# Up Close with Elranatamab

This section provides an overview of elranatamab-bcmm (ELREXFIO™).

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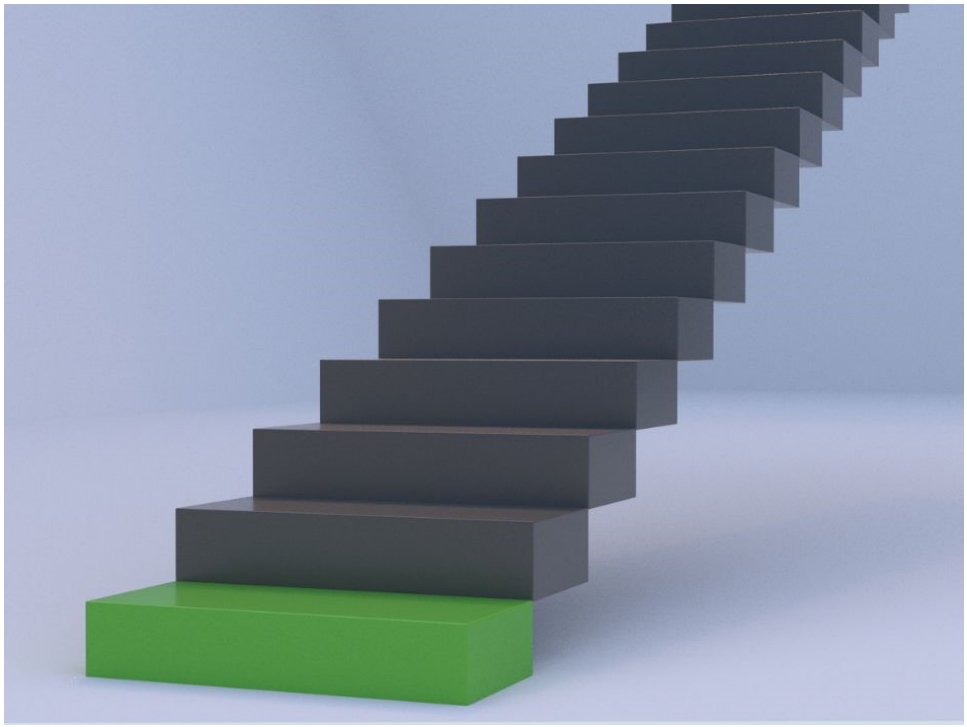
## 🏷️ Indications

Elranatamab is a **bispecific B-cell maturation antigen (BCMA)-directed CD3 T-cell engager** indicated for adult patients with:

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

**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



Elranatamab is administered **subcutaneously once weekly for 24 week**s, then once every 2 weeks in patients that have **achieved a partial response (PR) or better and maintained this response for at least 2 months**. Treatment is continued until disease progression or unacceptable toxicity.

- **Step-up dosing schedule:** 2 step-up doses on Days 1 and 4, followed by the first treatment dose on Day 8 to reduce the incidence and severity of CRS.
    - Per the US Package Insert, **patients should be hospitalized for 48 hour**s after administration of the **first step-up dose**, and for **24 hours** after administration of the **second step-up dose**.
    - A **minimum of 2 days** should be maintained **between step-up dose 1** (12 mg) and **step-up dose 2** (32 mg).
    - A **minimum of 3 days** should be maintained **between step-up dose 2** (32 mg) and the **first 76-mg dose.**
- After step-up dosing, elranatamab is administered as a **76-mg dose once weekly** starting at Week 3.
    - A minimum of 6 days should be maintained between weekly doses.

