

Patient leaflet in accordance with the Pharmacists' Regulation (Preparations) - 1986

This medicine is dispensed with a doctor's prescription only.

IMDELLTRA® 1 MG

IMDELLTRA® 10 MG

Powder for concentrate for solution for infusion

Active Ingredient

The active ingredient is tarlatamab. Each vial contains 1.34 mg or 11.3 mg of tarlatamab.

For Inactive ingredients and allergens in the medicine – see section 6 “Additional information”.

Read this leaflet carefully and until the end before using this medicine. This leaflet contains concise information about the medicine. If you have additional questions, contact your doctor or pharmacist.

This medicine is prescribed for treating your illness. Do not pass it on to others. It may cause them harm even if it appears to you that their medical condition is similar.

In addition to the patient leaflet, **IMDELLTRA** has Patient Alert Card and Educational Brochure for healthcare professionals. The Card includes important safety information that you should be aware of before starting treatment and during treatment with **IMDELLTRA** and act accordingly. The patient card and the patient leaflet should be read prior treatment initiation with this product. The card should be kept for additional reading as needed.

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.

1. What is this Medicine Intended for?

IMDELLTRA 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.

Therapeutic group: IMDELLTRA belongs to a group of medicines called antineoplastic agents which target cancer cells.

2. **Before Using this Medicine**

Don't use this medicine if:

- you are allergic to the active substance (tarlatamab) or any of the other ingredients of this medicine (refer to the listed ingredients in section 6).

Special warnings regarding the usage of the medicine

Before treatment with the medicine tell your doctor if:

You suffer from various medical conditions, including an infection, pregnancy or a plan to become pregnant.

Additional special warnings during treatment:

If you experience any of the following reactions whilst receiving IMDELLTRA tell your doctor immediately as there may be a need to treat the symptoms:

- Cytokine Release Syndrome (CRS). CRS is very common during treatment with IMDELLTRA and can also be serious or life-threatening. The symptoms may include: fever, low blood pressure, tiredness, hypoxia, fast heartbeat, headache, nausea and vomiting (see section 4 “side effects”).
- Neurological problems – Immune effector cell-associated neurotoxicity syndrome (ICANS)- that can be very common during treatment with IMDELLTRA and can also be serious or life-threatening. Your doctor may refer you to a doctor who specializes in neurologic problems. Tell your doctor right away if you develop any signs or symptoms of neurologic problems, such as: encephalopathy, confusion, delirium, seizure, balance problems (ataxia), neurotoxicity, tremor and headache (see section 4 “side effects”).

Your doctor may temporarily stop or completely stop your treatment with IMDELLTRA if you develop CRS, neurologic problems, or any other side effects that are severe. You may be hospitalized if you develop signs or symptoms of CRS or neurologic problems during treatment with IMDELLTRA.

Children and adolescents

The safety and efficacy of IMDELLTRA has not been studied in children and adolescents. Treatment with IMDELLTRA is currently not recommended in patients under 18 years of age.

Tests and monitoring

Your doctor will do bloodwork before and during treatment with IMDELLTRA.

Prior to treatment with IMDELLTRA, before each dose, and as clinically indicated a complete blood count, liver enzymes and bilirubin tests should be performed.

Your doctor will examine you to identify signs and symptoms of an infection before and during treatment with IMDELLTRA.

Your doctor will monitor you for signs and symptoms of CRS and neurologic problems during treatment with IMDELLTRA, as well as other side effects, and treat you as needed.

Drug interactions

Tell your doctor, pharmacist, or nurse if you are taking, have recently taken or might take any other medicines.

Pregnancy and breast-feeding

Pregnancy

Tell your doctor if you are pregnant or plan to become pregnant before you start treatment with IMDELLTRA.

IMDELLTRA may cause fetal harm when administered to a pregnant woman.

Your doctor will refer you to do a pregnancy test before you start treatment with IMDELLTRA. You should use an effective form of birth control (contraception) during treatment with IMDELLTRA, and for 2 months after your last dose of IMDELLTRA.

Tell your doctor right away if you become pregnant or think that you may be pregnant during treatment with IMDELLTRA.

Brest-feeding

Tell your doctor or nurse if you are breastfeeding or plan to breastfeed. It is not known if IMDELLTRA passes into human milk or the effects on the breastfed child or/and on milk production. Because of the potential for serious adverse reactions in a breastfed child, do not breastfeed during treatment with IMDELLTRA and for 2 months after the last dose of IMDELLTRA.

