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Teprotumumab-trbw

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Disclaimer

Medical policies are a set of written guidelines that support current standards of practice. They are based on current generally accepted standards of and developed by nonprofit professional association(s) for the relevant clinical specialty, third-party entities that develop treatment criteria, or other federal or state governmental agencies. A requested therapy must be proven effective for the relevant diagnosis or procedure. For drug therapy, the proposed dose, frequency and duration of therapy must be consistent with recommendations in at least one authoritative source. This medical policy is supported by FDA-approved labeling and/or nationally recognized authoritative references to major drug compendia, peer reviewed scientific literature and generally accepted standards of medical care. These references include, but are not limited to: MCG care guidelines, DrugDex (IIa level of evidence or higher), NCCN Guidelines (IIb level of evidence or higher), NCCN Compendia (IIb level of evidence or higher), professional society guidelines, and CMS coverage policy.

Carefully check state regulations and/or the member contract.

Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Legislative Mandates

EXCEPTION: For HCSC members residing in the state of Ohio, § 3923.60 requires any group or individual policy (Small, Mid-Market, Large Groups, Municipalities/Counties/Schools, State Employees, Fully-Insured, PPO, HMO, POS, EPO) that covers prescription drugs to provide for the coverage of any drug approved by the U. S. Food and Drug Administration (FDA) when it is prescribed for a use recognized as safe and effective for the treatment of a given indication in one or more of the standard medical reference compendia adopted by the United States Department of Health and Human Services or in medical literature even if the FDA has not approved the drug for that indication. Medical literature support is only satisfied when safety and efficacy has been confirmed in two articles from major peer-reviewed professional medical journals that present data supporting the proposed off-label use or uses as generally safe and effective. Examples of accepted journals include, but are not limited to, Journal of

American Medical Association (JAMA), New England Journal of Medicine (NEJM), and Lancet. Accepted study designs may include, but are not limited to, randomized, double blind, placebo controlled clinical trials. Evidence limited to case studies or case series is not sufficient to meet the standard of this criterion. Coverage is never required where the FDA has recognized a use to be contraindicated and coverage is not required for non-formulary drugs.

Coverage

Teprotumumab-trbw (Tepezza) **may be considered medically necessary** for the treatment of thyroid eye disease when **ALL** the following criteria are met:

- Individual is 18 years of age or older; **and**
- Individual has moderate-to-severe disease confirmed by at least 1 of the following:
  - Lid retraction of 2 or more millimeters; or
  - Moderate to severe soft tissue involvement; or
  - Exophthalmos ≥ 3 millimeters or more; or
  - Presentation of diplopia; or
  - Corneal exposure.

Teprotumumab-trbw (Tepezza™) **is considered experimental, investigational, and/or unproven** for all other non-Food and Drug Administration approved indications or when used as a repeat course of treatment (beyond the initial 8 doses).

Policy Guidelines

None.

Description

Diagnosis

Thyroid eye disease (TED), also known as thyroid associated orbitopathy, is a progressive systemic autoimmune process often linked to Graves' disease (GD) but can also occur in association with hypothyroidism, euthyroidism, and Hashimoto's thyroiditis. This condition affects the thyroid gland, pretibial skin and orbit. Ocular manifestations typically occur in up to 50 percent of patients with GD and usually presents in the 3rd to 5th decade of life with women more commonly affected. Clinical manifestations may include but are not limited to periorbital edema and erythema, eyelid retraction, proptosis, strabismus, chemosis, increased intraocular pressure, exposure keratopathy and reduced vision from corneal ulceration or compressive optic neuropathy. The disease is divided into two phases: active phase and stable (inactive) phase. The active phase is clinically progressive and is characterized by orbital inflammation and usually lasts between 6 months and 2 years. Subsequent tissue remodeling, and fibrosis is present when the disease becomes inactive. (2, 3)

Treatment

Supportive ophthalmic management for TED is usually indicated for mild orbitopathy and consists of ocular surface lubrication and prismatic correction of binocular diplopia. For moderate or severe cases, treatment strategies include corticosteroids, orbital irradiation, or orbital decompression. When surgical intervention is indicated, orbital decompression is performed, followed by strabismus surgery and then eyelid surgery. (2) The goal of treatment is to alter the course of the disease, preventing sight-threatening complications, and obviate the need for surgical rehabilitation. Additional treatment may also impact health-related quality of life (QOL) by preventing facial disfigurement and improving ocular function. (3)

