Medical Policy Bulletin
Title:
Teprotumumab (Tepezza®)
Policy #:
MA08.115c

The Company makes decisions on coverage based on the Centers for Medicare and Medicaid Services (CMS) regulations and guidance, benefit plan documents and contracts, and the member's medical history and condition. If CMS does not have a position addressing a service, the Company makes decisions based on Company Policy Bulletins. Benefits may vary based on contract, and individual member benefits must be verified. The Company determines medical necessity only if the benefit exists and no contract exclusions are applicable. Although the Medicare Advantage Policy Bulletin is consistent with Medicare's regulations and guidance, the Company's payment methodology may differ from Medicare.

When services can be administered in various settings, the Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition. This decision is based on the member's current medical condition and any required monitoring or additional services that may coincide with the delivery of this service.

This Policy Bulletin document describes the status of CMS coverage, medical terminology, and/or benefit plan documents and contracts at the time the document was developed. This Policy Bulletin will be reviewed regularly and be updated as Medicare changes their regulations and guidance, scientific and medical literature becomes available, and/or the benefit plan documents and/or contracts are changed.

Policy

Coverage is subject to the terms, conditions, and limitations of the member's Evidence of Coverage.

The Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition.

MEDICALLY NECESSARY

Teprotumumab-trbw (Tepezza) is considered medically necessary and, therefore, covered for adult individuals with active or inactive thyroid eye disease (TED) who have a confirmed diagnosis of Graves' disease, when all of the following criteria listed below are met, including dosing and frequency:

- Individual has moderate to severe TED with documentation of one or more of the following:
  - lid retraction ≥2 mm
  - moderate or severe soft-tissue involvement
  - proptosis ≥3 mm above normal values, as determined by professional provider
  - periodic or constant diplopia
- Individual has documentation of symptomatic TED, characterized by one or more of the following symptoms:
  - dry eye
  - exposure keratitis
  - inflammation, pain, or redness of the eye/eyelids
  - lagophthalmos (incomplete or defective closure of the eyelids) with excessive lacrimation
  - strabismus
- Individual is euthyroid or with mild hypo- or hyperthyroidism defined as free thyroxine (FT4) and free tri-iodothyronine (FT3) levels less than 50% above or below the normal limits.
- Individual does not have planned surgical ophthalmological intervention for proptosis repair
- Prescribed by an ophthalmologist, or endocrinologist in consultation with an ophthalmologist
- Dosing and frequency: 10 mg/kg for first infusion, followed by 20 mg/kg every 3 weeks for seven additional infusions (maximum of eight doses or one cycle)

EXPERIMENTAL/INVESTIGATIONAL

All other uses of teprotumumab-trbw (Tepezza), including subsequent treatment/retreatment therapy beyond a total of eight doses, are considered experimental/investigational and, therefore, not covered unless the indication is

supported as an accepted off-label use, as defined in the medical policy on off-label coverage for prescription drugs and biologics.

COSMETIC SERVICES

Requests for teprotumumab-trbw (Tepezza) that do not meet the medical necessity criteria listed in this policy (i.e., solely for the purpose of improving an individual's appearance) are considered cosmetic services. Services that are cosmetic are a benefit contract exclusion for all products of the Company. Therefore, they are not eligible for reimbursement consideration.

DOSING AND FREQUENCY REQUIREMENTS

The Company reserves the right to modify the Dosing and Frequency Requirements listed in this policy to ensure consistency with the most recently published recommendations for the use of teprotumumab-trbw (Tepezza). Changes to these guidelines are based on a consensus of information obtained from resources such as, but not limited to: the US Food and Drug Administration (FDA); Company-recognized authoritative pharmacology compendia; or published peer-reviewed clinical research. The professional provider must supply supporting documentation (i.e., published peer-reviewed literature) in order to request coverage for an amount of teprotumumab-trbw (Tepezza) outside of the Dosing and Frequency Requirements listed in this policy. For a list of Company-recognized pharmacology compendia, view our policy on off-label coverage for prescription drugs and biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of this drug. If the member's dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider must submit those changes to the Company for a new approval based on those changes as part of the utilization management process. The Company reserves the right to conduct postpayment review and audit procedures for any claims submitted for teprotumumab-trbw (Tepezza).