| Elranatamab Dosing Schedule | | | |
|---|---|---|---|
| **Dosing Schedule** | **Day of Treatment** | **Elranatamab Dose / Route** | |
| **Step-up Dosing Schedule** | 1 | Step-up dose 1 | 12 mg SQ |
| | 4 | Step-up dose 2 | 32 mg SQ |
| | 8 | First treatment dose | 76 mg SQ |
| **Weekly Dosing Schedule** | One week after first treatment dose and weekly thereafter through week 24 | Subsequent treatment doses | 76 mg SQ |
| **Every 2 Week Dosing Schedule**<br><br>***Responders only, Week 25 onward*** | Week 25 and every 2 weeks thereafter | Subsequent treatment doses | 76 mg SQ |
| SQ, subcutaneously | | | |

| Recommendations for Restarting Therapy with Elranatamab After Dosage Delay | | |
|---|---|---|
| **Last Dose Administered** | **Time Since the Last Dose Administered** | **Action for Next Dose** |
| **Step-up dose 1 (12 mg)** | 2 weeks or less (≤ 14 days) | Restart elranatamab at step-up dose 2 (32 mg).* If tolerated, increase to 76 mg 4 days later. |
| | Greater than 2 weeks (> 14 days) | Restart elranatamab step-up dosing schedule at step-up dose 1 (12 mg).* |
| **Step-up dose 2 (32 mg)** | 2 weeks or less (≤ 14 days) | Restart elranatamab at 76 mg.* |
| | Greater than 2 weeks to less than or equal to 4 weeks (15 days to ≤ 28 days) | Restart elranatamab at step-up dose 2 (32 mg).* If tolerated, increase to 76 mg 1 week later. |
| | Greater than 4 weeks (> 28 days) | Restart elranatamab step-up dosing schedule at step-up dose 1 (12 mg).* |
| **Any treatment dose (76 mg)** | 6 weeks or less (≤ 42 days) | Restart elranatamab at 76 mg. |
| | Greater than 6 weeks to less or equal to 12 weeks (43 days to ≤ 84 days)† | Restart elranatamab at step-up dose 2 (32 mg).* If tolerated, increase to 76 mg 1 week later. |
| | Greater than 12 weeks (> 84 days)† | Restart elranatamab step-up dosing schedule at step-up dose 1 (12 mg).* |
| *Administer pretreatment medication prior to elranatamab dose and monitor patients accordingly.<br><br>† Consider benefit-risk of restarting elranatamab in patients who require a dose delay of more than 42 days due to an adverse reaction. | | |

## Recommended Pre-Treatment Medications

Administer the following pre-treatment medications **approximately 1 hour before the first 3 doses of elranatamab** in the **step-up dosing schedule**, which includes step-up dose 1, step-up dose 2, and the first treatment dose to reduce the risk of CRS.

- acetaminophen (or equivalent) 650 mg orally
- dexamethasone (or equivalent) 20 mg orally or intravenously
- diphenhydramine (or equivalent) 25 mg orally

## ⚠️ 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 **58%** of patients who received elranatamab at the recommended dosage, in the clinical trial, MagnetisMM-3.

- **Most CRS events** were reported in the **step-up dosing schedule**, either at s**tep-up dose 1 (43%)**, **step-up dose 2 (35%)**, or the **initial treatment dose (24%**) and were **primarily Grade 1 (50%)**.
    - CRS did **reoccur in approximately 33% patients** regardless of their dosing schedule.
- The **median time to onset** of CRS across all doses was **2 days** (range: 1 to 6) post-administration. The **median duration** of CRS was **2 days** (range: 1 to 9).
- Care teams should monitor for signs/symptoms of CRS and **withhold or permanently discontinue elranatamab 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 **59% of patients** in MagnetisMM-3, and **Grade 3 or 4 neurological toxicity** was reported in **7% of patients**. The most common neurological toxicities included: headache, sensory neuropathy, encephalopathy, and Guillain-Barré Syndrome.

- **ICANS** specifically, was reported in **3.3% of patients** and **reoccurred in 1.1% of patients**.
    - **Most ICANS events** were reported in the **step-up dosing schedule**, at step-up dose 1 (2.7%), however one patient reported ICANS during step-up dose 2 (0.5%). Following the introduction of the treatment dose as part of the weekly dosing schedule, 1.8% of patients reported ICANS.
        - The most commonly reported manifestation of ICANS included Grade 1 or 2 Immune Effector Cell-Associated Encephalopathy (ICE) scores and a depressed level of consciousness.

    - The **median time to onset** of ICANS across all doses was **3 days** (range: 1 to 4) post-administration. The **median duration** of ICANS was **2 days** (range: 1 to 8).
    - 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 neurological toxicity/ICANS.
    - **Patients should be discouraged 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 should **consider withholding or permanently discontinuing elranatamab based on severity**.