To date, teprotumumab-trbw is the first U.S. Food and Drug Administration (FDA) approved human monoclonal antibody for the treatment of adults with TED. (4) Evidence suggests that autoantibodies to the insulin-like growth factor 1 receptor (IGF-1R), along with the thyroid-stimulating hormone receptor (TSHR), mediate the pathogenesis in susceptible individuals. (5) Teprotumumab-trbw, targets and binds to IGF-1R and blocks its activation and signaling. Based on the mechanism of action, teprotumumab-trbw is believed to decrease inflammation and tissue growth therefore, reducing the signs and symptoms of TED. (5, 6)

Regulatory Status
On January 21, 2020, the U.S. FDA approved teprotumumab-trbw (Tepezza; Horizon Therapeutics) for the treatment of adults with TED. On April 14, 2023, the U.S. FDA approved updated indication language for the use of teprotumumab-trbw to specify use in patients with TED regardless of disease activity or duration. The FDA approval was based on supporting data from a phase 4 clinical trial. (4, 7)

The FDA recommends the initial dose of 10 mg/kg given via intravenous (IV) infusion followed by an IV infusion of 20 mg/kg every 3 weeks for 7 additional infusions. Teprotumumab-trbw is administered IV over 60 to 90 minutes. (1)

Rationale

This policy is based on the United States (U.S.) Food and Drug Administration (FDA) approved labeled indications for Tepezza (teprotumumab-trbw) and a professional society guideline.

Tepezza (teprotumumab-trbw) (1)
Tepezza was evaluated in two randomized, double-masked, placebo controlled clinical trials in 171 patients with thyroid eye disease (TED): Study 1 (NCT01868997) and Study 2 (NCT03298867). Patients were randomized to receive Tepezza or placebo 1:1. Patients were given intravenous (IV) infusions (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. Patients had a clinical diagnosis of TED with presence of and were euthyroid or had thyroxine and free triiodothyronine levels less than 50% above or below normal limits. Prior surgical treatment for TED was not permitted. Proptosis ranged from 16 to 33 mm and 125 patients (73%) diplopia at baseline.

A total of 84 patients were randomized to Tepeeza and 87 patients were randomized to placebo. The median age was 52 years (range 20 to 79 years), 86% were White, 9% were Black or African American, 4% were Asian and 1% identified as Other. The majority (73%) were female. At baseline, 27% of patients were smokers.

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. Results for proptosis are found in Table 1.

Table 1. Efficacy Results in Patients with Thyroid Eye Disease in Study 1 and 2

	Study 1			**Study 2**		
	Teprotumumab (N=42)	**Placebo (N=45)**	**Difference (95% CI)**	**Teprotumumab (N=41)**	**Placebo (N=42)**	**Difference (95% CI)**
Proptosis respond-er rate at week 24, % (n) [1]	71% (30)	20% (9)	51% (33, 69)	83% (34)	10% (4)	73% (59, 88)
Proptosis (mm) average change from baseline through week 24, LS Mean (SE) [2]	-2.5 (0.2)	-0.2 (0.2)	-2.3 (-2.8, -1.8)	-2.8 (0.2)	-0.5 (0.2)	-2.3 (-2.8, -1.8)

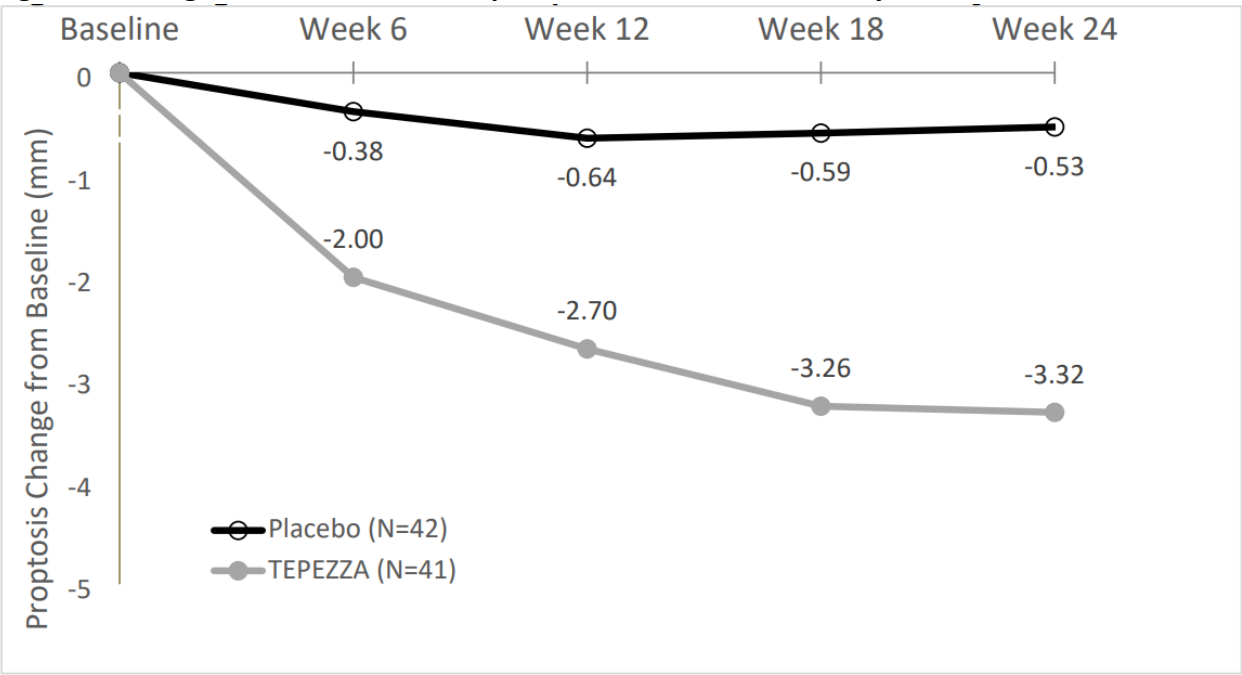
LS: least squares; SE: standard error.

