IMDELLTRA®: Dosing, Administration & Pharmacy Guide

IMDELLTRA® J-Code J9026, Injection, tarlatamab-dlle, 1 mg[1,]*

*The HCPCS billing unit for J9026 is 1 mg. J9026 can be used for both 1 mg and 10 mg IMDELLTRA® vials. It is the responsibility of the provider to report the number of billing units administered.

Coding and coverage policies change periodically and often without warning. The healthcare provider is solely responsible for determining coverage and reimbursement parameters and appropriate coding for his/her own patients and procedures. This information is not a guarantee of coverage or reimbursement.

INDICATION

IMDELLTRA® (tarlatamab-dlle) is 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.

This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

IMPORTANT SAFETY INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME AND NEUROLOGIC TOXICITY including IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME

- **Cytokine release syndrome (CRS), including serious or life-threatening reactions, can occur in patients receiving IMDELLTRA®. Initiate treatment with IMDELLTRA® using the step-up dosing schedule to reduce the incidence and severity of CRS. Withhold IMDELLTRA® until CRS resolves or permanently discontinue based on severity.**
- **Neurologic toxicity, including immune effector cell-associated neurotoxicity syndrome (ICANS), including serious or life-threatening reactions, can occur in patients receiving IMDELLTRA®. Monitor patients for signs and symptoms of neurologic toxicity, including ICANS, during treatment and treat promptly. Withhold IMDELLTRA® until ICANS resolves or permanently discontinue based on severity.**

Please see additional Important Safety Information, including BOXED WARNINGS, on pages 18–19.

IMDELLTRA®
(tarlatamab-dlle) for injection 1 mg & 10 mg single-use vials

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IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

- **Cytokine Release Syndrome (CRS):** IMDELLTRA® can cause CRS including serious or life-threatening reactions. In the pooled safety population, CRS occurred in 55% of patients who received IMDELLTRA®, including 34% Grade 1, 19% Grade 2, 1.1% Grade 3 and 0.5% Grade 4. Recurrent CRS occurred in 24% of patients, including 18% Grade 1 and 6% Grade 2.

  Most events (43%) of CRS occurred after the first dose, with 29% of patients experiencing any grade CRS after the second dose and 9% of patients experiencing CRS following the third dose or later. Following the Day 1, Day 8, and Day 15 infusions, 16%, 4.3% and 2.1% of patients experienced ≥ Grade 2 CRS, respectively. The median time to onset of all grade CRS from most recent dose of IMDELLTRA® was 13.5 hours (range: 1 to 268 hours). The median time to onset of ≥ Grade 2 CRS from most recent dose of IMDELLTRA® was 14.6 hours (range: 2 to 566 hours).

  Clinical signs and symptoms of CRS included pyrexia, hypotension, fatigue, tachycardia, headache, hypoxia, nausea, and vomiting. Potentially life-threatening complications of CRS may include cardiac dysfunction, acute respiratory distress syndrome, neurologic toxicity, renal and/or hepatic failure, and disseminated intravascular coagulation (DIC).

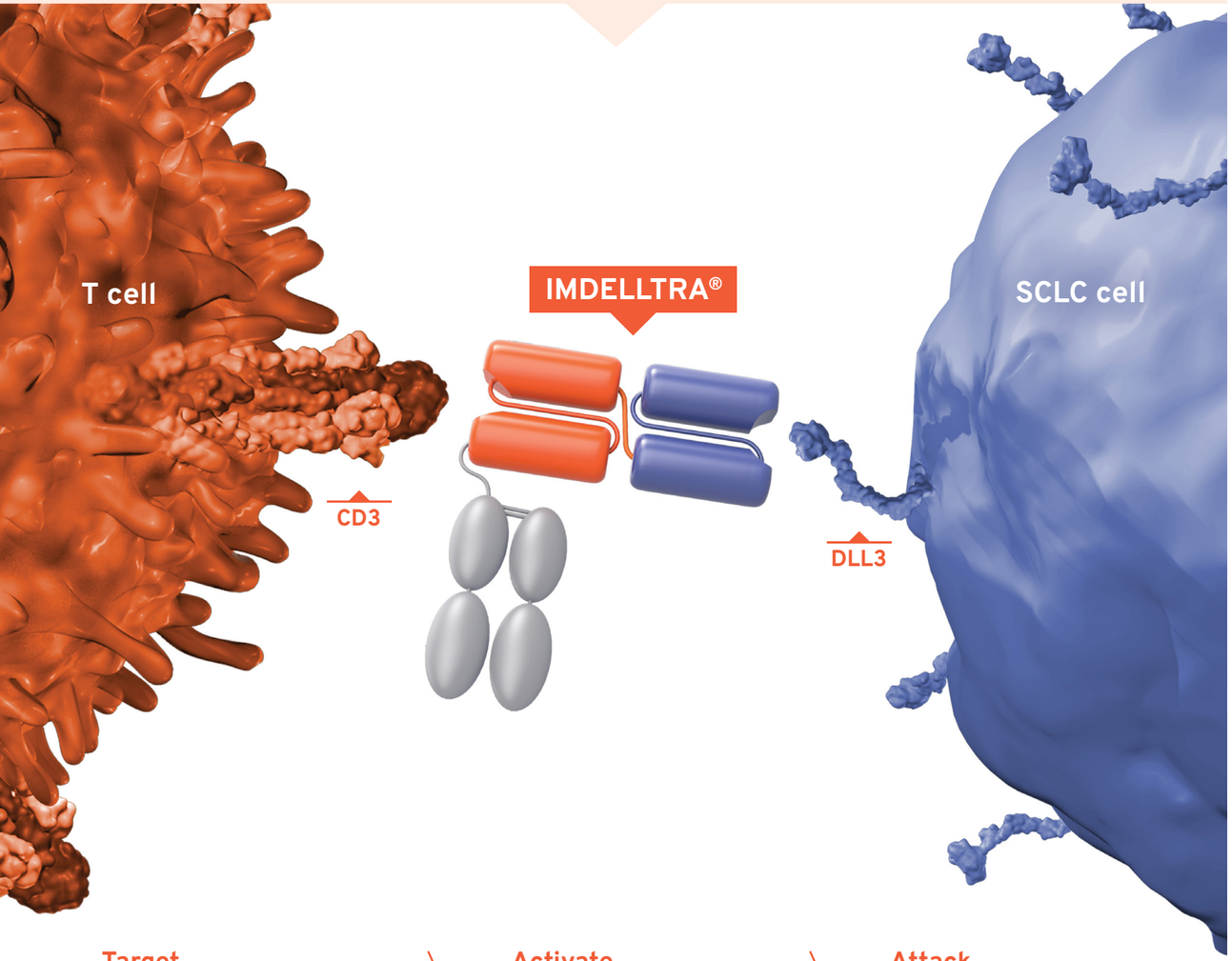
  Administer IMDELLTRA® following the recommended step-up dosing and administer concomitant medications before and after Cycle 1 IMDELLTRA® infusions as described in Table 3 of the Prescribing Information (PI) to reduce the risk of CRS. Administer IMDELLTRA® in an appropriate health care facility equipped to monitor and manage CRS. Ensure patients are well hydrated prior to administration of IMDELLTRA®.