Driving and using machines

Do not drive, operate heavy or potentially dangerous machinery or do other dangerous activities, including work-related activities, during treatment with IMDELLTRA if you develop dizziness, confusion, tremors, sleepiness, or any other symptoms that impair consciousness until your signs and symptoms go away. These may be signs and symptoms of neurologic problems.

3. How to use this Medicine?

Always use this medicine exactly as your doctor has told you. Check with your doctor or a pharmacist if you are not sure.

The dosage and treatment regimen will be determined solely by your doctor. The usual dosage and treatment regimen are:

IMDELLTRA will be given to you by your doctor in a hospital under medical supervision by intravenous (IV) infusion through a needle placed in a vein. The infusion will take about 1 hour.

Your IMDELLTRA treatment schedule is divided into cycles that are usually 28 days (4 weeks) long.

Your doctor will decide how many treatment cycles you will receive.

Do not exceed the recommended dose.

Due to the risk of CRS, IMDELLTRA treatment will be given on a “step-up dosing schedule”:

The step-up dosing schedule is when you receive a smaller dose of IMDELLTRA on Day 1 of your first treatment cycle (Cycle 1).

You will receive the full treatment dose of IMDELLTRA on Day 8 and Day 15 of Cycle 1. You will receive the full treatment dose 1 time every 2 weeks after Day 15 of Cycle 1.

If your dose of IMDELLTRA is delayed for any reason, you may need to repeat the “step-up dosing schedule”.

Before receiving your Day 1 and Day 8 doses of Cycle 1 of IMDELLTRA, you will be given an additional medicine to help reduce your risk of CRS. This will be given into your vein by intravenous (IV) infusion. You will also receive IV fluids after each of your Cycle 1 doses of IMDELLTRA (on Day 1, Day 8, and Day 15). Your doctor will decide if you need to receive additional medicines to help reduce your risk of CRS with future doses.

- **After the doses given in Cycle 1 on Day 1 and Day 8** your doctor will monitor you for **22 to 24 hours from the start of IMDELLTRA infusion. You should plan to stay within 1 hour of the hospital for a total of 48 hours** from the start of the IMDELLTRA infusion after your Day 1 and Day 8 of Cycle 1 doses **and be accompanied by a caregiver.**
- **After Day 15 of Cycle 1 and Cycle 2 doses,** your doctor will watch you for **6 to 8 hours** after the IMDELLTRA infusion.
- **After Cycle 3 and Cycle 4 doses,** your doctor will watch you for **3 to 4 hours** after the IMDELLTRA infusion.
- **After Cycle 5 and later doses,** your doctor will watch you for **2 hours** after the IMDELLTRA infusion.

If a higher dose was accidentally given to you

Contact your doctor or pharmacist immediately.

If you forgot to take the medicine

Coordinate the timing of your next dose with your doctor, you may need to repeat the “step-up dosing schedule”. Then, contact your doctor who will tell you when you should schedule your next dose, and follow the new schedule exactly as your doctor has told you.

If you stop treatment with the medicine

Even if there is an improvement in your health, do not stop treatment with the medicine without consulting first with the doctor.

Do not take medicines in the dark! Check the label and the dose each time you take medicine. Wear glasses if needed.

If you have any additional questions on the use of this medicine, consult a doctor or a pharmacist.

4. Side Effects

Like any medicine, using IMDELLTRA may cause side effects in some of the users. Do not be alarmed by reading the list of side effects. It is possible that you will not suffer from any one of them.

Tell your doctor immediately and seek immediate medical treatment if you get any of the following or combination of the following side effects:

- **Cytokine Release Syndrome (CRS)** (very common side effect that may affect more than 1 in 10 patients): fever of 38°C or higher; low blood pressure; tiredness; fast heart beat or dizziness; headache, shortness of breath or trouble breathing; hypoxia, nausea and vomiting; confusion, restlessness, or feeling anxious; problems with balance and movement, such as trouble walking; heart, liver, or kidney problems; unusual bleeding or bleeding that lasts a long time.
- **Neurologic problems (including ICANS) may happen days or weeks after you receive IMDELLTRA** (very common side effect that may affect more than 1 in 10 patients): trouble speaking, memory loss, or personality changes; confusion, delirium, feeling disoriented, slow thinking or not being able to think clearly; seizure; problems with walking or loss of balance or coordination; weakness or numbness of your arms or legs; shakiness (tremor); headache; numbness or tingling of your hands or feet; dizziness; trouble sleeping; insomnia; fainting or loss of consciousness; muscular weakness, feeling like you have no energy; somnolence.
- **Low blood cell counts (cytopenia)** (very common side effect that may affect more than 1 in 10 patients): decreased blood cell counts are common with IMDELLTRA and can also be severe. Low white blood cells can increase your risk for infection (neutropenia); low red blood cell counts (anemia); low red blood cells can cause tiredness and shortness of breath; low platelet counts (thrombocytopenia); low platelet counts can cause bruising or bleeding problems; decreased hemoglobin and febrile neutropenia.
- **Infections** (very common side effect that may affect more than 1 in 10 patients): IMDELLTRA can cause serious infections that can be life-threatening and may lead to death. The most frequent infections are