[1] Difference and its corresponding 95% Confidence Interval (CI) is based on a weighted average of the difference within each randomization stratum (tobacco user, tobacco non-use) using Cochran–Mantel–Haenszel (CMH) weights.

[2] Results were obtained from a mixed-model repeated measures (MMRM) with an unstructured covariance matrix and including treatment, smoking status, baseline value, visit, treatment by visit, and visit by baseline value interaction as fixed effects. A change from Baseline of 0 was imputed at the first post-Baseline visit for any subject without a post-Baseline value.

In Study 2, improvement of proptosis as measured by mean change from Baseline was observed as early as 6 weeks and continued to improve through week 24 as shown in Figure 1. Similar results were seen in Study 1.

Figure 1. Change from Baseline in Proptosis over 24 Weeks in Study 2



P<0.01 at each timepoint

Tepezza also led to improvement in the less severely impacted "fellow" eye. Diplopia (double vision) was evaluated in a subgroup of patients that had diplopia at baseline in Study 1 and 2. Results are shown in Table 2.

Table 2. Diplopia in Patients with Thyroid Eye Disease in Study 1 and 2

Parameter	Tepezza (n=66)	Placebo (n=59)
Diplopia Responder rate[a] at week 24, % (n)	53% (35)	25% (15)

P<0.01

[a] Diplopia was evaluated on a 4-point scale where scores ranged from 0 for no diplopia to 3 for constant diplopia. A diplopia responder was defined as a patient with baseline diplopia >0 and a score of 0 at week 24.

Following discontinuation of treatment in Study 1, 53% of patients (16 of 30 patients) who were proptosis responders at week 24 maintained proptosis response 51 weeks after the last TEPEZZA infusion. 67% of patients (12 of 18) who were diplopia responders at week 24 maintained diplopia response 51 weeks after the last Tepezza infusion.

Subgroups

Examination of age and gender subgroups did not identify differences in response to Tepezza among these subgroups. Reduction in proptosis was similar between smokers and non-smokers in both studies.

Guidelines and Position Statements

European Group on Graves' Orbitopathy

In 2021, the European Group on Graves' Orbitopathy (EUGOGO) published guidance on the medical management of Graves' orbitopathy (8) which considers teprotumumab-trbw (in addition to other second-line treatment options) as a second-line treatment option for moderate-to-severe and active Graves' orbitopathy if the response to primary treatment is poor and Graves' orbitopathy is still moderate to severe and active. (Strength of recommendation 1 and level of evidence moderate quality)

The 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 TED is defined as lid retraction ≥ 2 mm, exophthalmos ≥ 3 mm, moderate to severe soft tissue involvement, and presence of diplopia. Sight-threatening TED is defined as presence of dysthyroid optic neuropathy and/or corneal breakdown.

American Thyroid Association

In 2016, the American Thyroid Association published guidelines for the diagnosis and management of hyperthyroidism and other causes of thyrotoxicosis which offers guidance on what criteria is used to define the clinical severity of Graves' orbitopathy. (9)

Table 1. Graves' Orbitopathy Severity Assessment (9)

Grade[b]	**Lid Retraction**	**Soft Tissues**	**Proptosis**[c]	**Diplopia**	**Corneal Exposure**	**Optic Nerve Status**
Mild	<2 mm	Mild involvement	<3 mm	Transient or absent	Absent	Normal
Moderate	≥ 2 mm	Moderate involvement	≥3 mm	Inconstant	Mild	Normal
Severe	≥ 2 mm	Severe involvement	≥3 mm	Constant	Mild	Normal
Sight Threatening	_	_	_	_	Severe	Compression

[b] Mild Graves' orbitopathy (GO): patients whose features of GO have only a minor impact on daily life, generally insufficient to justify immunosuppressive or surgical treatment. Moderate-to-severe GO: patients without sight-threatening GO whose eye disease has sufficient impact on daily life to justify the risks of immunosuppression (if active) or surgical intervention (if inactive). Sight-threatening GO: patients with dysthyroid optic neuropathy and/or corneal breakdown. This category warrants immediate intervention.

