

Up Close with Tarlatamab

This section provides an overview of tarlatamab-dlle (IMDELLTRA™).

-  Indications
-  Dosing and Administration
-  CRS
-  Neurotoxicity (including ICANS)
-  Other Toxicities

Indications

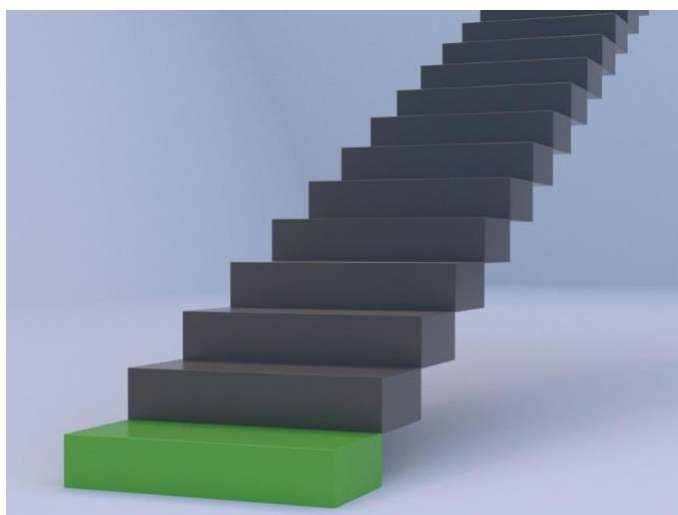


Tarlatamab is a **bispecific delta-like ligand 3 (DLL3)-directed CD3 T-Cell engager** indicated for the treatment of adult patients with:

- **Extensive stage small cell lung cancer (ES-SCLC) with disease progression on or after platinum-based chemotherapy**

Note: These indications are 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



Tarlatamab is administered via an **intravenous (IV) infusion over 1-hour** (rate of 250 mL/hour) with unique **step-up dosing** only during Cycle 1 (Days 1, 8, and 15) to reduce the risk and severity of cytokine release syndrome (CRS) as shown below.

Dosing Schedule	Day of Treatment	Tarlatamab Dose/ Route		Administration Instructions	Tarlatamab Monitoring Recommendations
Cycle 1 (Step-Up) ^a	Day 1	Step-up Dose 1	1 mg IV	Administer over a 1-hour infusion at an appropriate healthcare setting.	Monitor patients from the start of infusion for 22 to 24 hours on in an appropriate healthcare setting.
	Day 8	10 mg IV			Recommend that patients remain within 1-hour of an appropriate healthcare setting for a total of 48 hours from start of the infusion accompanied by a caregiver.
	Day 15	10 mg IV			Observe patients for 6-8 hours post infusion. ^b
Cycle 2	Day 1	10 mg IV		Administer over a 1-hour infusion at an appropriate healthcare setting.	Observe patients for 6-8 hours post infusion. ^b
	Day 15	10 mg IV			
Cycles 3-4	Day 1	10 mg IV		Administer over a 1-hour infusion at an appropriate healthcare setting.	Observe patients for 3-4 hours post infusion. ^b
	Day 15	10 mg IV			
Cycles 5+	Day 1	10 mg IV		Administer over a 1-hour infusion at an appropriate healthcare setting.	Observe patients for hours post infusion. ^b
	Day 15	10 mg IV			

^aAdminister concomitant medication before and after tarlatamab infusion (**Cycle 1 only**)

- Prior to tarlatamab infusion (Cycle 1 Days 1 and 8):
 - Administer 8 mg of dexamethasone intravenously (or equivalent) within 1 hour of tarlatamab infusion
- Post-tarlatamab infusion (Cycle 1 Days 1, 8, 15):
 - Administer 1 liter of normal saline intravenously over 4-5 hours immediately following completion of tarlatamab infusion

^bExtended monitoring in a healthcare setting is not required unless the patient experiences Grade ≥ 2 CRS, ICANS or neurological toxicity during prior treatments

