TEPEZZA™
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Infusion Guide

Instructions for administering TEPEZZA

Please see Important Safety Information on pages 24 and 25 and accompanying Full Prescribing Information.

It’s Time for a Breakthrough in TED Treatment

As the first and only FDA-approved treatment for Thyroid Eye Disease (TED), TEPEZZA is a breakthrough treatment for patients with this debilitating disease. By administering TEPEZZA infusions, you are part of a new era in TED treatment.[1,2]

This infusion guide, developed in collaboration with infusion nurses, contains step-by-step instructions to help you feel confident and prepared to infuse TEPEZZA.

Table of Contents

Please see Important Safety Information on pages 24 and 25 and accompanying Full Prescribing Information.

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TED and Patient Considerations

Thyroid Eye Disease (TED), or Graves' orbitopathy, is a progressive autoimmune eye disease with debilitating and vision-threatening consequences[2,3]

Help patients with TED feel more comfortable during their infusion:

Dim the lights: Painful light sensitivity is a common symptom of TED. When possible, dim the overhead lights or utilize window coverings. Patients may wear sunglasses or a hat during treatment.[4,5]

Reduce air drafts: Patients with TED often suffer from severely dry eyes. If possible, seat patients away from any air drafts created by fans, air conditioners, or blowing vents.[4,6]

Provide assistance for vision impairment: Patients with TED may have difficulty seeing small type, driving at night, or using peripheral vision. They may need assistance with reading and traveling to the infusion center.[4,7,8]

Empathize with psychological and emotional challenges: Patients with TED may struggle with the physical disfigurement associated with the disease. Help them feel welcome during their time at the infusion center.[7]

TED is commonly associated with a separate condition called Graves' disease, which causes an overproduction of thyroid hormones (hyperthyroidism)[4,9]

Help accommodate patients with this condition:

Keep the temperature comfortable: Patients with fluctuating thyroid levels can struggle with moderating body temperature. Have blankets and cold packs available to help patients stay warm or cool down during their infusion.[10]

Allow for time to settle in: Hyperthyroidism can cause high blood pressure, irregular heartbeat, hand tremors, anxiety, and irritability. With this in mind, give patients time to settle in and relax before their infusion.[11-13]

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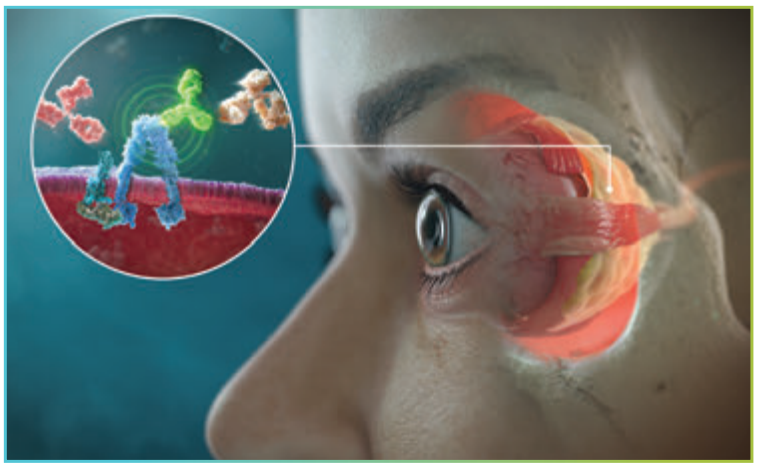
About TEPEZZA

TEPEZZA has a novel, breakthrough mechanism in TED designed to block IGF-1R, a key mediator[1,2,14-16]

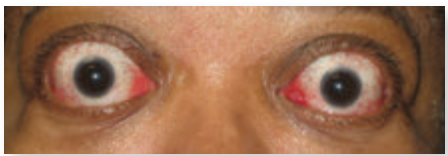


- TEPEZZA is a fully human monoclonal antibody inhibitor of the insulin-like growth factor-1 receptor (IGF-1R)[1,17]
- TEPEZZA **blocks IGF-1R** and **decreases proptosis** by reducing inflammation, preventing muscle and fat-tissue remodeling, and **preventing tissue expansion behind the eye**[1,2,15,18]

SELECT IMPORTANT SAFETY INFORMATION

Infusion Reactions have been reported in approximately 4% of patients treated with TEPEZZA. Reported infusion reactions have usually been mild or moderate in severity. Signs and symptoms may include transient increases in blood pressure, feeling hot, tachycardia, dyspnea, headache, and muscular pain.

