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

Policy Number: CSPA2025D0089D
Effective Date: April 1, 2025

Ü Instructions for Use

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Related Policies
None

Application

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

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 thyroid eye disease (TED); **and**
- Presence of moderately to severe disease, associated with at least **one** of the following:
  - **Both** of the following:
    - Presence of symptomatic, active disease; **and**
    - **One** of the following:
      - Lid retraction ≥ 2 mm
      - Moderate or severe soft tissue involvement
      - Proptosis ≥ 3 mm above normal for race and sex
      - Diplopia

  or
  - **Both** of the following:
    - Presence of stable, chronic (inactive) disease; **and**
    - **One** of the following:
      - Greater than or equal to 3 mm in proptosis from before diagnosis of TED; **or**
      - Proptosis ≥ 3 mm above normal values for race and sex (i.e., 19 and 21 mm for white female and male patients, respectively; and 23 and 24 mm for black female and male patients, respectively)

  and
- **One** of the following:
  - History of intolerance, failure, or contraindication to oral or intravenous glucocorticoids (e.g., prednisone, methylprednisolone); **or**
  - Patient with history of significant proptosis, soft tissue involvement and/or diplopia

  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 hyperthyroidism (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 hyperthyroidism to maintain a euthyroid state; **or**
- Patient has been initiated on antithyroid medication

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.

Requests outside of this criteria will be reviewed for medical necessity on a case-by-case basis.

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

Diagnosis Code	Description
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.

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 10 mg/kg for the first infusion and 20 mg/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

American Thyroid Association and European Thyroid Association

The American Thyroid Association and the European Thyroid Association issued a consensus statement in 2022 for the management of thyroid eye disease. The Task Force notes “active” thyroid eye disease as disease with a clinical activity score (CAS) of ≥ 3 or if the patient has history or documentation of progression of thyroid eye disease based on subjective or objective worsening of vision, soft tissue inflammation, motility, or proptosis. CAS assesses seven items (spontaneous retrobulbar pain, pain on attempted up or lateral gaze, redness of the eyelids, redness of the conjunctiva, swelling of the eyelids, inflammation of the caruncle and/or plica, and conjunctival edema); each item is given one point if present. The severity of disease is divided into three groups: mild (features of disease have a minor impact on daily life insufficient to justify treatment), moderate-to-severe (patient does not have sight-threatening disease but disease has sufficient impact on daily life to justify the risks of medical or surgical intervention), or sight-threatening (patient with dysthyroid optic neuropathy and/or corneal breakdown and/or globe subluxation). Patients with moderate-to-severe TED usually have any one or more of the following: lid retraction ≥ 2 mm, moderate or severe soft tissue involvement, proptosis ≥ 3 mm above normal for race and sex, or diplopia (Gorman score 2–3). Pharmacologic treatment includes oral or IV glucocorticoids, mycophenolate, rituximab, Tepezza, and Actemra (tocilizumab IV infusion). Intravenous glucocorticoid (IVGC) therapy is noted as a preferred treatment for active moderate-to-severe TED when disease activity is the prominent feature in the absence of either significant proptosis or diplopia. Tepezza is noted as a preferred therapy, if available, in patients with active moderate-to-severe TED with significant proptosis and/or diplopia. The Task Force used the term ‘significant proptosis’ rather than a numerical threshold (i.e., ≥ 3 mm above the upper limit for race and sex) as a numerical definition would exclude some patients who might otherwise benefit from therapy. In keeping with the definition of moderate-to-severe TED, a degree of proptosis < 3 mm above the upper limit for race and sex would be regarded as ‘significant proptosis’ if it impacted sufficiently on daily life and would justify the risks of treatment.

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

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8. Burch HB, Perros P, Bednarczuk T, et al. Management of thyroid eye disease: a Consensus Statement by the American Thyroid Association and the European Thyroid Association. *Eur Thyroid J*. 2022;11(6):e220189.
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Policy History/Revision Information

Date	Summary of Changes
04/01/2025	**Coverage Rationale** • Revised coverage criteria: o Added criterion requiring: § Presence of moderately to severe disease, associated with presence of stable, chronic (inactive) disease and one of the following: – Greater than or equal to 3 mm in proptosis from before diagnosis of TED; or – Proptosis ≥ 3 mm above normal values for race and sex (i.e., 19 and 21 mm for white female and male patients, respectively; and 23 and 24 mm for black female and male patients, respectively) o Replaced criterion requiring: § "Diagnosis of *Graves' disease associated with active* thyroid eye disease (TED)" with "diagnosis of thyroid eye disease (TED)" § "Presence of moderately to *severely active TED*, associated with at least one of the following: lid retraction ≥ 2 mm, moderate or severe soft tissue involvement, *exophthalmos* ≥ 3 mm above normal for race and *gender*, or diplopia" with "presence of moderately to *severe disease*, associated with *the presence of symptomatic, active disease and* one of the following: lid retraction ≥ 2 mm, moderate or severe soft tissue involvement, *proptosis* ≥ 3 mm above normal for race and *sex*, or diplopia" **Supporting Information** • Updated *Background*, *Clinical Evidence*, and *References* sections to reflect the most current information • Removed *Definitions* section • Archived previous policy version CSPA2024D0089C

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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