Recommendations for Restarting Tarlatamab Following Dose Delay			
Last Administered Cycle/Day of Tarlatamab	Last Dose of Tarlatamab Administered	Time Since Last Administered Dose of Tarlatamab	Recommended Action ^a
Cycle 1 Day 1	1 mg	≤ 14 days	Administer tarlatamab 10 mg, then resume the treatment plan as scheduled.
		> 14 days	Administer tarlatamab step-up dose 1 mg. If dose is tolerated, increase to 10 mg (one week later) and resume treatment plan as scheduled.
Cycle 1 Day 8	10 mg	≤ 21 days	Administer tarlatamab 10 mg, then resume the treatment plan as scheduled.
		> 21 days	Administer tarlatamab step-up dose 1 mg. If dose is tolerated, increase to 10 mg (one week later) and resume treatment plan as scheduled.
Cycle 1 Day 15 and Subsequent cycles every 2 weeks thereafter	10 mg	≤ 28 days	Administer tarlatamab 10 mg, then resume the treatment plan as scheduled.
		> 28 days	Administer tarlatamab step-up dose 1 mg. If dose is tolerated, increase to 10 mg (one week later) and resume treatment plan as scheduled.
^a Administer concomitant medication before and after tarlatamab infusion (Cycle 1 only) • Prior to tarlatamab infusion (Cycle 1 Days 1 and 8): ◦ Administer 8 mg of dexamethasone intravenously (or equivalent) within 1 hour of tarlatamab infusion • Post-tarlatamab infusion (Cycle 1 Days 1, 8, 15): ◦ Administer 1 liter of normal saline intravenously over 4-5 hours immediately following completion of tarlatamab infusion ^b Extended monitoring in a healthcare setting is not required unless the patient experiences Grade ≥ 2 CRS, ICANS or neurological toxicity during prior treatments			

⚠ 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 **55%** of patients who received tarlatamab in the studies DeLLphi-300 and DeLLphi-301.

- Most CRS events occurred during **Cycle 1**, with the highest events occurring with the first dose of tarlatamab (43%), followed by the second dose (29%) and third or subsequent doses (9%).
 - **≥ Grade 2 CRS events** occurred on the following days of Cycle 1
 - Day 1 (16%)
 - Day 8 (4.3%)
 - Day 15 (2.1%)
 - CRS events were primarily Grade 1 (34%) with Grade 3 and 4 events occurring in 1.1% and 0.5% of patients, respectively.
- The **median time to onset** of CRS following administration of the most recent dose of tarlatamab was 13.5 hours (range: 1 to 268).
 - The median time to onset of ≥ Grade 2 CRS events following administration of the most recent dose of tarlatamab was 14.6 hours (range: 1 to 566).
- Care teams should monitor patients for signs/symptoms of CRS during treatment with tarlatamab.
 - **At first sign of CRS**, care teams should **immediately discontinue the tarlatamab infusion** and evaluate the patient for need of hospitalization and supportive care measures.

The bottom line. CRS was primarily low-grade and predictable throughout Cycle 1 and for subsequent cycles.

🧠 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 **47%** of patients in a pooled analysis of the two clinical trials, **10%** of which were reported as **Grade 3**.

- **Neurological toxicity consistent with ICANS** was reported in **9%** of patients treated with tarlatamab, including **recurrent** events in **1.6%** of patients.
 - $\geq$ Grade 2 CRS events occurred on the following days of Cycle 1: Day 1 (16%), Day 8 (4.3%), and Day 15 (2.1%); however, most patients experienced ICANS after receiving tarlatamab on Cycle 2 Day 1 (24%).
- The **median time to onset** of ICANS following administration of the **first** dose of tarlatamab was **29.5 days** (range: 1 to 154), though it can occur at any point several weeks following its administration.
- The **median time to resolution** of ICANS was **33 days** (range: 1 to 93).
- Care teams should advise their patients to avoid driving or operating heavy machinery in the event of any neurological symptoms, until these events resolve.
 - Tarlatamab **may need to be withheld or permanently discontinued based on the severity**.