See the TEPEZZA difference[19]



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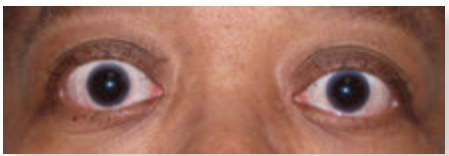

POST-TREATMENT (WEEK 24)

Patient treated with TEPEZZA in a clinical trial. Results shown are with no surgical intervention. Individual results may vary.[20]

In clinical trials, TEPEZZA was proven to[1,16,17]:

- Decrease proptosis (bulging eyes)
- Improve diplopia (double vision)
- Reduce signs and symptoms (pain, redness, and swelling)

TEPEZZA met its primary endpoint vs placebo in 2 randomized, placebo-controlled trials (P<0.01; N=171) defined as proptosis responder rate at Week 24 (percentage of patients with ≥2-mm reduction in proptosis from baseline in the study eye, without ≥2-mm increase in non-study eye).[1,16,20]

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Storage Instructions

Prior to reconstitution:

Store inside the box[1]

Protect from light[1]

Refrigerate between 2°C to 8°C (36°F to 46°F)[1]

Do not freeze[1]

TEPEZZA is supplied as a lyophilized powder for reconstitution. Each single-dose vial contains 500 mg of teprotumumab antibody.[1]

After reconstitution:

The combined storage time of reconstituted solution in the vial and diluted solution in the infusion bag is a total of:

Up to
4 hours
at room
temperature

20°C to 25°C
(68°F to 77°F)[1]

OR

Up to
48 hours
in refrigeration

2°C to 8°C
(36°F to 46°F)[1]

If not administered immediately, protect from light[1]

If refrigerated, allow the diluted solution to reach room temperature prior to infusion[1]

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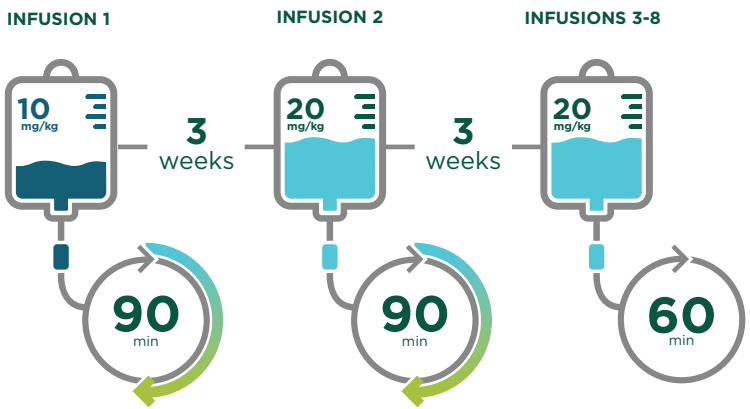
Dosing

TEPEZZA is given once every 3 weeks for a total of 8 infusions[1]



- TEPEZZA is dosed according to the patient's actual weight[1]
- If not well tolerated, the minimum infusion duration should remain at 90 minutes[1]
- No special considerations or monitoring required for patients with mild or moderate renal impairment[1]

SELECT IMPORTANT SAFETY INFORMATION

Infusion Reactions have been reported in approximately 4% of patients treated with TEPEZZA. Reported infusion reactions have usually been mild or moderate in severity. Signs and symptoms may include transient increases in blood pressure, feeling hot, tachycardia, dyspnea, headache, and muscular pain.

