

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

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

TEPEZZA®

Powder for concentrate for solution for infusion

Active Ingredient

Each vial of powder contains 500 mg of teprotumumab.

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.

1. What is this Medicine Intended for?

TEPEZZA is indicated for the treatment of moderate to severe Thyroid Eye Disease regardless of activity and duration.

Therapeutic group: TEPEZZA is a monoclonal antibody, an immunosuppressant.

2. Before Using this Medicine

Don't use this medicine if:

- you are allergic to the active ingredient (teprotumumab) 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 have previously experienced infusion-related reactions, such as shortness of breath, increased heart rate, high blood pressure, headache, or muscle pain. (See Section 4 "Side Effects").
- You suffer from inflammatory bowel disease (IBD). It is possible that TEPEZZA may cause worsening of your symptoms if you suffer from inflammatory bowel disease (IBD). IBD has been reported in some patients without a prior diagnosis of IBD. Your doctor will monitor you for signs and symptoms of IBD. If a worsening is suspected, discontinuation of TEPEZZA should be considered. (See Section 4 "Side Effects").
- You have hyperglycemia (increased blood sugar), diabetes, or pre-diabetes. If you have pre-existing diabetes mellitus, your doctor will ensure that your

diabetes is under control before starting TEPEZZA. (See Section "Tests and Monitoring").

Additional warnings:

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

- **Infusion-related Reactions** (reactions related to your injection of medicine): These reactions are usually mild or moderate in severity, in patients who experience an infusion reaction, consideration should be given to pre-medicating with an antihistamine, antipyretic, corticosteroid and/or administering all subsequent infusions at a slower infusion rate. (See Section 4 "Side Effects").
- **Hearing Impairment:** It is possible that TEPEZZA may cause hearing loss or impairment. This is usually temporary but in some cases it can be permanent. Your healthcare provider will assess your hearing before, during and after treatment with TEPEZZA. (See Section "Tests and Monitoring" and Section 4 "Side Effects").

Children and adolescents

There is no data regarding the use of TEPEZZA in children and adolescents under 18 years of age. Safety and effectiveness have not been established in this population.

Testing and monitoring

Before starting the treatment with TEPEZZA, your doctor will refer you to test your blood sugar and hearing.

Your doctor will continue to monitor you during and after TEPEZZA treatments.

Women of childbearing age should have a pregnancy test performed by their doctor before starting treatment with TEPEZZA.

Drug interactions

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

Pregnancy, breast-feeding and fertility

Pregnancy:

You must not use this medicine if you are pregnant. TEPEZZA may cause harm to your unborn baby. Your doctor should advise you about using contraception before start treatment with TEPEZZA and for at least 6 months after the last dose of TEPEZZA. You must inform your doctor if you are pregnant or suspect you might be pregnant.

In case of pregnancy during treatment, TEPEZZA should be discontinued since there is a potential risk to the fetus.

Breast-feeding:

There is no information regarding the presence of TEPEZZA in human milk, the effects on the breast-fed infant or the effects on milk production. Tell your doctor if you are breast-feeding or are planning to breast-feed.

Fertility:

Fertility studies have not been performed with TEPEZZA.

Driving and using machines

TEPEZZA has a minor influence on the ability to drive and use machines. Fatigue and headaches have been reported with the use of teprotumumab.

3. How to use this Medicine?

Always use the product exactly as instructed by your doctor. You should check with your doctor or pharmacist if you are not sure about the dosage or how to use the product.

TEPEZZA is given under the supervision of a healthcare professional.

The dosage and method of administration will be determined by the doctor only. The commonly used dosage is:

TEPEZZA is given to you through an intravenous infusion of 10 mg/kg for the initial dose followed by an intravenous infusion of 20 mg/kg every three weeks for 7 additional infusions.

Do not exceed the recommended dose.

The medical staff will prepare and dilute the product before the infusion.

The diluted solution should be administered intravenously over at least 90 minutes for the first two infusions. If well tolerated, the minimum time for subsequent infusions can be reduced to 60 minutes. If not well tolerated, the minimum time for subsequent infusions should remain at 90 minutes, and pre-medication is recommended for subsequent infusions.

If you experience immediate allergic reactions or infusion-related reactions during an infusion of TEPEZZA your doctor may provide appropriate treatment as required and/or will administer all subsequent infusions at a slower infusion rate to reduce the risk of a reaction.

If you were accidentally given a higher dose

Contact your doctor or pharmacist immediately.