  Closely monitor patients for signs and symptoms of CRS during treatment with IMDELLTRA®. At the first sign of CRS, immediately discontinue IMDELLTRA® infusion, evaluate the patient for hospitalization and institute supportive care based on severity. Withhold or permanently discontinue IMDELLTRA® based on severity. Counsel patients to seek medical attention should signs or symptoms of CRS occur.

Please see additional Important Safety Information, including BOXED WARNINGS, on pages 18–19.

IMDELLTRA® (tarlatamab-dlle) for injection 1 mg & 10 mg single-use vials

IMDELLTRA® is the first and only DLL3-targeting Bispecific T-cell Engager (BiTE®) therapy that activates the patient's own T cells to attack DLL3-expressing cells[2]



Target

IMDELLTRA® targets the DLL3 antigen while simultaneously engaging the patient's own T cells through the CD3 antigen[2]

Activate

The binding of IMDELLTRA® results in the formation of a synapse between T cells and DLL3-expressing cells, including tumor cells, leading to T-cell activation[2]

Attack

The activated T cells cause release of inflammatory cytokines and lysis of DLL3-expressing cells[2,*]

*IMDELLTRA® had anti-tumor activity in mouse models of SCLC.[2]
CD, cluster of differentiation; DLL3, delta-like ligand 3; SCLC, small cell lung cancer.

Please see additional Important Safety Information, including BOXED WARNINGS, on pages 18–19.

IMDELLTRA® dosing

		CONCOMITANT MEDICATION Pre-IMDELLTRA® Dose[2]	IMDELLTRA® ADMINISTRATION 1-hour IV infusion[2]	CONCOMITANT MEDICATION Post-IMDELLTRA® Dose[2]	PATIENT MONITORING[2]
STEP-UP DOSING SCHEDULE CYCLE 1	Day 1	**8 mg IV dexamethasone (or equivalent)** within 1 hour prior to dose Flush IV line†	1 mg Step-up dose	**1 L normal saline IV** over 4–5 hours immediately following infusion	Monitor for 22–24 hours from the start of the IMDELLTRA® infusion in an appropriate healthcare setting
	Day 8		10 mg		
	Day 15		10 mg		Observe for 6–8 hours post infusion
CYCLE 2	Day 1		10 mg		Observe for 6–8 hours post infusion
	Day 15				
CYCLES 3–4	Day 1		10 mg		Observe for 3–4 hours post infusion
	Day 15				
CYCLES 5+	Day 1		10 mg		Observe for 2 hours post infusion
	Day 15				

On Day 1 and Day 8 of Cycle 1, recommend patients remain within 1 hour of an appropriate healthcare setting for a total of 48 hours from start of the IMDELLTRA® infusion, accompanied by a caregiver.[2]

All IMDELLTRA® infusions and monitoring should take place in an appropriate healthcare setting.[2]

After Days 1 and 8 of Cycle 1, extended monitoring in a healthcare setting is not required unless the patient experiences Grade ≥ 2 CRS, ICANS, or neurological toxicity during prior treatments.[1] See the IMDELLTRA® full Prescribing Information for monitoring recommendations.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

- **Neurologic Toxicity, Including ICANS:** IMDELLTRA® can cause serious or life-threatening neurologic toxicity, including ICANS. In the pooled safety population, neurologic toxicity, including ICANS, occurred in 47% of patients who received IMDELLTRA®, including 10% Grade 3. The most frequent neurologic toxicities were headache (14%), peripheral neuropathy (7%), dizziness (7%), insomnia (6%), muscular weakness (3.7%), delirium (2.1%), syncope (1.6%), and neurotoxicity (1.1%).

  ICANS occurred in 9% of IMDELLTRA®-treated patients. Recurrent ICANS occurred in 1.6% of patients. Most patients experienced ICANS following Cycle 2 Day 1 (24%). Following Day 1, Day 8, and Day 15 infusions, 0.5%, 0.5% and 3.7% of patients experienced ≥ Grade 2 ICANS, respectively. The median time to onset of ICANS from the first dose of IMDELLTRA® was 29.5 days (range: 1 to 154 days). ICANS can occur several weeks following administration of IMDELLTRA®. The median time to resolution of ICANS was 33 days (range: 1 to 93 days).

†The IV catheter for concomitant medications administration can be used to administer the IMDELLTRA® infusion. To ensure patency, flush the IV catheter over 3–5 minutes using 0.9% Sodium Chloride for Injection.[2]

CRS, cytokine release syndrome; ICANS, immune effector cell–associated neurotoxicity syndrome; IV, intravenous.

