Up Close with Talquetamab

This section provides an overview of talquetamab-tgvs (TALVEY®).

- 🏷️ Indications
- 💊 Dosing and Administration
- ⚠️ CRS
- 🧠 Neurotoxicity (including ICANS)
- 🚨 Other toxicities

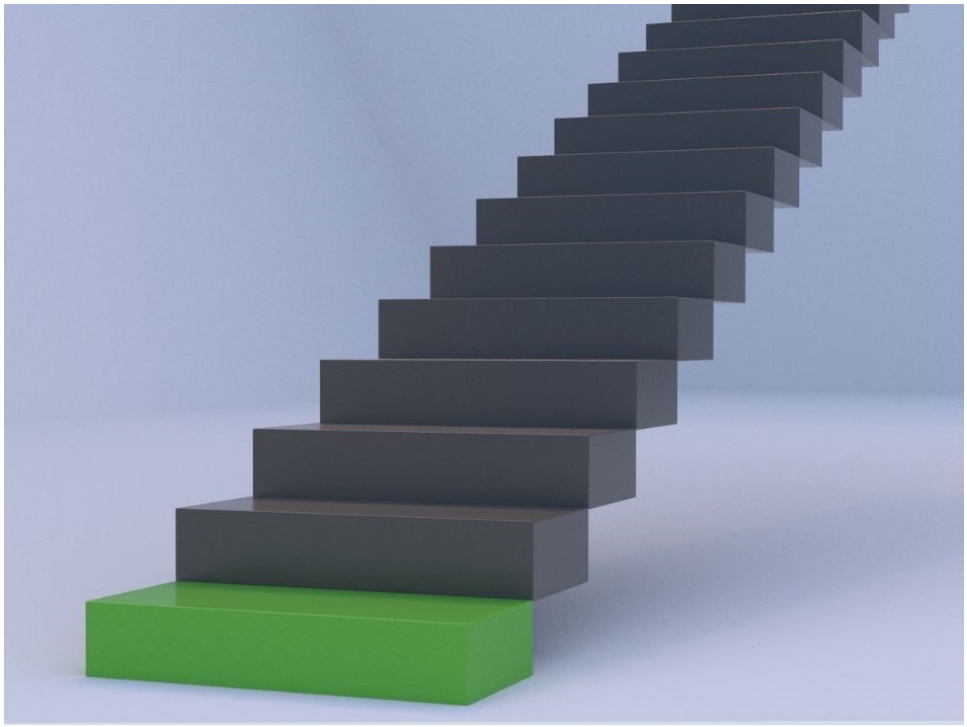
🏷️ Indications

Talquetamab is **bispecific G protein-coupled receptor class C group 5 member D (GPRC5D) directed CD3 T-cell engager**, indicated for adult patients with:

- **Relapsed or refractory multiple myeloma**, who have **previously received 4 or more lines of therapy** including an immunomodulatory agent, anti-CD38 monoclonal antibody, and a proteasome inhibitor.

Note: This indication is approved under accelerated approval based on response rate and durability of response. Continued approval may be contingent upon verification of clinical benefit in confirmatory trials.

💊 Dosing and Administration



Talquetamab is administrated **subcutaneously (SQ)** as part of a **weekly (7 day) or biweekly (14 day)-cycle**. With an overall aim to reduce the risk of cytokine release syndrome (CRS), talquetamab has a unique **step-up dosing** schedule as described below.

Talquetamab Weekly Dosing Schedule			
Dosing Schedule		**Day**	**Dose[a] / Route**
Step-up Dosing Schedule *	**Step-up Dose 1**	Day 1	0.01 mg/kg SQ
	Step-up Dose 2	Day 4[b]	0.06 mg/kg SQ
	Treatment Dose	Day 7[b]	0.4 mg/kg SQ
Weekly Dosing Schedule		One week following first treatment dose (Cycle 1 Day 7) and weekly thereafter[c]	0.4 mg/kg once weekly SQ

[a]Based on actual body weight
[b]Dose may be administered between 2 to 4 days after the previous dose and may be given up to 7 days after the previous dose to allow for resolution of adverse reactions
[c]Maintain a minimum of 6 days between weekly doses
*Administer the following pre-medications 1 to 3 hours before each dose in the step-up dosing cycle

- Dexamethasone 16 mg IV/PO (or equivalent)
- Diphenhydramine 50 mg IV/PO (or equivalent)
- Acetaminophen 650 mg to 1000 mg IV/PO (or equivalent)

Talquetamab Biweekly Dosing Schedule			
Dosing Schedule		**Day**	**Dose[a] / Route**
3 Step-up Dosing Schedule*	**Step-up Dose 1**	Day 1	0.01 mg/kg SQ
	Step-up Dose 2	Day 4[b]	0.06 mg/kg SQ
	Step-up Dose 3	Day 7[b]	0.4 mg/kg SQ