Sample dosing calculations for a 75-kg patient[1]

- Find complete dosing calculations for patients weighing 50 kg to 120 kg in the Dosing Calculations flashcard

	Infusion 1 (10 mg/kg)	Infusions 2 to 8 (20 mg/kg)	Notes
1. Determine patient's actual weight	165 lb / 2.2 lb/kg = **75 kg**	165 lb / 2.2 lb/kg = **75 kg**	• Confirm patient weight prior to each infusion
2. Calculate weight-based dose	75 kg x 10 mg/kg = **750 mg**	75 kg x 20 mg/kg = **1500 mg**	• Multiply the patient weight (kg) by the dosage (mg/kg)
3. Determine number of vials required	750 mg / 500 mg = 1.5 → **2 vials**	1500 mg / 500 mg = 3 → **3 vials**	• Each vial delivers 500 mg of TEPEZZA • Always round up when determining the number of vials
4. Convert dose (mg) to volume of solution to withdraw (mL)	750 mg / 47.6 mg/mL = **15.8 mL**	1500 mg / 47.6 mg/mL = **31.5 mL**	• After reconstitution, each vial will contain 10.5 mL of reconstituted solution • The final concentration is 47.6 mg/mL
5. Select appropriate size saline bag	**100 mL**	**100 mL**	• If dose is <1800 mg, use a 100-mL bag • If dose is ≥1800 mg, use a 250-mL bag
6. Calculate wastage	2 vials required x 500 mg/vial = 1000 mg – 750 mg = **250 mg**	3 vials required x 500 mg/vial = 1500 mg – 1500 mg = **0 mg**	• Multiply the number of vials required by the 500 mg of TEPEZZA per vial, then subtract the dose given*

*Reference payer guidelines for wastage documentation requirements.

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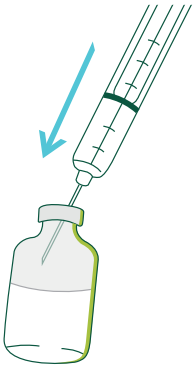
Preparation and Administration

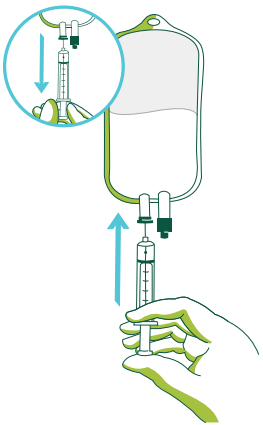


> Reconstitute each vial with 10 mL of sterile water.

Reconstitute[1]

- Using appropriate aseptic technique, reconstitute each TEPEZZA vial with 10 mL of Sterile Water for Injection, USP
- Ensure that the stream of diluent is not directed onto the lyophilized powder, which has a cake-like appearance
- Gently swirl the solution by rotating the vial until the lyophilized powder is dissolved. Do not shake
- Note: The reconstituted solution has a volume of 10.5 mL. The final concentration is 47.6 mg/mL
- Visually inspect the solution. It should be colorless or slightly brown, clear to opalescent. Discard the solution if any particulate matter or discoloration is observed

For illustrative purposes only.



> After removing the appropriate volume of saline, transfer the reconstituted TEPEZZA solution into the IV bag.

Dilute[1]

- The reconstituted TEPEZZA solution must be further diluted in 0.9% Sodium Chloride Injection, USP prior to infusion. Select the appropriate size saline bag based on the dose
- To maintain a constant volume in the infusion bag, use a sterile syringe and needle to remove the volume of saline equal to the amount of reconstituted TEPEZZA solution to be placed into the bag. Discard the saline withdrawn
- Withdraw the required volume from the TEPEZZA vial(s) based on the dose and transfer into the infusion bag
- Mix diluted solution by gentle inversion. Do not shake
- The combined storage time of reconstituted TEPEZZA solution in the vial and the diluted solution in the infusion bag is a total of 4 hours at room temperature or up to 48 hours under refrigerated conditions while protected from light

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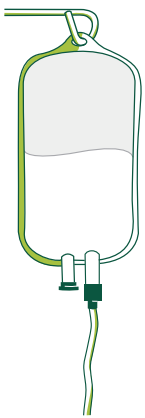
Preparation and Administration (cont'd)



>Infuse the diluted solution for the appropriate duration.