IMDELLTRA® (tarlatamab-dlle) for injection 1 mg & 10 mg single-use vials

Administer IMDELLTRA® in an appropriate healthcare setting as a 1-hour IV infusion every 2 weeks (Q2W) after an initial step-up dosing schedule to reduce the incidence and severity of CRS[2]

Dosing schedule[2]

- Administer 1 mg of IMDELLTRA® on Day 1 of Cycle 1, followed by 10 mg of IMDELLTRA® on Days 8, 15, and every 2 weeks thereafter
- Treat with IMDELLTRA® until disease progression or unacceptable toxicity
- Prior to administration of IMDELLTRA®, evaluate complete blood count, liver enzymes, and bilirubin before each dose, and as clinically indicated
- Ensure patients are well hydrated prior to administration of IMDELLTRA®

Recommended concomitant medications for Cycle 1 administration[2]

- On Days 1 and 8 of Cycle 1, administer 8 mg IV dexamethasone (or equivalent) within 1 hour prior to IMDELLTRA® dose
- On Days 1, 8, and 15 of Cycle 1, administer 1 L normal saline IV over 4–5 hours immediately after completion of IMDELLTRA® infusion
- No concomitant medications are recommended for all subsequent infusions of IMDELLTRA® treatment
  - Patients may experience treatment-related AEs that may require medication and/or management strategies

Administration[2]

- The IV catheter for concomitant medications administration can be used to administer the IMDELLTRA® infusion. To ensure patency, flush the IV catheter over 3–5 minutes using 0.9% Sodium Chloride for Injection
- Administer the reconstituted and diluted IMDELLTRA® as an IV infusion over 1 hour at a constant flow rate (250 mL/hr) using an infusion pump. The pump should be programmable, lockable, non-elastomeric, and have an alarm

Post-infusion monitoring for potential CRS & ICANS[2]

- On Days 1 and 8 of Cycle 1, monitor patients from the start of the IMDELLTRA® infusion for 22 to 24 hours in an appropriate healthcare setting
- On Day 15 of Cycle 1, observe patients for 6–8 hours post infusion
- On Days 1 and 15 of Cycle 2, observe patients for 6–8 hours post infusion
- On Days 1 and 15 of Cycles 3 and 4, observe patients for 3–4 hours post infusion
- On Days 1 and 15 of Cycle 5 and all subsequent infusions, observe patients for 2 hours post infusion

Post-infusion patient instruction[2]

- On Days 1 and 8 of Cycle 1, it is recommended that patients remain within 1 hour of an appropriate healthcare setting for a total of 48 hours from the start of the IMDELLTRA® infusion, accompanied by a caregiver
- After Days 1 and 8 of Cycle 1, extended monitoring in a healthcare setting is not required unless the patient experiences Grade ≥ 2 CRS, ICANS, or neurological toxicity during prior treatments. See the IMDELLTRA® full Prescribing Information for monitoring recommendations

Please see the full Prescribing Information for additional information on Dosing, Administration, and Monitoring

AE, adverse event; CRS, cytokine release syndrome; hr, hour; ICANS, immune effector cell–associated neurotoxicity syndrome; IV, intravenous.

Please see additional Important Safety Information, including BOXED WARNINGS, on pages 18–19.

IMDELLTRA® storage and handling, and package contents and vials

IMDELLTRA® for injection is supplied as a sterile, preservative free, white to slightly yellow, lyophilized powder in a single-dose vial for reconstitution and further dilution[2]

NDC (10 Digit)[2]	Strength[2]	Quantity	J Code
55513-059-01	1 mg	• One single-dose 1 mg vial of IMDELLTRA® (NDC 55513-103-01)[2,3] • Two 7 mL vials of IVSS (NDC 55513-068-01)[2,3]	J9026[1]
55513-077-01	10 mg	• One single-dose 10 mg vial of IMDELLTRA® (NDC 55513-069-01)[2,3] • Two 7 mL vials of IVSS (NDC 55513-068-01)[2,3]	J9026[1]

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Coding and coverage policies change periodically and often without warning. The healthcare provider is solely responsible for determining coverage and reimbursement parameters and appropriate coding for his/her own patients and procedures. This information is not a guarantee of coverage or reimbursement.

- Store IMDELLTRA® and IVSS vials refrigerated at 2°C to 8°C (36°F to 46°F) in the original carton to protect from light until time of use. Do not freeze[2]
- IMDELLTRA® and IVSS vials may be kept at room temperature between 20°C to 25°C (68°F to 77°F) for up to 24 hours in the original carton to protect from light[2]

Please see full Prescribing Information for preparation and administration instructions

HCPCS, Healthcare Common Procedure Coding System; IVSS, IV solution stabilizer; NDC, National Drug Code.

IMDELLTRA® (tarlatamab-dlle) for injection 1 mg & 10 mg single-use vials

Information on material compatibility

- IV bags composed of ethyl vinyl acetate (EVA), polyolefin, and polyvinyl chloride (PVC), have been shown to be compatible with IMDELLTRA® at the specified administration conditions[2]
- IV line and catheter materials composed of polyolefin, PVC, and polyurethane have been shown to be compatible with IMDELLTRA® at the specified administration conditions[2]
- The use of Closed System Transfer Device (CSTD) is not recommended due to potential wrong dose medication error risk. Amgen has not performed compatibility testing of vial adaptor CSTDs with IMDELLTRA®[2]

Step 1 Reconstitute IMDELLTRA® vial with Sterile Water for Injection

Amount of Sterile Water for Injection required to reconstitute IMDELLTRA® [2,*]

IMDELLTRA® vial strength	Sterile Water for Injection required to reconstitute IMDELLTRA®	Resulting concentration
1 mg	1.3 mL	0.9 mg/mL
10 mg	4.4 mL	2.4 mg/mL

*Each vial contains overfill to allow for withdrawal of 1.1 mL (1 mg vial) or 4.2 mL (10 mg vial) after reconstitution to ensure delivery at the stated concentration of labeled vial strength.[2]

- **Do not use IVSS for reconstitution of IMDELLTRA®.** The IVSS is used to coat the IV bag prior to addition of reconstituted IMDELLTRA® to prevent adsorption of IMDELLTRA® to IV bags and IV tubing[2]

1 Using a needle and syringe filled with the required amount of sterile water, inject the sterile water against the glass vial. Avoid injecting the water directly onto the powder to prevent foaming[2]

2 Gently swirl the contents to mix. Do not shake[2]

3 Inspect parenteral drug products for particulate matter and discoloration prior to administration. Inspect that the solution is clear to opalescent, colorless to slightly yellow. Do not use if the solution is cloudy or has particulates[2]

4 Further dilute reconstituted IMDELLTRA®[2]

5 The reconstituted IMDELLTRA® must be further diluted within 4 hours of reconstitution, or discarded[2]

IV, intravenous; IVSS, IV solution stabilizer.