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

When coverage of teprotumumab-trbw (Tepezza) is requested outside of the Dosing and Frequency Requirements listed in this policy, the prescribing professional provider must supply documentation (i.e., published peer-reviewed literature) to the Company that supports this request.

Guidelines

There is no Medicare coverage determination addressing teprotumumab-trbw (Tepezza); therefore, the Company policy is applicable.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable Evidence of Coverage, teprotumumab-trbw (Tepezza) for intravenous infusion is covered under the medical benefits of the Company's Medicare Advantage products when the medical necessity criteria and Dosing and Frequency Requirements listed in this medical policy are met.

However, services that are identified in this policy as experimental/investigational are not eligible for coverage or reimbursement by the Company.

Services that are cosmetic are a benefit contract exclusion for all products of the Company. Therefore, they are not eligible for reimbursement consideration.

CLASSIFICATION OF SEVERITY OF GRAVES' ORBITOPATHY

- **Mild disease, at least one of the following:**

    - Minor lid retraction (<2 mm)
    - Mild soft-tissue involvement
    - Exophthalmos <3 mm above normal values, as determined by professional provider
    - No or intermittent diplopia
    - Corneal exposure responsive to lubricants
- **Moderate-to-severe disease, at least one of the following:**
    - Lid retraction ≥2 mm
    - Moderate or severe soft-tissue involvement
    - Exophthalmos ≥3 mm above normal values, as determined by professional provider
    - Inconstant or constant diplopia
- **Sight-threatening disease, at least one of the following:**
    - Dysthyroid optic neuropathy (DON)
    - Corneal breakdown

Source: 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.* 2021;185(4):G43-G67.

US FOOD AND DRUG ADMINISTRATION (FDA) STATUS

Teprotumumab-trbw (Tepezza) was approved by the FDA on January 21, 2020, for treatment of thyroid eye disease (TED).

PEDIATRIC USE
The safety and effectiveness of teprotumumab-trbw (Tepezza) in pediatric individuals have not been established.

Description

Teprotumumab-trbw (Tepezza) is a fully human antibody that targets the insulin-like growth factor-1 receptor (IGF-1R) indicated for the treatment of active thyroid eye disease (TED)/Graves' disease in adult individuals 18 years of age and older. TED is a rare, autoimmune disease, in which the muscles and fatty tissues behind the eye become inflamed, causing the eyes to be pushed forward and bulge outwards (proptosis).

TED is characterized by proptosis (outward bulging of the eye) that can cause a variety of symptoms such as eye pain, double vision, light sensitivity, or difficulty closing the eye. This disease affects a relatively small population, with women more commonly affected than men. Although this condition affects relatively few individuals, TED can be incapacitating. For example, the troubling ocular symptoms can lead to the progressive inability of people with TED to perform important daily activities, such as driving or working.

The US Food and Drug Administration (FDA) granted this application Priority Review, in addition to Fast Track and Breakthrough Therapy Designation. Additionally, teprotumumab-trbw (Tepezza) received Orphan Drug designation, which provides incentives to assist and encourage the development of drugs for rare diseases or conditions.

PEER-REVIEWED LITERATURE

Summary of Literature for Active TED

Two trials have investigated teprotumumab-trbw (Tepezza) Tepeza. Both trials enrolled participants with active TED. The participants received either teprotumumab-trbw (Tepezza) or placebo by intravenous infusion every 3 weeks for a total of eight infusions.

After the trials' end (24 weeks), the researchers reported on the percentage of individuals who achieved the trials' primary outcomes of a reduction greater than 2 mm in proptosis between the two treatment groups.

In a randomized, double-masked, placebo-controlled, phase 3 multicenter trial, participants with active TED were assigned in a 1:1 ratio to receive intravenous infusions of the IGF-IR inhibitor teprotumumab-trbw (Tepezza) (10 mg/kg of body weight for the first infusion and 20 mg/kg for subsequent infusions) or placebo once every 3 weeks for 21 weeks.

A total of 41 individuals were assigned to the teprotumumab-trbw (Tepezza) group and 42 to the placebo group. At

week 24, the percentage of patients with a proptosis response was higher with teprotumumab-trbw (Tepezza) than with placebo (83% [34 patients] vs. 10% [four patients]; *P*<0.001). The treatment arm resulted in better outcomes with respect to proptosis, Clinical Activity Score (CAS), diplopia, and quality of life than placebo in individuals with active TED.