[c] Proptosis refers to the variation compared to the upper limit of normal for each race/sex or the patient's baseline, if available.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	None
HCPCS Codes	J3241

*Current Procedural Terminology (CPT®) ©2024 American Medical Association: Chicago, IL.

References

U.S. Food and Drug Administration Label:

1. U.S. Food and Drug Administration, Drugs@FDA. Highlights of Prescribing Information: Tepezza (teprotumumab-trbw). (9/2025). Available at <https://www.accessdata.fda.gov> (accessed September 5, 2025).

Other:

2. Wang Y, Patel A, Douglas R, et al. Thyroid eye disease: How a novel therapy may change the treatment paradigm. Ther Clin Risk Manag. Nov 2019; 15:1305-1318. PMID 31814726
3. Gupta S, Douglas R. The pathophysiology of thyroid eye disease (TED): Implications for immunotherapy. Curr Opin Ophthalmol. Sept 2011; 22(5):385-390. PMID 21730841
4. FDA news release: FDA approves teprotumumab for thyroid eye disease. Jan 21 2020. Available at <https://fda.gov> (accessed September 5, 2025).
5. Douglas R. Teprotumumab, an insulin-like growth factor-1 receptor antagonist antibody, in the treatment of active thyroid eye disease: a focus on proptosis. Eye. Feb 2019; 33(2):183-190. PMID 30575804
6. Wang Y, Smith TJ. Current concepts in the molecular pathogenesis of thyroid-associated ophthalmopathy. IOVS. Mar 2014; 55(3):1735-1748. PMID 24651704
7. Horizon Therapeutics plc announces FDA approval of an update to the indication language for Tepezza® (teprotumumab-trbw) to specify its use in thyroid eye disease (TED) patients regardless of disease activity or duration. PressRelease. Dublin, Ireland: Horizon Therapeutics; Apr 14, 2023. Available at <https://www.drugs.com> (accessed August 19, 2025).
8. Bartalena L, Kahaly GJ, Baldeschi L, et al. The 2021 European Group on Graves' Orbitopathy (EUGOGO) clinical practice guidelines for the medical management of Graves' orbitopathy. Eur J Endocrinol. Aug 27 2021; 185(4):G43-G67. PMID 34297684
9. Ross DS, Burch HB, Cooper DS, et al. 2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis. Thyroid. Oct 2016; 26(10):1343-1421. PMID 27521067

Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision	
Date	**Description of Change**
11/01/2025	Document updated. The following changes were made to Coverage: 1) Added "for the treatment of thyroid eye disease" to the medically necessary statement; and 2) Removed "individual has documented active thyroid eye disease"; and 3) Removed "significant" and replaced with "moderate to severe" for soft tissue involvement; and 4) Added "non-Food and Drug Administration approved" to the existing experimental, investigational and/or unproven statement. Title changed from “Teprotumumab”. No new references added; others updated or removed.
07/15/2024	Reviewed. No changes.
11/01/2023	Document updated with literature review. The following change was made in Coverage: Removed requirement for clinical activity score (CAS) and Note 1 which defined the CAS score. Added reference 7, 8, 12; others updated.
04/01/2023	Document updated with literature review. The following change was made to Coverage: Updated the criteria for moderate to severe disease from “Proptosis of 3 millimeters or more” to “Exophthalmos ≥ 3 millimeters or more”. Added reference 9, 11; others updated.
07/01/2022	Reviewed. No changes.
06/01/2021	Document updated with literature review. The following change was made to Coverage: Modified clinical activity score (CAS) criterion from “greater than 4” to “greater than or equal to 4”. No new references added.
11/01/2020	New medical document. 1) Teprotumumab (Tepezza) may be considered medically necessary when ALL of the following criteria are met: Member is 18 years of age or older; and member has documented active thyroid eye disease with a clinical activity score (CAS) greater than 4 (defined in NOTE 1); and member has moderate-to-severe disease confirmed by at least one of the following: Lid retraction of 2 or more millimeters; or significant soft tissue involvement; or proptosis of 3 millimeters or more; or presentation of diplopia; or corneal exposure. 2) Teprotumumab (Tepezza) is considered experimental, investigational, and/or unproven for all other indications or

	when used as a repeat course of treatment (beyond the initial 8 doses). 3) Added Note 1 to reflect 7-point Clinical Activity Score.