If you forgot to go and receive the medicine

You should coordinate the timing of your next dose with your doctor. 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 TEPEZZA 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 if you get any of the following or combination of the following side effects:

- High blood sugar (Hyperglycemia)
- Any changes in hearing, hearing impairment including hearing loss:
 - Deafness, including hearing loss due to inner ear or nerve damage (Sensorineural deafness)
 - Muffled hearing (Eustachian tube dysfunction)
 - Hearing your own voice louder than normal (Autophony)
 - Sensitivity to particular sounds (Hyperacusis)
 - Partial loss of hearing (Hypoacusis)
 - Ringing in the ears (Tinnitus)
- Infusion-related reactions (e.g., transient increases in blood pressure, feeling hot, tachycardia, dyspnea, headache and muscular pain). These reactions may occur during any of the infusions or within 1.5 hours after an infusion. Reported infusion reactions are usually mild or moderate in severity.
- Inflammatory bowel disease (IBD) with symptoms such as: diarrhea, with or without blood or rectal bleeding, associated with abdominal pain or cramping/colic, urgency, tenesmus or incontinence

Other side effects include:

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

- Muscle spasms
- Nausea
- Hair loss (Alopecia)
- Diarrhea
- Tiredness (Fatigue)
- Changes in menstrual cycle, such as:
 - Missing one or more periods (Amenorrhea)
 - Menstrual cramps (Dysmenorrhea)
 - Heavy menstrual bleeding (Metrorrhagia)

Common side effects (may affect up to 1 in 10 patients):

- Change in the sense of taste (Dysgeusia)
- Headache
- Dry skin
- Weight decreased

- Brittle or discoloring of the nails (Nail disorders)

Not known side effects (frequency cannot be estimated from the available data):

- Metabolism and Nutrition Disorders: diabetic ketoacidosis, hyperosmolar hyperglycemic state (HHS)

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.

Storage conditions:

Unopened vials:

Store and transport refrigerated (2°C - 8°C).

Do not freeze.

Keep the vial in the outer carton in order to protect from light.

Reconstituted and/or diluted solution:

The combined storage time of reconstituted solution in the vial and the diluted solution in the infusion bag containing 0.9% Sodium Chloride Injection is a total of 4 hours at room temperature 20°C to 25°C or up to 48 hours under refrigerated conditions 2°C to 8°C, protected from light.

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. Contents of the pack and other information

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

Excipients:

- α , α -Trehalose dihydrate
- L-Histidine hydrochloride monohydrate,
- L-Histidine,
- Polysorbate 20

How the medicine looks and what is the content of the package?

TEPEZZA is a preservative-free powder for concentrate and solution for infusion. The powder is a white to off white lyophilized powder supplied in a single-dose vial. Each pack contains one vial. Sterile Water for Injection (not included) should be used to reconstitute TEPEZZA.

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.

Registration number of the medicine in the National Drugs Registry at the Ministry of Health: 38100

Revised in October 2025.

The following preparation instructions are intended for healthcare professionals only:

Step 1: Calculate the dose (mg) and determine the number of vials needed for the 10 or 20 mg/kg dosage based on patient weight. Each TEPEZZA vial contains 500 mg of the teprotumumab antibody.

Step 2: Using appropriate aseptic technique, reconstitute each TEPEZZA vial with 10 mL of Sterile Water for Injection. Ensure that the stream of diluent is not directed onto the lyophilized powder, which has a cake-like appearance. Do not shake, but gently swirl the solution by rotating the vial until the lyophilized powder is dissolved. The reconstituted solution has a total volume of 10.5 mL. Withdraw 10.5 mL of reconstituted solution to obtain 500 mg. After reconstitution, the final concentration is 47.6 mg/mL.

Step 3: The reconstituted TEPEZZA solution must be further diluted in 0.9% Sodium Chloride Injection prior to infusion. To prepare the diluted solution, use 100 mL infusion bags for a dose less than 1800 mg, and 250 mL infusion bags for a dose equal to or greater than 1800 mg. To maintain a constant volume in the infusion bag, a sterile syringe and needle should be used to remove the volume equivalent to the amount of the reconstituted TEPEZZA solution to be placed into the infusion bag. Discard the volume of 0.9% Sodium Chloride withdrawn.

Step 4: Withdraw the required volume from the reconstituted TEPEZZA vial(s) based on the patient's weight (in kg) and transfer into the intravenous bag containing 0.9% Sodium Chloride Injection. Mix diluted solution by gentle inversion. Do not shake. If refrigerated prior to administration, allow the diluted solution to reach room temperature prior to infusion.