Tepezza® (Teprotumumab-Trbw) (for Louisiana Only)

Policy Number: CSLA2024D0089H
Effective Date: October 1, 2024

➲ Instructions for Use

Table of Contents **Page**

Application

This Medical Benefit Drug Policy only applies to the state of Louisiana.

Coverage Rationale

Thyroid Eye Disease

Tepezza is proven and medically necessary for the treatment of thyroid eye disease when all of the following criteria are met:

- Diagnosis of Graves' disease associated with active thyroid eye disease (TED) with a Clinical Activity Score (CAS) ≥ 4 in the most severely affected eye; **and**
- Presence of moderately to severely active TED, associated with at least **one** of the following:[2,4]
  - Lid retraction ≥ 2 mm; **or**
  - Moderate or severe soft tissue involvement; **or**
  - Exophthalmos ≥ 3 mm above normal for race and gender; **or**
  - Diplopia

  and
- History of intolerance, failure, or contraindication to oral or intravenous glucocorticoids (e.g., prednisone, methylprednisolone)
  and
- **One** of the following:
  - Patient is euthyroid [defined as free triiodothyronine (T3) and thyroxine (T4) levels within the normal limits]; **or**
  - Presence of mild hypo- or hyper-thyroidism [defined as free T3 and T4 levels less than 50% above or below the normal limits] and patient is undergoing treatment to correct the mild hypo- or hyper-thyroidism to maintain a euthyroid state

  and
- Tepezza is prescribed by an endocrinologist or ophthalmologist; **and**
- Tepezza will not be used in combination with another biologic immunomodulator [e.g., rituximab (Rituxan®, Ruxience®, Truxima®, Riabni™), Actemra® (tocilizumab), Kevzara® (sarilumab)]; **and**
- Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
- Authorization will be issued for a maximum of 8 doses per lifetime

Reauthorization/Continuation of Care Criteria

The clinical benefit of Tepezza has not been demonstrated beyond 8 infusions in phase 3 clinical trials. The continued use of Tepezza beyond 8 infusions in the patient's lifetime is unproven and not medically necessary.

Definitions

Exophthalmos: Proptosis can be confirmed with exophthalmometry, which measures the distance between the lateral angle of the bony orbit and the cornea; normal values are < 20 mm to < 22 mm. An Exophthalmometer is an instrument used for measuring the degree of forward displacement of the eye in Exophthalmos. The device allows measurement of the forward distance of the lateral orbital rim to the front of the cornea. CT or MRI is often useful to confirm the diagnosis.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state, or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J3241	Injection, teprotumumab-trbw, 10 mg

Diagnosis Code	Description
E05.00	Thyrotoxicosis with diffuse goiter without thyrotoxic crisis or storm
E05.01	Thyrotoxicosis with diffuse goiter with thyrotoxic crisis or storm
H05.20	Unspecified exophthalmos
H05.211	Displacement (lateral) of globe, right eye
H05.212	Displacement (lateral) of globe, left eye
H05.213	Displacement (lateral) of globe, bilateral
H05.219	Displacement (lateral) of globe, unspecified eye
H05.221	Edema of right orbit
H05.222	Edema of left orbit
H05.223	Edema of bilateral orbit
H05.229	Edema of unspecified orbit
H05.231	Hemorrhage of right orbit
H05.232	Hemorrhage of left orbit
H05.233	Hemorrhage of bilateral orbit
H05.239	Hemorrhage of unspecified orbit
H05.241	Constant exophthalmos, right eye
H05.242	Constant exophthalmos, left eye
H05.243	Constant exophthalmos, bilateral
H05.249	Constant exophthalmos, unspecified eye
H05.251	Intermittent exophthalmos, right eye
H05.252	Intermittent exophthalmos, left eye
H05.253	Intermittent exophthalmos, bilateral
H05.259	Intermittent exophthalmos, unspecified eye
H05.261	Pulsating exophthalmos, right eye
H05.262	Pulsating exophthalmos, left eye
H05.263	Pulsating exophthalmos, bilateral
H05.269	Pulsating exophthalmos, unspecified eye

Background

Teprotumumab is an insulin-like growth factor-1 receptor inhibitor (IGF-1R), a fully human IgG1 monoclonal antibody. The mechanism of action of teprotumumab in patients with thyroid eye disease has not been fully characterized. Teprotumumab binds to IGF-1R and blocks its activation and signaling.