	Treatment Dose	Day 10[c]	0.8 mg/kg SQ
Biweekly (every 2 weeks) Dosing Schedule		Two weeks after first treatment dose and every 2 weeks thereafter[d]	0.8 mg/kg once every 2 weeks

IV, intravenously; PO, oral

[a]Based on actual body weight
[b]Dose may be administered between 2 to 4 days after the previous dose and may be given up to 7 days after the previous dose to allow for resolution of adverse reactions
[c]Maintain a minimum of 6 days between weekly doses
[d]Maintain a minimum of 12 days between biweekly (every 2 week) doses
*Administer the following pre-medications 1 to 3 hours before each dose in the step-up dosing cycle

- Dexamethasone 16 mg IV/PO (or equivalent)
- Diphenhydramine 50 mg IV/PO (or equivalent)
- Acetaminophen 650 mg to 1000 mg IV/PO (or equivalent)

Recommendations for Restarting Talquetamab after Dose Delay			
	Last Dose Administered	**Time from Last Dose Administered**	**Talquetamab Recommendation***
Talquetamab Weekly Dosing Schedule	0.01 mg/kg	> 7 days	Restart step-up dosing schedule (weekly) at step-up dose 1 (0.01 mg/kg).
	0.06 mg/kg	8 to 28 days	Repeat step-up dose 2 (0.06 mg/kg) and continue step-up dosing schedule (weekly) as planned.
		> 28 days	Restart step-up dosing schedule (weekly) at step-up dose 1 (0.01 mg/kg).
	0.4 mg/kg	8 to 28 days	Continue dosing schedule (weekly) at treatment dose (0.4 mg/kg/weekly).
		29 to 56 days	Restart step-up dosing schedule (weekly) at step-up dose 2 (0.06 mg/kg).
		> 56 days	Consider permanent discontinuation. If restarting, begin with the step-up dosing schedule at step-up dose 1 (0.01 mg/kg).
Talquetamab Biweekly Dosing Schedule	0.01 mg/kg	> 7 days	Restart step-up dosing schedule (biweekly) at step-up dose 1 (0.01 mg/kg).
	0.06 mg/kg	8 to 28 days	Repeat step-up dose 2 (0.06 mg/kg) and continue step-up dosing schedule (biweekly) as planned.
		> 28 days	Restart step-up dosing schedule (biweekly) at step-up dose 1 (0.01 mg/kg).
	0.4 mg/kg	8 to 28 days	Repeat step-up dose 3 (0.4 mg/kg) and continue step-up dosing schedule (biweekly) as planned.
		29 to 56 days	Restart step-up dosing schedule (biweekly) at step-up dose 2 (0.06 mg/kg).
		> 56 days	Consider permanent discontinuation. If restarting, begin with the step-up dosing schedule (biweekly) at step-up dose 1 (0.01 mg/kg).
	0.8 mg/kg	15 to 28 days	Continue dosing schedule (biweekly) dosing schedule at treatment dose (0.8 mg/kg every 2 weeks).

		29 to 56 days	Restart step-up dosing schedule (biweekly) at step-up dose 3 (0.4 mg/kg).
		> 56 days	Consider permanent discontinuation. If restarting, begin with the step-up dosing schedule (biweekly) at step-up dose 1 (0.01 mg/kg).

IV, intravenously; PO, oral.

*Administer the following pre-medications 1 to 3 hours before each dose in the step-up dosing cycle

- Dexamethasone 16 mg IV/PO (or equivalent)
- Diphenhydramine 50 mg IV/PO (or equivalent)
- Acetaminophen 650 mg to 1000 mg IV/PO (or equivalent)

⚠️ 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 **76%** of patients who received talquetamab **at the recommended dosage**, in the clinical trial, MonumenTAL-1.

- **Most CRS events were reported** in the step-up dosing schedule, either at **step-up dose 1 (29%)** or **step-up dose 2 (44%)** and were primarily **Grade 1 (57%)**.

    - CRS **reoccurred** in approximately **30%** of patients regardless of their dosing schedule.
    - The **median time to onset** of CRS across all doses was **27 hours** (range: 0.1 to 167) post-administration. The **median duration** of CRS was 1**7 hours** (range: 0 to 622).
- Care teams should **monitor for signs/symptoms of CRS** and **withhold or permanently discontinu**e talquetamab **based on severity**.

The bottom line. While CRS was primarily low grade, predictable, and manageable.

🧠 Neurotoxicity (including ICANS)

What is it? Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) is characterized by various neurological symptoms resulting from the activation of the immune system and the resultant inflammatory processes.