COVID-19, urinary tract infection, pneumonia, respiratory tract infection, and candida infection. Possible symptoms of these infections are: fever of 38°C or higher; cough; chest pain; tiredness; shortness of breath; painful rash; sore throat; pain during urination; feeling weak or generally unwell.

- **Liver problems** (very common side effect that may affect more than 1 in 10 patients): IMDELLTRA might cause increased liver enzymes and bilirubin in your blood. Symptoms of liver problems can be: tiredness; loss of appetite; pain in your right upper stomach-area (abdomen); dark urine; yellowing of your skin or the white part of your eyes.
- **Allergic reactions** (unknown frequency): IMDELLTRA can cause allergic reactions that can be severe. Go to the nearest emergency room or get medical help right away if you develop any signs or symptoms of a severe allergic reaction during treatment with IMDELLTRA, including shortness of breath or trouble breathing; pain or tightness in your chest and back; wheezing; coughing; feeling lightheaded or dizzy; rash.

Additional side effects include:

Very common side effects (may affect more than 1 in 10 patients):

- tiredness
- fever
- a bad or metallic taste in your mouth
- decreased appetite
- muscle or bone pain
- constipation
- nausea
- cough
- shortness of breath
- decreased sodium
- increased uric acid

Common side effects (may affect more than 1 in 100 patients):

- increased clotting time
- decreased potassium
- tumor lysis syndrome

Uncommon side effects (may affect up to 1 in 100 patients):

- aspiration
- pulmonary embolism
- respiratory acidosis
- respiratory failure

If a side effect has appeared, if any of the side effects get worse or when you suffer from a side effect that has not been mentioned in the leaflet, you should consult the doctor.

Reporting of side effects

You can report adverse reactions to the Ministry of Health by clicking on the link "report on adverse reactions following medication treatment" located on the homepage of the Ministry of Health website (www.health.gov.il) which directs you to the online form for reporting adverse reactions or by using the link:

<https://sideeffects.health.gov.il/>

5. How to Store the Medicine?

Prevent poisoning! This medicine, as well as any other medicine, should be stored in a closed area out of the reach and sight of children and/or infants, thereby preventing poisoning. Do not induce vomiting without explicit instruction from your doctor.

Do not use this medicine after the expiry date which is stated on the carton after EXP. The expiry date refers to the last day of that month.

Unopened vials:

- Store and transport refrigerated (2°C - 8°C). It can be stored at a temperature of 23°C - 25°C in the original packaging for up to 24 hours.
- Do not freeze.
- Store in the original carton in order to protect from light.

Prepared IMDELLTRA (infusion bag)

- Once at room temperature 23°C to 25°C, store no longer than 8 hours.
- When refrigerated (2°C to 8°C), the infusion bag must be used within 7 days.

The maximum storage time is the total time from when the powder is reconstituted in the IMDELLTRA vial until the end of the infusion.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Additional information

In addition to the active ingredient, this medicine also contains:

Excipients of powder:

- Sucrose,
- L-glutamic acid,
- Polysorbate 80,
- Sodium Hydroxide,
- Water for injections.

Excipients of stabilizer solution:

- Lysine Hydrochloride,

- Citric acid monohydrate,
- Polysorbate 80,
- Sodium Hydroxide,
- Water for injections

What does the medicine look like and what are the contents of the package?

IMDELLTRA is a white to slightly yellow powder in a vial. The packaging also contains a stabilizer solution for infusion.

- 1 mg pack contains: 1 glass vial of 1 mg IMDELLTRA and 2 vials of 7 mL stabiliser solution for infusion.
- 10 mg pack contains: 1 glass vial of 10 mg IMDELLTRA and 2 vials of 7 mL stabiliser solution for infusion.

Sterile Water for Injection (not included) should be used to reconstitute IMDELLTRA.

Registration Holder's name and address:

Amgen Europe B.V.
P.O. BOX 53313, Tel - Aviv, Israel.