Thyroid eye disease (TED) is also known as thyroid associated orbitopathy (TAO) and Grave's orbitopathy (GO). This disease is an autoimmune inflammatory condition affecting the orbit and ocular adnexa of the eye. TED is associated with distinct clinical features, including upper eyelid retraction, restrictive strabismus, and proptosis. TED can threaten vision through compressive optic neuropathy or corneal decompensation from exposure keratopathy.

The European Group on Graves' Orbitopathy (EUGOGO) defines mild TED disease as the presence of mild lid retraction (< 2 mm), mild Exophthalmos (< 3 mm), mild soft tissue involvement, and corneal exposure that is responsive to topical lubrication. Moderate to severe TAO is defined as lid retraction > 2 mm, Exophthalmos > 3 mm, moderate to severe soft tissue involvement, and presence of diplopia. Sight-threatening TAO is defined as presence of direct optic neuropathy or corneal breakdown.

Clinical Evidence

The efficacy and safety of teprotumumab was evaluated in 2 randomized, double-masked, placebo-controlled trials in 171 patients diagnosed with thyroid eye disease (TED). Patients were randomized to either receive teprotumumab (n = 84) or placebo (n = 87) in a 1:1 ratio. Patients receiving teprotumumab were infused 10mg/kg for the first infusion and 20mg/kg for the remaining 7 infusions every 3 weeks for a total of 8 infusions. The proptosis responder rate at week 24 was defined as the percentage of patients with ≥ 2 mm reduction in proptosis in the study eye from baseline, without deterioration in the non-study eye (≥ 2 mm increase) in proptosis. Additional evaluations included signs and symptoms of TED including pain, gaze evoked orbital pain, swelling, eyelid erythema, redness, chemosis, inflammation, clinical activity score and assessments of functional vision and patient appearance.

In study 1, in the intention-to-treat population, 29 of 42 patients who received teprotumumab (69%), as compared with 9 of 45 patients who received placebo (20%), had a response at week 24 ($p < 0.001$). Therapeutic effects were rapid; at week 6, a total of 18 of 42 patients in the teprotumumab group (43%) and 2 of 45 patients in the placebo group (4%) had a response ($p < 0.001$). Differences between the groups increased at subsequent time points. The only drug-related adverse event was hyperglycemia in patients with diabetes; this event was controlled by adjusting medication for diabetes.

In study 2 (n = 83), at week 24, the percentage of patients with a proptosis response was higher with teprotumumab than with placebo [83% (34 patients) vs. 10% (4 patients), $p < 0.001$], with a number needed to treat of 1.36. All secondary outcomes were significantly better with teprotumumab than with placebo, including overall response [78% of patients (32) vs. 7% (3)], Clinical Activity Score (CAS) of 0 or 1 [59% (24) vs. 21% (9)], the mean change in proptosis (−2.82 mm vs. −0.54 mm), diplopia response [68% (19 of 28) vs. 29% (8 of 28)], and the mean change in GO-QOL overall score (13.79 points vs. 4.43 points) ($p \leq 0.001$ for all). Reductions in extraocular muscle, orbital fat volume, or both were observed in 6 patients in the teprotumumab group who underwent orbital imaging. Most adverse events were mild or moderate in severity; two serious events occurred in the teprotumumab group, of which one (an infusion reaction) led to treatment discontinuation. Among patients with active thyroid eye disease, teprotumumab resulted in better outcomes with respect to proptosis, Clinical Activity Score, diplopia, and quality of life than placebo; serious adverse events were uncommon.

The efficacy and safety of teprotumumab in TED patients regardless of disease activity or duration was established by a randomized, double-masked, placebo-controlled, parallel-group, multicenter, Phase 4 clinical trial that evaluated adult patients with chronic TED and low levels of disease activity. The primary efficacy objective was to measure the effect of teprotumumab versus placebo in the change of proptosis measurements in the study eye from baseline at Week 24. All study participants were required to have an initial diagnosis of TED two to 10 years prior to screening, and a CAS of ≤ 1 in both eyes for at least one year prior to screening or all of the following one year prior to screening: no progression in proptosis, no progression in diplopia and no new inflammatory TED symptoms. Participants could not have had prior orbital irradiation, orbital decompression surgery or strabismus surgery. The mean duration of disease for teprotumumab and placebo patients was 5.1 years (SD 1.88) and 5.4 years (SD 1.61), respectively. The mean CAS for teprotumumab and placebo patients was 0.3 (SD 0.47) and 0.5 (SD 0.51), respectively. At Week 24, per the pre-specified primary analysis method (intent-to-treat), patients treated with teprotumumab achieved a statistically significant reduction in proptosis from baseline compared to those receiving placebo (2.41 mm vs. 0.92 mm; $p = 0.0004$). In addition, in the pre-

specified per-protocol analysis, the differences between patients treated with teprotumumab and patients treated with placebo increased (2.44 mm vs. 0.69 mm; p = 0.0006).