- **Signs and symptoms:** encephalopathy, headaches, seizures, aphasia, motor deficits, ataxia, and tremor.
- ICANS is frequently graded using the ASTCT consensus criteria.

Why it matters. Neurological toxicity, including ICANS, occurred in **55%** of patients in MonumenTAL-1, and **Grade 3 or 4 neurological toxicity** was reported in **6%** of patients.

- The most common neurological toxicities included: headache, sensory neuropathy, encephalopathy, and motor dysfunction.

- **ICANS** specifically, was reported in **9%** (N= 23/265) of patients and **reoccurred** in **3%** of patients.
    - Most ICANS events were reported in the **step-up dosing schedule**, either at step-up dose 1 (3%) or step-up dose 2 (3%), step-up dose 3 (of biweekly schedule) (1.8%). Following the introduction of the treatment dose as part of the weekly or biweekly dosing schedule, 2.6% and 3.7% of patients experienced ICANS, respectively.
    - The **median time to onset of ICANS** across all doses was **2.5 days** (range: 1 to 16) post-administration. The **median duration of ICANS** was **2 days** (range: 1 to 22). The onset of ICANS may be experienced concurrently with CRS, in the absence of CRS, or even following the resolution of CRS.
- Care teams should monitor for signs/symptoms of ICANS and **discourage patients from driving or operating heavy machinery** that may be considered potentially dangerous **during the step-up dosing schedule and 48 hours following completion** of the step-up schedule the in event of any new onset of neurological toxicity occurs or until symptoms resolve.
    - Additionally, care teams **withhold or permanently discontinue** talquetamab **based on severity**.

The bottom line. ICANS events were less common compared to CRS but resolved relatively quickly over a few days.

🚨 Other Toxicities

Talquetamab may cause other adverse reactions such as **weight loss, infection, and other toxicities like skin, oral, hepato- and embryo-fetal toxicity**.

Why it matters. In addition to the risks of CRS and neurotoxicity (including ICANS), care teams need to be on the lookout for other talquetamab-associated toxicities.

Oral Toxicity/Weight Loss. Talquetamab may cause oral toxicities including d**ry mouth, dysphagia, dysgeusia, and stomatitis which can increase the risk of weight loss**.

- In MonumenTAL-1 **80%** of patients experienced **oral toxicity**, with **Grade 3** toxicity being reported in **2.1%** of patients who received talquetamab at the recommended dosages.
    - The **medium time to onset was 15 days** (range: 1 to 634 days) and the **medium time to resolution to baseline was 43 days** (range: 1 to 530 days). In **65%** of patients, oral toxicity **did not resolve to baseline**.
- Regardless of experiencing oral toxicity, **62%** of patients in MonumenTAL-1 **reported weight loss**, primarily **Grade 2 (29%)** weight loss at 10% or greater from baseline.
    - The **medium time to onset was 67 days** (range: 6 to 407) and the **medium time to resolution to baseline was 50 days** (range: 1 to 403). In **57% of patients**, weight **did not resolve to baseline**.

The bottom line. Care teams should monitor patients for **signs and symptoms of oral toxicity and weight loss** during treatment and **consider withholding or permanent discontinuation based on the severity**.

Infections. Talquetamab may cause serious and fatal infections.

- **Serious infections**, including opportunistic infections, occurred in **16% of patients**, with **Grade 3 or 4 infections in 17%, and fatal infections in 1.5%**.
    - The most common serious infections reported bacterial infections which included sepsis and COVID-19.

The bottom line. Care teams should **monitor patients for signs of infection before and during treatment** and **consider withholding or permanent discontinuation based on the severity**.

- Additionally, care teams should **administer prophylactic antimicrobials according to the local guidelines**.

Cytopenia. Talquetamab may cause neutropenia and thrombocytopenia.

- In MonumenTAL-1, **Grade 3 or 4 neutropenia and thrombocytopenia** occurred in **35% and 22%** of patients, respectively.
    - The **medium time to onset** for Grade 3 or 4
        - Neutropenia was **22 days** (range: 1 to 312)
        - Thrombocytopenia was **12 days** (range: 2 to 183)
    - The **medium time to resolution** for **Grade 2 or lower**
        - Neutropenia was **8 days** (range: 1 to 72)
        - Thrombocytopenia was **10 days** (range: 1 to 64)

The bottom line. Care teams should monitor **complete blood counts throughout treatment** and **consider withholding or permanent discontinuation** talquetamab **based on the severity**.