Infuse[1]

- If refrigerated prior to administration, allow the diluted solution to reach room temperature prior to infusion
- Infuse the diluted solution for the appropriate duration

! **Do not** administer as an intravenous push or bolus

! **Do not** infuse concomitantly with other agents

- Use your normal protocol to monitor for infusion reactions. If an infusion reaction occurs, interrupt or slow the rate of infusion and use appropriate medical management
- Discard vial(s) and all unused contents

For illustrative purposes only.

Administration Supplies

- ☐  TEPEZZA vial(s)
- ☐  Sterile syringe and needle
- ☐  Sterile Water for Injection, USP
- ☐  IV infusion bag containing 0.9% Sodium Chloride Solution, USP (100 mL or 250 mL)
- ☐  Infusion administration set (no special tubing required)
- ☐  Routine infusion supplies (e.g., alcohol swabs, gauze pads, bandages, and biohazard containers)
- ☐  In-line filters with a 0.2-µm pore size (optional)

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Infusion Reactions

4% rate of infusion reactions[1]

What to look for[1]:

- Signs and symptoms of an infusion reaction include:

Transient increase in blood pressure	**Dyspnea**
Feeling hot	**Headache**
Tachycardia	**Muscular pain**

- Infusion reactions may occur during any of the infusions or within 1.5 hours after an infusion[1]
- Reported infusion reactions are usually mild or moderate in severity and can usually be successfully managed with corticosteroids and antihistamines[1]

If an infusion reaction occurs[1]:

- Interrupt or slow the rate of infusion and use appropriate medical management
- For subsequent infusions, consider premedicating with an antihistamine, antipyretic, or corticosteroid and/or slowing the rate of infusion

In clinical trials:

- Pretreatment medications were not routinely required[21]
- No antidrug antibodies were observed in patients treated with TEPEZZA[1]

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Patient Counseling

Risk during pregnancy

- Advise females of reproductive potential that TEPEZZA can cause harm to a fetus and to inform their healthcare provider of a known or suspected pregnancy[1]
- Educate and counsel these patients about the need to use effective contraception prior to initiation, during treatment, and for 6 months after the last dose[1]

Infusion reactions

- Advise patients that TEPEZZA may cause infusion reactions that can occur at any time[1]
- Instruct patients to recognize the signs and symptoms of an infusion reaction and to contact their healthcare provider immediately if they experience these signs or symptoms[1]

Worsening of IBD

- Advise patients on the risk of inflammatory bowel disease (IBD)[1]
- Instruct patients to seek medical advice immediately if they experience diarrhea (with or without blood or rectal bleeding) associated with abdominal pain or cramping/colic, urgency, tenesmus, or incontinence[1]

Increased blood sugar

- Advise patients on the risk of hyperglycemia. Diabetic patients should discuss this with their healthcare provider to adjust glycemic control medications as appropriate[1]
- Encourage compliance with glycemic control[1]

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Patient FAQs

Helpful answers to commonly asked questions from patients

1 What are the potential side effects of TEPEZZA?

The most common side effects of TEPEZZA include muscle cramps or spasms, nausea, hair loss, diarrhea, feeling tired, high blood sugar, hearing problems, taste changes, headache, and dry skin.[1]

2 Why can't I take TEPEZZA as a pill?

Some medicines need to be given in a particular way for them to work. TEPEZZA is given by a process known as intravenous (IV) infusion.[1]

3 This is my first time receiving an infusion—what should I expect?

We want you to be as comfortable as possible during your infusion. Our staff is trained on the proper way to give IV medicines, which are medicines that are given through a needle that is placed in your arm. You'll receive your TEPEZZA in an infusion chair, which is a cushioned armchair a lot like a recliner. There may be a TV to help you pass the time, or you can enjoy your own books, magazines, or your tablet or phone. There may be other patients nearby receiving medicines for a variety of conditions, not just TED.[1]

