# Tepezza® (Teprotumumab-Trbw)

Policy Number: CS2021D0089E
Effective Date: June 1, 2021

Instructions for Use

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| • Tepezza® (Teprotumumab-Trbw) |

## Application

This Medical Benefit Drug Policy does not apply to the states listed below; refer to the state-specific policy/guideline, if noted:

| State | Policy/Guideline |
|---|---|
| Indiana | Tepezza® (Teprotumumab-Trbw) (for Indiana Only) |
| Kansas | None |
| Kentucky | Tepezza® (Teprotumumab-Trbw) (for Kentucky Only) |
| Louisiana | Tepezza® (Teprotumumab-Trbw) (for Louisiana Only) |
| North Carolina | None |

## 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); and
- Presence of moderately to severely active TED, associated with at least one of the following:[2,4]
  - Lid retraction ≥ 2 mm
  - Moderate or severe soft tissue involvement
  - Exophthalmos ≥ 3 mm above normal for race and gender
  - Diplopia

  and
- One of the following:
  - Patient must be euthyroid with thyroid function under control
  - Mild hypothyroidism or hyperthyroidism undergoing treatment to correct and/or maintain euthyroid

  and

- Tepezza is prescribed by, or in consultation with, an endocrinologist or specialist with expertise in the treatment of Graves' disease associated with TED; 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 |

| Diagnosis Code | Description |
|---|---|
| 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. 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 Thyroid Eye Disease 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 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≤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.

### Professional Societies

In 2016, the European Thyroid Association (ETA) and European Group on Graves' Orbitopathy (EUGOGO) jointly published a guideline for the management of Graves' Orbitopathy/TED. Some of the recommendations are as follows:

- Quit Smoking: Physicians should urge all patients with Graves' hyperthyroidism, irrespective of the presence/absence of GO, to refrain from smoking, if necessary with the help of specialized smoking cessation programs or clinics.
- Thyroid Dysfunction: Euthyroidism be promptly restored and stably maintained in all patients with GO.
- Steroid Prophylaxis: Oral prednisone prophylaxis, starting with a daily dose of 0.3–0.5 mg prednisone/kg body weight, should be given in radioiodine-treated patients at high risk of progression or de novo development of GO. Lower-dose prednisone can be used in low-risk patients. Patients with inactive GO can safely receive radioiodine without steroid cover, as long as hypothyroidism is avoided, if other risk factors for GO progression, particularly smoking, are absent.
- First-Line Treatment for Moderate-to-Severe and Active GO: High-dose intravenous glucocorticoids (GC) be considered as first-line treatment for moderate-to-severe and active GO. Intravenous GC therapy should be performed in experienced centers that can safely manage potentially serious adverse events.
- Second-Line Treatments for Moderate-to-Severe and Active GO: Shared decision-making as an appropriate approach to select a second-line therapy in patients with moderate-to-severe and active GO.

## 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]. Lake Forest, IL: Horizon Therapeutics USA, Inc.; January 2020.
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, Baldeschi L, Boboridis K, European Group on Graves' Orbitopathy (EUGOGO), et al. The 2016 European Thyroid Association/European Group on Graves' Orbitopathy Guidelines for the Management of Graves' Orbitopathy. Eur Thyroid J. 2016;5(1):9–26.


## Policy History/Revision Information

| Date | Summary of Changes |
|---|---|
| 08/01/2021 | Application<br>• Added language to indicate this policy does not apply to the state of North Carolina |
| 06/01/2021 | Template Update<br>• Removed *CMS* section<br>Application<br>• Added language to indicate this policy does not apply to the state of Indiana; refer to the state-specific policy version |

| Date | Summary of Changes |
|---|---|
| | **Coverage Rationale**<br>• Revised coverage criteria for proven and medically necessary treatment; replaced language indicating "authorization will be issued for *no more than* 8 doses" with "authorization will be issued for *a maximum of* 8 doses *per lifetime*"<br>***Reauthorization/Continuation of Care Criteria***<br>• Revised reauthorization guidelines; replaced language indicating "the continued use of Tepezza beyond 8 infusions is unproven and not medically necessary" with "the continued use of Tepezza beyond 8 infusions *in the patient's lifetime* is unproven and not medically necessary"<br>**Supporting Information**<br>• Archived previous policy version CS2021D0089D |

# 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.

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