Manufacturer's name and address:

Amgen Europe B.V.
Minervum 7061, Breda, The Netherlands.

Approved in February 2025.

Registration number of the medicine in the National Drugs Registry at the Ministry of Health: 37928, 37927

The following preparation instructions are intended for healthcare professionals only:

Material Compatibility Information

- 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.
- IV line and catheter materials composed of polyolefin, PVC, and polyurethane have been shown to be compatible with IMDELLTRA at the specified administration conditions.
- 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.

Step 1: Reconstitute IMDELLTRA with Sterile Water for Injection

- Table 1 provides the required amount of sterile water for injection required to reconstitute IMDELLTRA 1 mg and 10 mg vials.

Do not use IV Solution Stabilizer (IVSS) to reconstitute IMDELLTRA.

The IV Solution Stabilizer (IVSS) is used to coat the intravenous bag prior to addition of reconstituted IMDELLTRA to prevent adsorption of IMDELLTRA to IV bags and IV tubing.

Table 1. Required Amount of Sterile Water for Injection to Reconstitute IMDELLTRA^a

IMDELLTRA Vial Strength	Amount of Sterile Water for Injection Needed to Reconstitute IMDELLTRA	Resulting Concentration
1 mg	1.3 mL	0.9 mg/mL
10 mg	4.4 mL	2.4 mg/mL

^a 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.

- 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.
- Gently swirl the contents to mix. Do not shake.
- 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.
- Further dilute reconstituted IMDELLTRA.
- The reconstituted IMDELLTRA must be further diluted within 4 hours of reconstitution or discarded.

Prepare the infusion bag: Steps 2 to 5

Step 2 : Withdraw 0.9% Sodium Chloride for Injection

- Using a 250 mL prefilled bag of 0.9% Sodium Chloride for Injection, withdraw the amount of sodium chloride specified in Table 2 and discard.

Table 2. Required Amount of 0.9% Sodium Chloride to Withdraw from 250 mL IV Bag

IMDELLTRA Vial Strength	IMDELLTRA Dose	Volume of 0.9% Sodium Chloride to Withdraw From 250 mL IV Bag
1 mg	1 mg	14 mL
10 mg	10 mg	17 mL

Step 3: Add IV Solution Stabilizer to the infusion bag

- Inject 13 mL of IV Solution Stabilizer (IVSS) into the 250 mL 0.9% Sodium Chloride infusion bag, see Table 3.
- Gently mix the contents of the infusion bag to avoid foaming. Do not shake.

Table 3. Required Amount of IV Solution Stabilizer (IVSS) to Add to IV Bag

IMDELLTRA Vial Strength	IMDELLTRA Dose	Volume of IV Solution Stabilizer (IVSS) to Add to IV Bag
1 mg	1 mg	13 mL
10 mg	10 mg	13 mL

Step 4: Dilute the reconstituted IMDELLTRA into the infusion bag

- Transfer the required volume of reconstituted IMDELLTRA listed in Table 4 to the infusion bag (*containing IV Solution Stabilizer*).

NOTE: the final concentrations for the different strength vials are NOT the same following reconstitution and further dilution.

Table 4. Required Amount of Reconstituted IMDELLTRA to Add to 250 mL IV Bag

IMDELLTRA Vial Strength	IMDELLTRA Dose	Volume of Reconstituted IMDELLTRA to Add to 250 mL IV Bag
1 mg	1 mg	1.1 mL
10 mg	10 mg	4.2 mL

- Gently mix the contents of the bag. Do not shake.

Step 5: Remove air from IV bag

Remove air from the prepared IV bag using an empty syringe to avoid foaming.

Step 6: Prime IV tubing

- Prime intravenous tubing with either 0.9% Sodium Chloride for Injection or with the final prepared product.
- See Table 5 for maximum storage time of prepared IMDELLTRA infusion.

Prepared IMDELLTRA Infusion Bag Storage Requirements

- Administer reconstituted and diluted IMDELLTRA immediately.
- Table 5 displays the maximum storage time for the prepared IMDELLTRA infusion bag.
- Maximum storage time includes total duration from the time of reconstitution of the vial of IMDELLTRA to the end of the infusion.

Table 5. Maximum Storage Time

	Room Temperature 23°C to 25°C	Refrigerated 2°C to 8°C
Prepared IMDELLTRA Infusion Bag	8 hours	7 days
<ul style="list-style-type: none"> • Discard IMDELLTRA infusion after maximum storage time (from time of reconstitution). • Do not re-refrigerate prepared infusion bag. 		