Please see additional Important Safety Information, including BOXED WARNINGS, on pages 18–19.

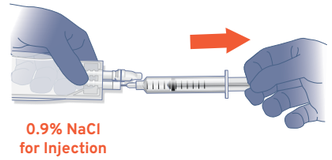
Preparation

Steps 2-5 Prepare IMDELLTRA® infusion bag

Volumes required for preparation of IMDELLTRA® infusion bag[2]

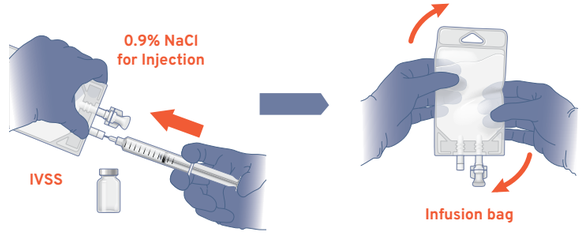
IMDELLTRA® vial strength	Volume of 0.9% Sodium Chloride to withdraw from 250 mL IV bag	Volume of IVSS to add to IV Bag	Volume of reconstituted IMDELLTRA® to add to 250 mL IV bag
1 mg	14 mL	13 mL	1.1 mL
10 mg	17 mL	13 mL	4.2 mL

Step 2: Withdraw 0.9% Sodium Chloride for Injection



1 Using a 250 mL prefilled bag of 0.9% Sodium Chloride for Injection, withdraw 14 mL (for 1 mg IMDELLTRA® dose) or 17 mL (for 10 mg IMDELLTRA® dose) and discard[2]

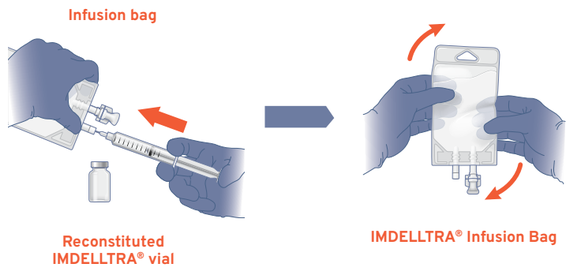
Step 3: Add IVSS to the infusion bag



1 Inject 13 mL of IVSS into the 250 mL 0.9% Sodium Chloride infusion bag[2]

2 Gently mix the contents of the infusion bag to avoid foaming. Do not shake[2]

Step 4: Dilute the reconstituted IMDELLTRA® into the infusion bag



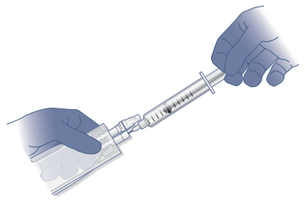
1 Transfer 1.1 mL (for 1 mg IMDELLTRA® dose) or 4.2 mL (for 10 mg IMDELLTRA® dose) of reconstituted IMDELLTRA® to the infusion bag containing IVSS[2]

- NOTE: the final concentrations for the different strength vials are NOT the same following reconstitution and further dilution[2]

2 Gently mix the contents of the bag. Do not shake[2]

IMDELLTRA® (tarlatamab-dlle) for injection 1 mg & 10 mg single-use vials

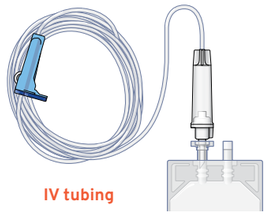
Step 5: Remove air from the IV bag



IMDELLTRA® infusion bag

1 Remove air from the prepared IV bag using an empty syringe to avoid foaming[2]

Step 6 Prime the IV tubing



IV tubing

1 Prime IV tubing with either 0.9% Sodium Chloride for Injection or with the final prepared product[2]

2 If the prepared IMDELLTRA® infusion bag is not used immediately, it can be stored at room temperature (20°C to 25°C or 68°F to 77°F) for 8 hours, or it can be refrigerated (2°C to 8°C or 36°F to 46°F) for 7 days[2]

- Discard IMDELLTRA® infusion after maximum storage time (from time of reconstitution)[2]
- Do not re-refrigerate the prepared infusion bag[2]

It is very important that the instructions for Dosing and Administration provided in the full Prescribing Information are strictly followed.

IV, intravenous.

Please see additional Important Safety Information, including BOXED WARNINGS, on pages 18–19.

Cytokine release syndrome (CRS)

- Administer IMDELLTRA® according to the step-up dosing schedule to reduce the incidence and severity of CRS[1]
- Diagnose CRS based on clinical presentation (See page 2 under “Warnings and Precautions”)[2]
- Evaluate for and treat other causes of fever, hypoxia, and hypotension. If CRS is suspected, manage according to the recommendations below[2]
- Monitor patients who experience Grade 2 or higher CRS with continuous cardiac telemetry and pulse oximetry. Perform laboratory testing to monitor for disseminated intravascular coagulation (DIC), hematology parameters, as well as pulmonary, cardiac, renal, and hepatic function.[2] Please see the full Prescribing Information for additional information

Dosage modifications and management strategies for CRS[2,*]