Summary of Literature for Inactive TED

According to the 2021 European Group on Graves' orbitopathy (EUGOGO) clinical practice guidelines for the medical management of Graves' orbitopathy (Bartalena et al., 2021), the management of inactive TED may require low dose immunosuppressives or surgical intervention. There have been a few case reports and small, retrospective, case series researching the use of teprotumumab-trbw (Tepezza) in individuals with inactive TED (also cited in the literature as chronic or stable TED). The researchers found benefit of this treatment in some individuals with inactive TED. In the OPTIC-X study (Douglas et al., 2022), there was exploratory evidence showing some benefit in five individuals. A clinical trial of 57 individuals with inactive TED is ongoing, with estimated study completion date of April 2023 (NCT04583735). Researchers are exploring the hypothesis that individuals with chronic TED maintain an IGF-1R overexpression. Due to the paucity of literature, more large, prospective trials are needed to confirm the benefit and safety of teprotumumab-trbw (Tepezza) in individuals with inactive TED.

Douglas et al. (2023) performed a randomized, double-masked, placebo-controlled, parallel-group, multicenter, phase 4 trial in adults with TED duration of 2 to 10 years and a CAS less than or equal to 1 (stable/inactive disease). Individuals had greater than or equal to 3-mm increase in proptosis from before diagnosis of TED and/or proptosis greater than or equal to 3 mm above normal values. Sixty-two individuals were randomly assigned (2:1) to receive intravenous teprotumumab-trbw (Tepezza) or placebo once every 3 weeks (total of eight infusions). The primary endpoint was proptosis (mm) improvement at Week 24, which resulted in greater improvement with teprotumumab-trbw (Tepezza) than with placebo (*P*=0.0004). Adverse reactions were similar among the two groups, with hyperglycemia reported in six (15%) versus two (10%), and hearing impairment in nine (22%) versus two (10%) with teprotumumab-trbw (Tepezza) and placebo, respectively.

Summary of Literature for Subsequent Treatments/Retreatment

The data for the role of subsequent treatments (or retreatment) of teprotumumab-trbw (Tepezza) after one course of therapy is still being investigated. In the OPTIC-X study (Douglas et al., 2022), researchers saw benefit in a few individuals who were non-responders to initial therapy. Due to the paucity of literature, more large, prospective trials are needed to confirm the benefit and safety of teprotumumab-trbw (Tepezza) in individuals who need subsequent treatments of teprotumumab-trbw (Tepezza).

COSMETIC USES

Cosmetic services are those provided to improve an individual's physical appearance, from which no significant improvement in physiologic function can be expected. Emotional and/or psychological improvement alone does not constitute improvement in physiologic function.

OFF-LABEL INDICATIONS

There may be additional indications contained in the Policy section of this document due to evaluation of criteria highlighted in the Company's off-label policy, and/or review of clinical guidelines issued by leading professional organizations and government entities.

References

American Hospital Formulary Service (AHFS). Drug Information 2024. Teprotumumab-trbw. [Lexicomp Online Web site]. 02/24/2020. Available at: http://online.lexi.com/lco/action/home [via subscription only]. Accessed January 4, 2024.

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.* 2021;185(4):G43-G67.

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. *Thyroid*. 2022;32(12):1439-1470.

Davies TF, Burch HB. Clinical features and diagnosis of Graves' orbitopathy (ophthalmopathy). 10/18/2023. Available at: Clinical features and diagnosis of Graves' orbitopathy (ophthalmopathy) - UpToDate. Accessed May 3, 2024.

Davies TF, Burch HB. Thyroid eye disease severity assessment. 2024. Available at: TED severity assessment - UpToDate. Accessed May 30, 2024.

Davies TF, Burch HB. Treatment of Graves' orbitopathy (ophthalmopathy). 04/17/2024. Available at: Treatment of Graves' orbitopathy (ophthalmopathy) - UpToDate. Accessed May 3, 2024.

Dickinson AJ, Perros P. Controversies in the clinical evaluation of active thyroid-associated orbitopathy: use of a detailed protocol with comparative photographs for objective assessment. *Clin Endocrinol (Oxf)*. 2001;55(3):283-303.