The bottom line: The majority of ICANS events occurred on Day 1 of the second cycle, however events that occurred during the first cycle were of a higher grade.

Other Toxicities



Tarlatamab may cause other adverse reactions such as **cytopenias, infections, hypersensitivity, and certain toxicities including 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 **tarlatamab**-associated toxicities.

Infections. Tarlatamab may cause serious and fatal infections.

- **Serious infections**, including opportunistic infections, occurred in **41%** of patients with **Grade 3 or 4** infections reported in **13%** of patients.
 - The most common serious infections reported were COVID-19 (of note, this trial was conducted during the COVID-19 pandemic), candida infections, pneumonia, and urinary tract infections.

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

- **Based on severity**, tarlatamab **may need to be withheld or permanently discontinued.**
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Cytopenias. Tarlatamab may cause cytopenias which include: thrombocytopenia, anemia, and neutropenia.

- In the pooled safety analysis, laboratory abnormalities resulted in **neutropenia (12%), anemia (58%), and thrombocytopenia (33%)** of patients who received tarlatamab.
 - These events do include **Grade 3 or 4 reductions** for neutropenia, anemia, and thrombocytopenia as followed: **6%, 5%, and 3.2%**.
- **Febrile neutropenia** occurred in **0.5%** of patients.

The bottom line. Care teams should **perform complete blood counts prior to treatment with each dose of tarlatamab and as clinically indicated** throughout treatment.

- **Withhold or discontinue tarlatamab based on neutropenia severity.**
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Hepatotoxicity. Tarlatamab may cause hepatotoxicity which can include in liver enzymes, including alanine aminotransferase (ALT), aspartate aminotransferase (AST) and markers like total bilirubin.

- Within the two clinical trials, **liver enzyme elevations, AST and ALT** were observed in **44%** and **42%** of patients and **total bilirubin elevations** occurred in **15%** of patients who received tarlatamab.
 - In addition, **Grade 3 or 4 AST** elevations occurred in **3.2%** of patients whereas **Grade 3 or 4 ALT** elevations occurred in **2.1%** of patients.
 - **Grade 3 or 4 total bilirubin elevations** occurred in **1.6%** of patients.

The bottom line. Care teams should **monitor liver enzymes routinely**, including AST/ALT/total bilirubin/total bilirubin prior to initiation of tarlatamab and during therapy.

- **Treatment with tarlatamab** may need to be **temporarily held or permanently discontinued based on severity.**
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Hypersensitivity. Tarlatamab may cause severe hypersensitivity reactions, including but not limited to rash or bronchospasms.

The bottom line. Care teams should **monitor their patients for any sign/symptoms of hypersensitivity** during treatment with tarlatamab.

- Care teams may need to **consider a temporary hold or permanent discontinuation based on severity.**
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Embryo-Fetal Toxicity. Tarlatamab 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 2 months** after the last dose.
 - Verify pregnancy status before initiating tarlatamab.
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Use in Specific Populations

- **Lactation:** Advise women not to breastfeed during treatment and for **2 months** after the last dose.
- **Pediatric Use:** The safety and efficacy of tarlatamab has not yet been established in the pediatric population.
- **Geriatric Use:** Of the total number of tarlatamab treated patients in these studies, 54% were 65 years of age and older and 12% were 75 years of age or older. No overall differences in safety or effectiveness were observed between these patients and younger patients.

Updated: 5/16/2025

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. [IMDELLTRA™ \(tarlatamab-dlle\) \[package insert\]. Amgen Inc. Thousand Oaks, CA. 2024.](#)
3. [Paz-Ares L, Goldman JW, Goto K, et al. Tarlatamab, a first-in-class DLL3-targeted bispecific T-cell engager, in recurrent small-cell lung cancer: an open-label, phase I study. J Clin Oncol. Published online 2024. doi:10.1200/JCO.23.XXXXX.](#)
4. [Ganti AK, Shuster D, Schneider BJ, et al. Tarlatamab for patients with previously treated small-cell lung cancer. N Engl J Med. Published online 2024. doi:10.1056/NEJMoaXXXXX.](#)