CRS Grade	Dosage Modifications	Management Strategies
Grade 1 • Symptoms require symptomatic treatment only (eg, fever ≥ 100.4°F without hypotension or hypoxia)	Withhold IMDELLTRA® until event resolves, then resume IMDELLTRA® at the next scheduled dose	Administer symptomatic treatment (eg, acetaminophen) for fever
Grade 2 • Symptoms require and respond to moderate intervention – Fever ≥ 100.4°F – Hypotension responsive to fluids not requiring vasopressors, and/or – Hypoxia requiring low-flow nasal cannula or blow-by	Withhold IMDELLTRA® until event resolves, then resume IMDELLTRA® at the next scheduled dose	• Recommend hospitalization for a minimum of 24 hours with cardiac telemetry and pulse oximetry • Administer symptomatic treatment (eg, acetaminophen) for fever • Administer supplemental oxygen and intravenous fluids (IVF) when indicated • Consider dexamethasone† (or equivalent) 8 mg IV • Consider tocilizumab (or equivalent) When resuming treatment at the next planned dose, monitor patients from the start of the IMDELLTRA® infusion for 22 to 24 hours in an appropriate healthcare setting
Grade 3 • Severe symptoms defined as temperature ≥ 100.4°F with: – Hemodynamic instability requiring a vasopressor (with or without vasopressin) or – Worsening hypoxia or respiratory distress requiring high-flow nasal cannula (> 6 L/min oxygen) or face mask	• Withhold IMDELLTRA® until the event resolves, then resume IMDELLTRA® at the next scheduled dose • For recurrent Grade 3 events, permanently discontinue IMDELLTRA®	In addition to Grade 2 treatment: • Recommend intensive monitoring (eg, ICU care) • Administer dexamethasone† (or equivalent) 8 mg IV every 8 hours up to 3 doses • Vasopressor support as needed • High-flow oxygen support as needed • Recommend tocilizumab (or equivalent) • Prior to the next dose, administer concomitant medications as recommended for Cycle 1 When resuming treatment at the next planned dose, monitor patients from the start of the IMDELLTRA® infusion for 22 to 24 hours in an appropriate healthcare setting
Grade 4 • Life-threatening symptoms defined as temperature ≥ 100.4°F with: – Hemodynamic instability requiring multiple vasopressors (excluding vasopressin) – Worsening hypoxia or respiratory distress despite oxygen administration requiring positive pressure	Permanently discontinue IMDELLTRA®	• ICU care • Per Grade 3 treatment • Recommend tocilizumab (or equivalent)

*CRS grading, dosage modifications, and management are based on American Society for Transplantation and Cellular Therapy (ASTCT) Consensus Grading (2019).[2]
†Taper steroids per standard-of-care guidelines.[2]

ICU, intensive care unit.

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Neurologic toxicity/immune effector cell–associated neurotoxicity syndrome (ICANS)

- At the first sign of neurologic toxicity, including ICANS, withhold IMDELLTRA® and consider neurology evaluation[2]
- Closely monitor patients for signs and symptoms of neurologic toxicity and ICANS during IMDELLTRA® treatment[2]
- Rule out other causes of neurologic symptoms. Provide supportive therapy, which may include intensive care, for severe or life-threatening neurologic toxicities, including ICANS[2]
- Manage according to the recommendations provided here.[2] Please see the full Prescribing Information for additional information

Dosage modifications and management strategies for ICANS[2,*]

ICANS Grade	Dosage Modifications	Management Strategies
Grade 1 ▪ Immune effector cell–associated encephalopathy (ICE) score 7–9[†] with no depressed level of consciousness	Withhold IMDELLTRA® until ICANS resolves, then resume IMDELLTRA® at the next scheduled dose	Supportive care
Grade 2 ▪ ICE score 3–6[†] and/or ▪ Mild somnolence awaking to voice	Withhold IMDELLTRA® until ICANS resolves, then resume IMDELLTRA® at the next scheduled dose	▪ Supportive care ▪ Dexamethasone[‡] (or equivalent) 10 mg IV. Can repeat every 6 hours or methylprednisolone 1 mg/kg IV every 12 hours if symptoms worsen ▪ Monitor neurologic symptoms and consider consultation with neurologist and other specialists for further evaluation and management ▪ Monitor patients for 22 to 24 hours following the next dose of IMDELLTRA®
Grade 3 ▪ ICE score 0–2[†] and/or ▪ Depressed level of consciousness awakening only to tactile stimulus and/or ▪ Any clinical seizure, focal or generalized, that resolves rapidly, or nonconvulsive seizures on EEG that resolve with intervention, and/or ▪ Focal or local edema on neuroimaging	▪ Withhold IMDELLTRA® until ICANS resolves, then resume IMDELLTRA® at the next scheduled dose ▪ If there is no improvement to Grade ≤ 1 within 7 days, or Grade 3 toxicity reoccurs within 7 days of reinitiation, permanently discontinue IMDELLTRA® ▪ For recurrent Grade 3 events, permanently discontinue IMDELLTRA®	▪ Recommend intensive monitoring (eg, ICU care) ▪ Consider mechanical ventilation for airway protection ▪ Dexamethasone[‡] (or equivalent) 10 mg IV every 6 hours or methylprednisolone 1 mg/kg IV every 12 hours ▪ Consider repeat neuroimaging (CT or MRI) every 2–3 days if patient has persistent Grade ≥ 3 neurotoxicity ▪ Monitor patients for 22 to 24 hours following the next dose of IMDELLTRA®
Grade 4 ▪ ICE score 0[†] (patient is unarousable and unable to perform ICE) and/or ▪ Stupor or coma and/or ▪ Life-threatening prolonged seizure (> 5 minutes) or repetitive clinical or electrical seizures without return to baseline in between and/or ▪ Diffuse cerebral edema on neuroimaging, decerebrate or decorticate posturing or papilledema, cranial nerve VI palsy, or Cushing's triad	Permanently discontinue IMDELLTRA®	▪ ICU care ▪ Consider mechanical ventilation for airway protection ▪ High-dose corticosteroids[‡] ▪ Consider repeat neuroimaging (CT or MRI) every 2–3 days if subject has persistent Grade ≥ 3 neurotoxicity ▪ Treat convulsive status epilepticus per institutional guidelines

[*]ICANS grading, dosage modifications, and management are based on ASTCT Consensus Grading (2019).[2] [†]If patient is arousable and able to perform ICE Assessment, assess: orientation (oriented to year, month, city, hospital = 4 points); naming (names 3 objects, eg, point to clock, pen, button = 3 points); following commands (eg, "show me 2 fingers" or "close your eyes and stick out your tongue" = 1 point); writing (ability to write a standard sentence = 1 point); and attention (count backwards from 100 by ten = 1 point). If patient is unarousable and unable to perform ICE Assessment (Grade 4 ICANS) = 0 points.[2] [‡]Taper steroids per standard-of-care guidelines.[2]

ASTCT, American Society for Transplantation and Cellular Therapy; CT, computed tomography; EEG, electroencephalogram; ICU, intensive care unit; IV, intravenous; MRI, magnetic resonance imaging.

Please see additional Important Safety Information, including BOXED WARNINGS, on pages 18–19.