4 How often are the infusions given and how long will I be on treatment?

TEPEZZA is given once every 3 weeks for a total of 8 doses. So completing your TEPEZZA treatment should take about 5 months. Make sure you complete your TEPEZZA treatment unless your doctor tells you to stop.[1]

5 Do I have to complete all 8 treatments?

Yes, people in clinical studies were given TEPEZZA 1 time every 3 weeks—a total of 8 treatments over the course of about 5 months. So it's important to complete all 8 treatments to see the best results.[1]

6 What if I become pregnant during treatment with TEPEZZA?

TEPEZZA can harm an unborn baby if given to a pregnant woman. You should use an effective form of birth control before treatment, during treatment, and for at least 6 months after your final infusion. Tell your doctor if you become pregnant or suspect you are pregnant during treatment with TEPEZZA.[1]

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TEPEZZA™
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Patient FAQs (cont'd)

7

What happens if I miss an infusion?

Making time for your infusions can be challenging, but in order to see the best results with TEPEZZA, it's important to receive your infusion every 3 weeks. If you are going to miss an appointment, contact your infusion center as soon as possible to reschedule.[1]

8

Is co-pay assistance available?

Yes! Part of Horizon's commitment to helping patients with TED is a one-on-one support program. You can call 1-833-4MY-TED1 to speak with a Horizon Patient Services™ professional who will connect you to your Patient Access Manager, or PAM for short. Your PAM can help figure out if you qualify for co-pay support or other financial assistance options.

Horizon Patient Services:

A partnership you and your patients can rely on throughout the treatment journey

Horizon Patient Services offers a wide array of services:

Patient Support

Infusion Logistics Assistance

Financial Assistance

Insurance Benefits Investigation

Upon enrollment, a dedicated Patient Access Manager (PAM) is assigned to coordinate care, so your patients receive an optimal experience—from treatment initiation through completion.

PAMs provide personalized one-on-one support and can even meet with your patient at the infusion center.

Ask your patient to call 1-833-4MY-TED1 to enroll

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INDICATION

TEPEZZA is indicated for the treatment of Thyroid Eye Disease.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

Infusion Reactions: TEPEZZA may cause infusion reactions. Infusion reactions have been reported in approximately 4% of patients treated with TEPEZZA. Reported infusion reactions have usually been mild or moderate in severity. Signs and symptoms may include transient increases in blood pressure, feeling hot, tachycardia, dyspnea, headache, and muscular pain. Infusion reactions may occur during an infusion or within 1.5 hours after an infusion. In patients who experience an infusion reaction, consideration should be given to premedicating with an antihistamine, antipyretic, or corticosteroid and/or administering all subsequent infusions at a slower infusion rate.

Preexisting Inflammatory Bowel Disease: TEPEZZA may cause an exacerbation of preexisting inflammatory bowel disease (IBD). Monitor patients with IBD for flare of disease. If IBD exacerbation is suspected, consider discontinuation of TEPEZZA.

Hyperglycemia: Increased blood glucose or hyperglycemia may occur in patients treated with TEPEZZA. In clinical trials, 10% of patients (two-thirds of whom had preexisting diabetes or impaired glucose tolerance) experienced hyperglycemia. Hyperglycemic events should be managed with medications for glycemic control, if necessary. Monitor patients for elevated blood glucose and symptoms of hyperglycemia while on treatment with TEPEZZA. Patients with preexisting diabetes should be under appropriate glycemic control before receiving TEPEZZA.

Adverse Reactions

The most common adverse reactions (incidence ≥5% and greater than placebo) are muscle spasm, nausea, alopecia, diarrhea, fatigue, hyperglycemia, hearing impairment, dysgeusia, headache, and dry skin.

For additional information on TEPEZZA, please see accompanying Full Prescribing Information.