Hepatotoxicity. Talquetamab may cause hepatotoxicity. In MonumenTAL-1, elevations of alanine aminotransferase (ALT), aspartate aminotransferase (AST), and bilirubin were reported as followed:

- **ALT:** 33% (Grade 3 or 4: 2.7%)
- **AST**: 31% (Grade 3 or 4: 3.3%)
- **Bilirubin:** 0.3% (Grade 3 or 4)

The bottom line. Care teams should **monitor liver enzymes and bilirubin throughout treatment** as clinically indicated and **consider withholding or permanent discontinuation** of talquetamab **based on the severity.**

Skin Toxicity. Talquetamab may cause serious skin infections including rash, maculopapular rash, erythema or erythematous rash.

- In MonumenTAL-1, skin reactions occurred in **62% of patients**, including **Grade 3 skin reactions** as reported in **0.3%** of patients.
    - The **medium time to onset** for these skin reactions was **25 days** (range: 1 to 630) and the **medium time to resolution or improvement** (Grade 1 or less) was **33 days**.

The bottom line. Care teams should **monitor patients for skin toxicity**, including rash progression throughout treatment as clinically indicated and **consider withholding** talquetamab **based on the severity**.

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

- Advise **females of reproductive potentia**l to use effective contraception **during treatment** and **for at least 3 months after** the last dose.
- Verify pregnancy status before initiating talquetamab.

Use in Specific Populations

- **Lactation:** Advise women not to breastfeed during treatment and for 3 months after the last dose.
- **Geriatric:** No overall difference in safety or effectiveness were observed in patients between 65 and 74 years of age compared to younger patients, however there was a higher rate of fatal adverse events in patients 75 years of age or older compared to younger patients.
- **Pediatric** Use: At this time, no safety and effectiveness data has been established in pediatric patients.

REMS

Talquetamab has a **Risk Evaluation and Mitigation Strategy (REMS)** to mitigate the risk of CRS and neurologic toxicity, including ICANS.

Why it matters. Prescribers, pharmacies, and healthcare settings have specific requirements per the TECVAYLI and TALVEY REMS to treat patients with talquetamab.

Notable requirements of the TECVAYLI and TALVEY REMS include the following:

- Prescribers must be certified with the program by enrolling and completing training.
- Prescribers must counsel patients receiving talquetamab about the risk of CRS and neurologic toxicity, including ICANS, and provide patients with Patient Wallet Card.
- Pharmacies and healthcare settings that dispense talquetamab must be certified with the TECVAYLI and TALVEY REMS program and must verify prescribers are certified through the TECVAYLI and TALVEY REMS program.
- Wholesalers and distributers must only distribute TECVAYLI to certified pharmacies or healthcare settings.

Steps for a prescriber to become certified:

1. Review the prescribing training program and adverse reaction management slides.
2. Successfully complete the knowledge assessment and submit it to the REMS
3. Complete the prescriber enrollment form and submit it to the REMS
4. Before treatment initiation (first step-up dose), counsel patients and/or their caregivers using the patient wallet card. Counsel patients that they should be hospitalized and monitored for signs and symptoms of CRS and neurologic toxicity, including ICANS, for 48 hours after administration of all doses within the step-up dosing schedule.

Steps for pharmacies and healthcare settings to become certified:

1. Designate an Authorized Representative (AR) for the pharmacy and healthcare setting
    a. The AR at the pharmacy can be a pharmacist, pharmacy technician, or any responsible individual assigned by the pharmacy.
    b. The AR at the healthcare setting can be a pharmacist, nurse, or any responsible individual assigned by the healthcare setting.
    c. Note: One delegate may be added to support the AR at each setting.
2. AR must review the Pharmacy and Healthcare Setting Training Program slides.
3. AR must complete the Pharmacy and Healthcare Setting Enrollment Form and submit it to the REMS
4. Train all relevant staff involved in dispensing talquetamab on the REMS requirements using the Pharmacy and Healthcare Setting Training Program slides.
    a. Before dispensing, obtain authorization to dispense each prescription by contacting the REMS to verify the prescriber is certified.

Go deeper. For more information on the TECVAYLI and TALVEY REMS program, click here.

Updated: 03/25/2025

References:

1. TALVEY™ (talquetamab-tgvs) [package insert]. Janssen Biotech, Inc. Horsham, PA. 2023.
2. ©Janssen Biotech, Inc. TECVAYLI® and TALVEY® Risk Evaluation and Mitigation Strategy (REMS). https://www.tec-talrems.com/#Main. Accessed March 2025.
3. Chari A, Minnema MC, Berdeja JG, et al. Talquetamab, a T-cell-redirecting GPRC5D bispecific antibody for multiple myeloma. *N Engl J Med*. 2022;387(24):2232-2244. doi:10.1056/NEJMoa2204591.
4. 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.