Neurologic toxicity/ICANS (cont'd)

ICE assessment tool[4]

Assessment	Points
Orientation: Orientation to year, month, city, hospital	**4**
Naming: Ability to name 3 objects (eg, point to clock, pen, button)	**3**
Following commands: Ability to follow simple commands (eg, "show me 2 fingers" or "close your eyes and stick out your tongue")	**1**
Writing: Ability to write a standard sentence (eg, "our national bird is the bald eagle")	**1**
Attention: Ability to count backwards from 100 by 10	**1**

Cytopenias

Dosage modifications for cytopenias[2]

Adverse Event	Severity[§]	Dosage Modifications
Cytopenias[†]	**Grade 3 or Grade 4 neutropenia**	▪ Withhold IMDELLTRA® until recovery to ≤ Grade 2 ▪ Consider administration of granulocyte colony stimulating factor (G-CSF) ▪ Permanently discontinue if recovery to ≤ Grade 2 does not occur within 3 weeks
	Recurrent Grade 4 neutropenia	Permanently discontinue IMDELLTRA®
	Febrile neutropenia	Withhold IMDELLTRA® until neutropenia recovers to ≤ Grade 2 and fever resolves
	Hemoglobin < 8 g/dL	Withhold IMDELLTRA® until hemoglobin is ≥ 8 g/dL
	Grade 3 or Grade 4 decreased platelet count	▪ Withhold IMDELLTRA® until platelet count is ≤ Grade 2 and no evidence of bleeding ▪ Permanently discontinue if recovery to ≤ Grade 2 does not occur within 3 weeks
	Recurrent Grade 4 decreased platelet count	Permanently discontinue IMDELLTRA®

[§]Severity based on National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), Version 5.[2]

Infections

Dosage modifications for infections[2]

Severity*	Dosage Modifications
All Grades	Withhold IMDELLTRA® in the step-up phase in patients until infection resolves
Grade 3	Withhold IMDELLTRA® during the treatment phase until infection improves to ≤ Grade 1
Grade 4	Permanently discontinue IMDELLTRA®

Hepatotoxicity

Dosage modifications for hepatotoxicity[2]

Severity*	Dosage Modifications
Grade 3 increased ALT or AST or bilirubin	Withhold IMDELLTRA® until adverse events improve to ≤ Grade 1
Grade 4 increased ALT or AST or bilirubin	Permanently discontinue IMDELLTRA®
AST or ALT > 3 × ULN with total bilirubin > 2 × ULN in the absence of alternative causes	Permanently discontinue IMDELLTRA®

Other adverse reactions

Dosage modifications for other adverse reactions[2]

Severity*	Dosage Modifications
Grade 3 or 4	• Withhold IMDELLTRA® until recovery to ≤ Grade 1 or baseline • Consider permanently discontinuing if adverse reaction does not resolve within 28 days • Consider permanent discontinuation for Grade 4 events

*Severity based on National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), Version 5.[2]

Restarting IMDELLTRA® after dosage delay

Dosage modifications[2]

- If a dose of IMDELLTRA® is delayed, restart therapy based on the recommendations provided here, and resume the dosing schedule accordingly[2]
- Administer recommended concomitant medications.[2] Please see the full Prescribing Information for additional information

Last Dose Administered	Time Since the Last Dose Administered	Action†
1 mg on Cycle 1 Day 1	2 weeks or less (≤ 14 days)	Administer IMDELLTRA® 10 mg, then resume with the planned dosage schedule
	Greater than 2 weeks (> 14 days)	Administer IMDELLTRA® step-up dose 1 mg. If tolerated, increase to 10 mg 1 week later, then resume with the planned dosage schedule
10 mg on Cycle 1 Day 8	3 weeks or less (≤ 21 days)	Administer IMDELLTRA® 10 mg, then resume with the planned dosage schedule
	Greater than 3 weeks (> 21 days)	Administer IMDELLTRA® step-up dose 1 mg. If tolerated, increase to 10 mg 1 week later, then resume with the planned dosage schedule
10 mg on Cycle 1 Day 15 and subsequent Cycles Q2W thereafter	4 weeks or less (≤ 28 days)	Administer IMDELLTRA® 10 mg, then resume with the planned dosage schedule
	Greater than 4 weeks (> 28 days)	Administer IMDELLTRA® step-up dose 1 mg. If tolerated, increase to 10 mg 1 week later, then resume with the planned dosage schedule

†Administer recommended concomitant medications before and after Cycle 1 IMDELLTRA® infusions and monitor patients accordingly.[2]

ALT, alanine aminotransferase; AST, aspartate aminotransferase; ULN, upper limit of normal.

Q2W, every 2 weeks.

Please see additional Important Safety Information, including BOXED WARNINGS, on pages 18–19.

AMGEN Support+

We're right here, right when you need us

Personalized support that you and your patients can count on across Amgen therapies

HCP Support Center

Our Amgen SupportPlus Representatives can assist with issues around patient coverage, prior authorizations, co-pay programs, and more.

Benefits Verification

- Verify patient's insurance plan coverage details

Prior Authorization Requirements

- Provide payer-specific prior authorization forms

Amgen SupportPlus Customer Portal

- A tool for managing patient benefits verification and more
- Submit, store, and retrieve benefit verifications electronically

Visit **myAmgenPortal.com** to register and submit forms online.

Amgen® Patient Navigator

A single point of contact to help answer questions about access and reimbursement, navigating treatment logistics, and to provide supplemental resources as your patients transition from hospital to outpatient care.

Amgen Patient Navigators can help with:

- Benefits verification and understanding coverage
- Prior authorization process
- Reimbursement and access resources

Visit AmgenSupportPlus.com to learn how an Amgen Patient Navigator can help.
Call Amgen SupportPlus at (866) 264-2778, Monday – Friday 9:00 AM – 8:00 PM ET

The Amgen Patient Navigator is not part of a patient's treatment team and does not provide medical advice or case management services. The Amgen Patient Navigator does not administer Amgen medications. Patients should always consult their healthcare provider regarding medical decisions or treatment concerns.

Financial Support

We know every patient has unique needs. And we're here to provide financial support information and resources, regardless of their current financial situation or what type of insurance they have.