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A Patient Access Manager (PAM) can help answer questions and support your patient throughout therapy.

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Learn more at TEPEZZAhcp.com

To contact medical information, call 1-866-479-6742.

References: 1. TEPEZZA (teprotumumab-trbw) [prescribing information] Horizon. **2.** Bahn RS. Graves' ophthalmopathy. *N Engl J Med.* 2010;362(8):726-738. **3.** Shan SJ, Douglas RS. The pathophysiology of thyroid eye disease. *J Neuroophthalmol.* 2014;34(2):177-185. **4.** Barrio-Barrio J, Sabater AL, Bonet-Farriol E, Velázquez-Villoria Á, Galofré JC. Graves' ophthalmopathy: VISA versus EUGOGO classification, assessment, and management. *J Ophthalmol.* 2015. doi:10.1155/2015/249125. **5.** Digre KB, Brennan KC. Shedding light on photophobia. *J Neuroophthalmol.* 2012;32(1):68-81. **6.** Ismailova DS, Fedorov AA, Grusha YO. Ocular surface changes in thyroid eye disease. *Orbit.* 2013;32(2):87-90. **7.** Ponto KA, Pitz S, Pfeiffer N, Hommel G, Weber MM, Kahaly GJ. Quality of life and occupational disability in endocrine orbitopathy. *Dtsch Arztebl Int.* 2009;106(17):283–289. **8.** McKeag D, Lane C, Lazarus JH, et al. Clinical features of dysthyroid optic neuropathy: a European group on Graves' orbitopathy (EUGOGO) survey. *Br J Ophthalmol.* 2007;91(4):455-458. **9.** Mayo Clinic. Graves' disease. Mayo Clinic website. https://www.mayoclinic.org/diseases-conditions/graves-disease/symptoms-causes/syc-20356240. Accessed December 1, 2019. **10.** Silva JE. The thermogenic effect of thyroid hormone and its clinical implications. *Ann Intern Med.* 2003;139(3):205-213. **11.** Prisant LM, Gujral JS, Mulloy AL. Hyperthyroidism: a secondary cause of isolated systolic hypertension. *J Clin Hypertens (Greenwich).* 2006;8(8):596-599. **12.** De Leo S, Lee SY, Braverman LE. Hyperthyroidism. *Lancet.* 2016;388(10047):906-918. **13.** Demet MM, Ozmen B, Deveci A, Boyvada S, Adigüzel H, Aydemir O. Depression and anxiety in hyperthyroidism. *Arch Med Res*. 2002;33(6):552-556. **14.** Patel A, Yang H, Douglas RS. A new era in the treatment of thyroid eye disease. *Am J Ophthalmol*. 2019;208:281-288. **15.** Douglas RS. Teprotumumab, an insulin-like growth factor-1 receptor antagonist antibody, in the treatment of active thyroid eye disease: a focus on proptosis. *Eye (Lond).* 2019;33(2):183-190. **16.** Douglas RS, Kahaly GJ, Patel A, et al. Teprotumumab for the treatment of active thyroid eye disease. *N Engl J Med*. 2020;382(4):341-352. **17.** Smith TJ, Kahaly GJ, Ezra DG, et al. Teprotumumab for thyroid-associated ophthalmopathy. *N Engl J Med.* 2017;376(18):1748-1761. **18.** Dik WA, Virakul S, van Steensel L. Current perspectives on the role of orbital fibroblasts in the pathogenesis of Graves' ophthalmopathy. *Exp Eye Res.* 2016;142:83-91. **19.** Data on File. Horizon, January 2020. **20.** Data on File. Horizon, December 2019. **21.** Smith TJ, Kahaly GJ, Ezra DG, et al. Teprotumumab for thyroid-associated ophthalmopathy. *N Engl J Med*. 2017;376(18)(protocol):1748-1761. https://www.nejm.org/doi/suppl/10.1056/NEJMoa1614949/suppl_file/nejmoa1614949_protocol.pdf.

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