step-up dosing** on Days 1, 8, and 15 to reduce the risk of cytokine release syndrome (CRS).

The recommended dosage of tebentafusp administered intravenously is:	**20 mcg on Day 1**
	30 mcg on Day 8
	68 mcg on Day 15
	68 mcg once every week thereafter

Continue treatment until disease progression or unacceptable toxicity.

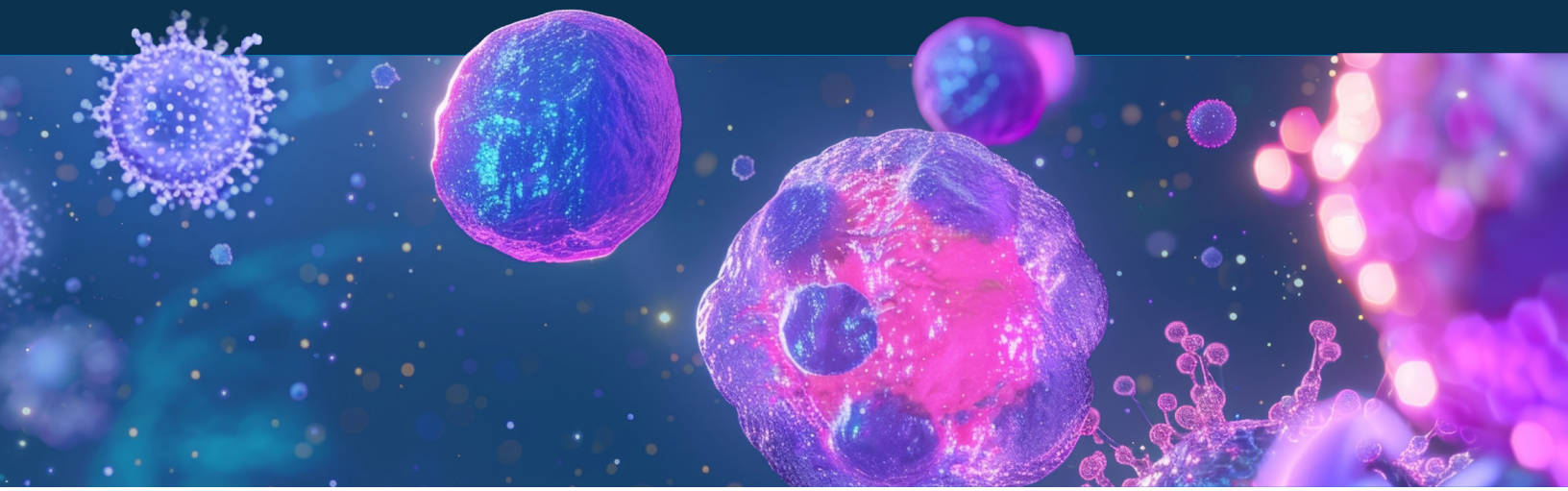
Administer the first three infusions of tebentafusp in an appropriate healthcare setting by intravenous infusion over 15-20 minutes. Monitor patients during the infusion and for at least 16 hours after the infusion is complete.

If the patient does not experience Grade 2 or higher hypotension (requiring medical intervention) during or after the third infusion, administer subsequent doses in an appropriate ambulatory care setting, and monitor patients for a minimum of 30 minutes following each of these infusions.

Recommendations for Restarting Therapy with Tebentafusp After Dosage Delay

The PI does not provide specific recommendations for restarting tebentafusp after a dosage delay. Dose reductions are not recommended.

Cytokine Release Syndrome



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:

- Chills
- Low tissue oxygen level
- Fever
- Rapid heartbeat
- Low blood pressure
- Trouble breathing

CRS is frequently graded using the American Society for Transplantation and Cellular Therapy (ASTCT) consensus criteria.

Why it matters:

Grade 2 or higher CRS occurred in **77%** of patients who received tebentafusp in the study IMCgp100-202. **Grade ≥2 CRS** occurred with **more than 1 infusion** in 60% of patients; the median number of events was 2 (range: 1–12)..

- Most CRS episodes (84%) began on the day of infusion. Among episodes that resolved, the median time to resolution was 2 days.
- CRS resulted in permanent discontinuation in 1.2% of patients. Systemic corticosteroids, supplemental oxygen, and vasopressors were required in 23%, 8%, and 0.8% of patients, respectively.
- Care teams should **withhold or discontinue** tebentafusp **based on the persistence and severity CRS**.

THE BOTTOM LINE:

CRS is very common with tebentafusp and may be life-threatening. Most episodes begin on the day of infusion and, among episodes that resolve, the median time to resolution is 2 days

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, pruritus, and cutaneous edema.

- In the study IMCgp100-202 **skin reactions** occurred in **91%** of patients treated with tebentafusp including **Grade 2 (44%)** and **Grade 3 (21%)**.
  - Specific skin reactions included:
    - Rash (83%)
    - Cutaneous edema (27%)
    - Erythema (25%)
    - Pruritus (69%)
- The median time to onset was **1 day** (range: 1–55 days), and the median time to improvement to Grade ≤1 was approximately **6 days**.

THE BOTTOM LINE:

Skin reactions are very common and have a median onset of 1 day after infusion; however, delayed reactions can occur.

- 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, **ALT or AST elevations** occurred in **65%** of patients and led to **permanent discontinuation in 0.4%**.
  - 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
  - For liver enzyme elevations occurring outside the setting of CRS, the median time to onset was **129 days.**
    - Grade ≥3 elevations occurred in ~8%.

THE BOTTOM LINE:

Liver enzyme elevations commonly occur during the first three infusions and may occur with or independently of CRS.

- **Monitor ALT, AST, and total bilirubin** before starting tebentafusp and throughout treatment. Withhold tebentafusp based on the severity of the elevations.

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.

Use in Specific Populations

- **Lactation:** Advise women not to breastfeed during treatment and for 1 week after the last dose.
- **Pediatric Use:** Safety and efficacy of tebentafusp has not yet been established in the pediatric population.
- **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 differences in safety and efficacy were observed when comparing patients 65 years of age or older to younger adult patients.

References:

1. KIMMTRAK® (tebentafusp-tebn) [package insert]. Immunocore Limited. Oxfordshire, United Kingdom. 2024.

2. 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.

3. 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