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

## 🚨 Other Toxicities


Elranatamab may cause other adverse reactions such as **infections, neutropenia, hepatotoxicity, 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 **elranatamab**-associated toxicities.

**Infections.** Elranatamab may cause serious and fatal infections.

- **Serious infections**, including opportunistic infections, occurred in **42% of patients**, with **Grade 3 or 4 infections in 31%**, and **fatal infections in 7%**.
    - The most common serious infections reported were pneumonia and sepsis.

**The bottom line.** Care teams should **monitor patients for signs of infection before and during treatment**; treat appropriately.

- Avoid administration in patients with active infections; withhold or discontinue elranatamab based on severity.
- Provide prophylactic antimicrobial and anti-viral medications according to current practice guidelines before starting elranatamab.
- Consider treatment with subcutaneous or intravenous immunoglobulin (IVIG) as appropriate.

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**Neutropenia.** Elranatamab may cause neutropenia and febrile neutropenia.

- In the MagnetisMM-3 trial, **decreased neutrophils** occurred in **62% of patients**, with **Grade 3 or 4 decreased neutrophils in 51%**.
    - **Febrile neutropenia** occurred in **2.2% of patients**.

**The bottom line.** Care teams should monitor complete blood counts throughout treatment.

- **Withhold or discontinue elranatamab based on neutropenia severity**; consider prophylactic granulocyte colony-stimulating factor.

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**Hepatotoxicity.** Elranatamab may cause hepatotoxicity.

- In the MagnetisMM-3 trial, **elevated ALT** occurred in **36% of patients**, with **Grade 3 or 4 ALT elevation occurring in 3.8%**; **elevated AST** occurred in **40% of patients**, with **Grade 3 or 4 AST elevation occurring in 6%**.
    - **Grade 3 or 4 total bilirubin** elevations occurred in **0.5% of patients.**
    - Liver enzyme elevation can occur with or without concurrent CRS.

**The bottom line.** Care teams should monitor liver enzymes and bilirubin throughout treatment as clinically indicated.

- **Withhold or consider permanent discontinuation** of elranatamab **based on severity**.

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

- Advise **females of reproductive potential** to use effective contraception **during treatment and for 4 months after** the last dose.
- Verify pregnancy status before initiating elranatamab.

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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:**
    - In MagnetisMM-3, 62% were 65 years of age or older, and 19% were 75 years of age or older.
    - No overall differences in safety or effectiveness were observed in patients 65-74 years of age compared to younger patients.
    - Clinical studies did not include sufficient numbers of patients 75 years of age or older to determine whether they respond differently from younger patients.
- **Pediatric Use:** At this time, no safety and effectiveness data has been established in pediatric patients.

# 🛑 REMS

Elranatamab 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 ELREXFIO REMS to treat patients with elranatamab.

**Notable requirements of the ELREXFIO REMS include the following:**

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

**Steps for a prescriber to become certified:**

1. Review the prescribing information, prescriber training program, and adverse reaction management guide.
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. Complete and provide patients or their caregivers with the patient wallet card.

**Steps for pharmacies and healthcare settings to become certified:**

1. Designate an Authorized Representative (AR) for the pharmacy and healthcare setting
    a. The AR can be a pharmacist, pharmacy technician, registered nurse, or any responsible individual assigned by the pharmacy or healthcare 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 elranatamab 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 ELREXFIO REMS program, click here.

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References


1. ELREXFIO™ (elranatamab-bcmm) [package insert]. New York, NY: Pfizer Inc.; 2023.
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3. ©Pfizer Inc. ELREXFIO™ Risk Evaluation and Mitigation Strategy (REMS). https://www.elrexfiorems.com/#Main/Home. Accessed March 2025.
4. Lesokhin AM, Tomasson MH, Arnulf B, et al. Elranatamab in relapsed or refractory multiple myeloma: phase 2 MagnetisMM-3 trial results. *Nat Med.* 2023;29(9):2259-2267. doi:10.1038/s41591-023-02528-9.