What if my patient doesn't have private or commercial insurance? Amgen SupportPlus can provide your patients with information about independent nonprofit foundations that may be able to help.*

Learn more about how Amgen SupportPlus can help your patients access their prescribed medication. Visit **AmgenSupportPlus.com** to learn more.

*Eligibility for resources provided by independent nonprofit patient assistance programs is based on the nonprofit's criteria. Amgen has no control over these programs and provides information as a courtesy only.

AMGEN THERAPY LOCATOR™

Amgen Therapy Locator™

Use this searchable database to locate alternative injection sites where IMDELLTRA® can be administered to your patients.†

Visit Amgen Therapy Locator™ at **AmgenTherapyLocator.com**

†The information on this website is self-reported by independent third-party sites that administer treatment to patients or dispense product. It is not a comprehensive list of all sites that provide the therapies listed, and Amgen does not confirm the accuracy or otherwise endorse any of the sites on this list, which is subject to change. The information provided is not a guarantee of coverage, reimbursement, or availability of a product.

Note: Coding and coverage policies change periodically and often without warning. The healthcare provider is solely responsible for determining coverage and reimbursement parameters and appropriate coding for his/her own patients and procedures. This information is not a guarantee of coverage or reimbursement.

Call **Amgen SupportPlus** at **(866) 264-2778**, Monday – Friday 9:00 AM – 8:00 PM ET.
Visit **AmgenSupportPlus.com** to learn how Amgen can help.

HCP, healthcare professional.

Please see additional Important Safety Information, including BOXED WARNINGS, on pages 18–19.

IMDELLTRA® (tarlatamab-dlle) for injection 1 mg & 10 mg single-use vials

IMPORTANT SAFETY INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME AND NEUROLOGIC TOXICITY including IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME

- **Cytokine release syndrome (CRS), including serious or life-threatening reactions, can occur in patients receiving IMDELLTRA®. Initiate treatment with IMDELLTRA® using the step-up dosing schedule to reduce the incidence and severity of CRS. Withhold IMDELLTRA® until CRS resolves or permanently discontinue based on severity.**
- **Neurologic toxicity, including immune effector cell-associated neurotoxicity syndrome (ICANS), including serious or life-threatening reactions, can occur in patients receiving IMDELLTRA®. Monitor patients for signs and symptoms of neurologic toxicity, including ICANS, during treatment and treat promptly. Withhold IMDELLTRA® until ICANS resolves or permanently discontinue based on severity.**

WARNINGS AND PRECAUTIONS

- **Cytokine Release Syndrome (CRS):** IMDELLTRA® can cause CRS including serious or life-threatening reactions. In the pooled safety population, CRS occurred in 55% of patients who received IMDELLTRA®, including 34% Grade 1, 19% Grade 2, 1.1% Grade 3 and 0.5% Grade 4. Recurrent CRS occurred in 24% of patients, including 18% Grade 1 and 6% Grade 2.

  Most events (43%) of CRS occurred after the first dose, with 29% of patients experiencing any grade CRS after the second dose and 9% of patients experiencing CRS following the third dose or later. Following the Day 1, Day 8, and Day 15 infusions, 16%, 4.3% and 2.1% of patients experienced ≥ Grade 2 CRS, respectively. The median time to onset of all grade CRS from most recent dose of IMDELLTRA® was 13.5 hours (range: 1 to 268 hours). The median time to onset of ≥ Grade 2 CRS from most recent dose of IMDELLTRA® was 14.6 hours (range: 2 to 566 hours).

  Clinical signs and symptoms of CRS included pyrexia, hypotension, fatigue, tachycardia, headache, hypoxia, nausea, and vomiting. Potentially life-threatening complications of CRS may include cardiac dysfunction, acute respiratory distress syndrome, neurologic toxicity, renal and/or hepatic failure, and disseminated intravascular coagulation (DIC).

  Administer IMDELLTRA® following the recommended step-up dosing and administer concomitant medications before and after Cycle 1 IMDELLTRA® infusions as described in Table 3 of the Prescribing Information (PI) to reduce the risk of CRS. Administer IMDELLTRA® in an appropriate health care facility equipped to monitor and manage CRS. Ensure patients are well hydrated prior to administration of IMDELLTRA®.

  Closely monitor patients for signs and symptoms of CRS during treatment with IMDELLTRA®. At the first sign of CRS, immediately discontinue IMDELLTRA® infusion, evaluate the patient for hospitalization and institute supportive care based on severity. Withhold or permanently discontinue IMDELLTRA® based on severity. Counsel patients to seek medical attention should signs or symptoms of CRS occur.
- **Neurologic Toxicity, Including ICANS:** IMDELLTRA® can cause serious or life-threatening neurologic toxicity, including ICANS. In the pooled safety population, neurologic toxicity, including ICANS, occurred in 47% of patients who received IMDELLTRA®, including 10% Grade 3. The most frequent neurologic toxicities were headache (14%), peripheral neuropathy (7%), dizziness (7%), insomnia (6%), muscular weakness (3.7%), delirium (2.1%), syncope (1.6%), and neurotoxicity (1.1%).

  ICANS occurred in 9% of IMDELLTRA®-treated patients. Recurrent ICANS occurred in 1.6% of patients. Most patients experienced ICANS following Cycle 2 Day 1 (24%). Following Day 1, Day 8, and Day 15 infusions, 0.5%, 0.5% and 3.7% of patients experienced ≥ Grade 2 ICANS, respectively. The median time to onset of ICANS from the first dose of IMDELLTRA® was 29.5 days (range: 1 to 154 days). ICANS can occur several weeks following administration of IMDELLTRA®. The median time to resolution of ICANS was 33 days (range: 1 to 93 days).

  The onset of ICANS can be concurrent with CRS, following resolution of CRS, or in the absence of CRS. Clinical signs and symptoms of ICANS may include but are not limited to confusional state, depressed level of consciousness, disorientation, somnolence, lethargy, and bradyphrenia.

  Patients receiving IMDELLTRA® are at risk of neurologic adverse reactions and ICANS resulting in depressed level of consciousness. Advise patients to refrain from driving and engaging in hazardous occupations or activities, such as operating heavy or potentially dangerous machinery, in the event of any neurologic symptoms until they resolve.