Professional Societies

In 2021, the European Group on Graves' Orbitopathy (EUGOGO) published a guideline for the management of Graves' Orbitopathy/TED. Some of the recommendations are as follows:

- Euthyroidism should be promptly restored and stably maintained in all patients with GO. Antithyroid drugs are preferred when managing Graves' hyperthyroidism.
- In mild and active GO, control of risk factors, local treatments, and selenium (selenium-deficient areas) are usually sufficient; if radioactive iodine (RAI) treatment is selected to manage GO, low-dose oral prednisone prophylaxis is needed, especially if risk factors coexist.
- In moderate-to-severe and active GO: High-dose intravenous glucocorticoids (GC) (methylprednisolone) with or without oral mycophenolate sodium (or mofetil) should be considered as first-line treatment for moderate-to-severe and active GO.
- Intravenous GC therapy is more effective and better tolerated than oral GC therapy and should be performed in experienced centers that can safely manage potentially serious adverse events.
- A cumulative dose of 4.5 g of i.v. methylprednisolone in 12 weekly infusions is the optimal regimen. Alternatively, higher cumulative doses not exceeding 8 g can be used as monotherapy in most severe cases and constant/inconstant diplopia.
- Second-Line Treatments for moderate-to-severe and active GO include (a) the second course of i.v. methylprednisolone (7.5 g) subsequent to careful ophthalmic and biochemical evaluation, (b) oral prednisone/prednisolone combined with either cyclosporine or azathioprine; (c) orbital radiotherapy combined with oral or i.v. glucocorticoids, (d) teprotumumab; (e) rituximab and (f) tocilizumab.
- Sight-threatening GO is treated with several high single doses of i.v. methylprednisolone per week and, if unresponsive, with urgent orbital decompression.
- Rehabilitative surgery (orbital decompression, squint, and eyelid surgery) is indicated for inactive residual GO manifestations.

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Tepezza (teprotumumab-trbw) is an insulin-like growth factor-1 receptor inhibitor indicated for the treatment of thyroid eye disease.

References

1. Tepezza [prescribing information]. Deerfield, IL: Horizon Therapeutics USA, Inc.; July 2023.
2. Douglas RS, Kahaly GJ, Patel A, et al. Teprotumumab for the Treatment of Active Thyroid Eye Disease. N Engl J Med. 2020 Jan 23;382(4):341-352.
3. Smith TJ, Kahaly GJ, Ezra DG, et al. Teprotumumab for Thyroid-Associated Ophthalmopathy. N Engl J Med. 2017 May 4;376(18):1748-1761.
4. Hodgson NM and Rajaii F. Current Understanding of the Progression and Management of Thyroid Associated Orbitopathy: A Systematic Review. Ophthalmol Ther. 2019 Dec 10.
5. Bartalena L, Kahaly G, Baldeschi L, Boboridis K, European Group on Graves' Orbitopathy (EUGOGO), et al. The 2016 2021 European Thyroid Association/European Group on Graves' Orbitopathy Clinical Practice Guidelines for the Medical Management of Graves' Orbitopathy. Eur Thyroid Endocrinology J. 202116;5(1):9–26. 185(4), G43-G67.
6. Horizon Therapeutics plc Announces Positive Topline Data from Tepezza (teprotumumab-trbw) Phase 4 Clinical Trial in Patients with Chronic/Low Clinical Activity Score (CAS) Thyroid Eye Disease (TED). 2023. Available at https://www.tepezza.com. Accessed May 2, 2023.
7. A Study Evaluating Tepezza Treatment in Patients with Chronic (Inactive) Thyroid Eye Disease. ClinicalTrials.gov identifier: NCT04583735. Updated April 11, 2023. Accessed May 2, 2023.
8. Hoang TD, Stocker DJ, Chou EL, Burch HB. 2022 Update on Clinical Management of Graves Disease and Thyroid Eye Disease. Endocrinol Metab Clin North Am. 2022 Jun;51(2):287-304. doi: 10.1016/j.ecl.2021.12.004. Epub 2022 May 11. PMID: 35662442; PMCID: PMC9174594.

Policy History/Revision Information

Date	Summary of Changes
10/01/2024	**Supporting Information** • Updated *FDA* and *References* sections to reflect the most current information • Archived previous policy version CSLA2024D0089G

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. The UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.