  Closely monitor patients for signs and symptoms of neurologic toxicity and ICANS during treatment. At the first sign of ICANS, immediately evaluate the patient and provide supportive therapy based on severity. Withhold IMDELLTRA® or permanently discontinue based on severity.
- **Cytopenias:** IMDELLTRA® can cause cytopenias including neutropenia, thrombocytopenia, and anemia. In the pooled safety population, decreased neutrophils occurred in 12% including 6% Grade 3 or 4 of IMDELLTRA®-treated patients. The median time to onset for Grade 3 or 4 neutropenia was 29.5 days (range: 2 to 213). Decreased platelets occurred in 33% including 3.2% Grade 3 or 4. The median time to onset for Grade 3 or 4 decreased platelets was 50 days (range: 3 to 420). Decreased hemoglobin occurred in 58% including 5% Grade 3 or 4. Febrile neutropenia occurred in 0.5% of patients treated with IMDELLTRA®.

  Monitor patients for signs and symptoms of cytopenias. Perform complete blood counts prior to treatment with IMDELLTRA®, before each dose, and as clinically indicated. Based on the severity of cytopenias, temporarily withhold, or permanently discontinue IMDELLTRA®.
- **Infections:** IMDELLTRA® can cause serious infections, including life-threatening and fatal infections.

  In the pooled safety population, infections, including opportunistic infections, occurred in 41% of patients who received IMDELLTRA®. Grade 3 or 4 infections occurred in 13% of patients. The most frequent infections were COVID-19 (9%, majority during the COVID-19 pandemic), urinary tract infection (10%), pneumonia (9%), respiratory tract infection (3.2%), and candida infection (3.2%).

  Monitor patients for signs and symptoms of infection prior to and during treatment with IMDELLTRA® and treat as clinically indicated. Withhold or permanently discontinue IMDELLTRA® based on severity.
- **Hepatotoxicity:** IMDELLTRA® can cause hepatotoxicity. In the pooled safety population, elevated ALT occurred in 42%, with Grade 3 or 4 ALT elevation occurring in 2.1%. Elevated AST occurred in 44% of patients, with Grade 3 or 4 AST elevation occurring in 3.2%. Elevated bilirubin occurred in 15% of patients; Grade 3 or 4 total bilirubin elevations occurred in 1.6% of patients. Liver enzyme elevation can occur with or without concurrent CRS. Monitor liver enzymes and bilirubin prior to treatment with IMDELLTRA®, before each dose, and as clinically indicated. Withhold IMDELLTRA® or permanently discontinue based on severity.
- **Hypersensitivity:** IMDELLTRA® can cause severe hypersensitivity reactions. Clinical signs and symptoms of hypersensitivity may include, but are not limited to, rash and bronchospasm. Monitor patients for signs and symptoms of hypersensitivity during treatment with IMDELLTRA® and manage as clinically indicated. Withhold or consider permanent discontinuation of IMDELLTRA® based on severity.
- **Embryo-Fetal Toxicity:** Based on its mechanism of action, IMDELLTRA® may cause fetal harm when administered to a pregnant woman. Advise patients of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with IMDELLTRA® and for 2 months after the last dose.

ADVERSE REACTIONS

- The most common (> 20%) adverse reactions were CRS (55%), fatigue (51%), pyrexia (36%), dysgeusia (36%), decreased appetite (34%), musculoskeletal pain (30%), constipation (30%), anemia (27%), and nausea (22%). The most common (≥ 2%) Grade 3 or 4 laboratory abnormalities were decreased lymphocytes (57%), decreased sodium (16%), increased uric acid (10%), decreased total neutrophils (6%), decreased hemoglobin (5%), increased activated partial thromboplastin time (5%), decreased potassium (5%), increased aspartate aminotransferase (3.2%), decreased white blood cells (3.8%), decreased platelets (3.2%), and increased alanine aminotransferase (2.1%).
- Serious adverse reactions occurred in 58% of patients. Serious adverse reactions in > 3% of patients included CRS (24%), pneumonia (6%), pyrexia (3.7%), and hyponatremia (3.6%). Fatal adverse reactions occurred in 2.7% of patients including pneumonia (0.5%), aspiration (0.5%), pulmonary embolism (0.5%), respiratory acidosis (0.5%), and respiratory failure (0.5%).

DOSAGE AND ADMINISTRATION: Important Dosing Information

- Administer IMDELLTRA® as an intravenous infusion over one hour.
- Administer IMDELLTRA® according to the step-up dosing schedule in the IMDELLTRA® PI (Table 1) to reduce the incidence and severity of CRS.
- For Cycle 1, administer recommended concomitant medications before and after Cycle 1 IMDELLTRA® infusions to reduce the risk of CRS reactions as described in the PI (Table 3).
- IMDELLTRA® should only be administered by a qualified healthcare professional with appropriate medical support to manage severe reactions such as CRS and neurologic toxicity including ICANS.
- Due to the risk of CRS and neurologic toxicity, including ICANS, monitor patients from the start of the IMDELLTRA® infusion for 22 to 24 hours on Cycle 1 Day 1 and Cycle 1 Day 8 in an appropriate healthcare setting.
- Recommend that patients remain within 1 hour of an appropriate healthcare setting for a total of 48 hours from start of the infusion with IMDELLTRA® following Cycle 1 Day 1 and Cycle 1 Day 8 doses, accompanied by a caregiver.
- Prior to administration of IMDELLTRA®, evaluate complete blood count, liver enzymes, and bilirubin before each dose, and as clinically indicated.
- Ensure patients are well hydrated prior to administration of IMDELLTRA®.

Please see IMDELLTRA® full Prescribing Information, including BOXED WARNINGS.

For more information, visit IMDELLTRAhcp.com

References: 1. Centers for Medicare & Medicaid Services. https://www.cms.gov/files/document/2024-hcpcs-application-summary-quarter-3-2024-drugs-and-biologicals.pdf. Accessed October 21, 2024. **2.** IMDELLTRA® (tarlatamab-dlle) prescribing information, Amgen. **3.** Data on file, Amgen; 2024. **4.** Lee DW, et al. *Biol Blood Marrow Transplant.* 2019;25:625-638.

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(tarlatamab-dlle) for injection 1 mg & 10 mg single-use vials