Douglas RS, Couch S, Wester ST, et al. Efficacy and Safety of Teprotumumab in Patients With Thyroid Eye Disease of Long Duration and Low Disease Activity. *J Clin Endocrinol Metab*. 2023;109(1):25-35.

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.

Douglas RS, Kahaly GJ, Ugradar S, et al. Teprotumumab Efficacy, Safety, and Durability in Longer-Duration Thyroid Eye Disease and Re-treatment: OPTIC-X Study. *Ophthalmology*. 2022 Apr;129(4):438-449.

Elsevier's Clinical Pharmacology Compendium. Teprotumumab-trbw. 04/14/2023. [Clinical Key Web site]. Available at: https://www.clinicalkey.com/pharmacology/ [via subscription only]. Accessed January 4, 2024.

Ho TC, Maamari RN, Kossler AL, et al. Outcomes of patients with thyroid eye disease partially treated with teprotumumab. *Ophthalmic Plast Reconstr Surg*. 2023;39(2):150-155.

Kahaly GJ, Douglas RS, Holt RJ, Sile S, Smith TJ. Teprotumumab for patients with active thyroid eye disease: a pooled data analysis, subgroup analyses, and off-treatment follow-up results from two randomised, double-masked, placebo-controlled, multicentre trials. *Lancet Diabetes Endocrinol.* 2021;9(6):360-372.

Lexi-Drugs Compendium. teprotumumab-trbw. 12/05/2023. [Lexicomp Online Web site]. Available at: http://online.lexi.com/lco/action/home [via subscription only]. Accessed January 4, 2024.

Mourits MP, Koornneef L, Wiersinga WM, et al. Clinical criteria for the assessment of disease activity in Graves' ophthalmopathy: a novel approach. *Br J Ophthalmol*. 1989;73(8):639-644.

National Organization of Rare Diseases (NORD). Thyroid eye disease. 2020. Available at: Thyroid Eye Disease - NORD (National Organization for Rare Disorders) (rarediseases.org). Accessed January 4, 2024.

Ozzello DJ, Dallalzadeh LO, Liu CY. Teprotumumab for chronic thyroid eye disease. *Orbit*. 2021; Jun 1:1-8.

Ozzello DJ, Kikkawa DO, Korn BS. Early experience with teprotumumab for chronic thyroid eye disease. *Am J Ophthalmol Case Rep*. 2020;19:100744.

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.* 2016;26(10):1343-1421.

Smith TJ, Kahaly GJ, Ezra DG, et al. Teprotumumab for thyroid-associated ophthalmopathy. *N Engl J Med.* 2017 May 4;376(18):1748-1761.

Truven Health Analytics. Micromedex® DrugDex® Compendium. teprotumumab-trbw. 12/13/2023. Greenwood Village, CO. [Micromedex® Solutions Web site]. Available at: http://www.micromedexsolutions.com/micromedex2/librarian [via subscription only]. Accessed January 4, 2024.

Ugradar S, Shi L, Wang Y, Mester T, Yang H, Douglas RS. Teprotumumab for non-inflammatory thyroid eye disease (TED): evidence for increased IGF-1R expression. *Eye (Lond)*. 2021;35(9):2607-2612.

US Food and Drug Administration. Center for Drug Evaluation and Research. Teprotumumab-trbw (Tepezza) Product Labeling. [FDA Web site]. 10/26/2021. Available at: https://www.accessdata.fda.gov/scripts/cder/daf/. Accessed May 3, 2024.

US Food and Drug Administration. Center for Drug Evaluation and Research. Teprotumumab-trbw (Tepezza) Approval Letter. [FDA Web site]. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2020/761143Orig1s000ltr.pdf. Accessed May 3, 2024.

Coding

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

CPT Procedure Code Number(s)

N/A

ICD - 10 Procedure Code Number(s)

N/A

ICD - 10 Diagnosis Code Number(s)

E05.00	Thyrotoxicosis with diffuse goiter without thyrotoxic crisis or storm
E05.10	Thyrotoxicosis with toxic single thyroid nodule without thyrotoxic crisis or storm
E05.20	Thyrotoxicosis with toxic multinodular goiter without thyrotoxic crisis or storm
E05.30	Thyrotoxicosis from ectopic thyroid tissue without thyrotoxic crisis or storm
E05.80	Other thyrotoxicosis without thyrotoxic crisis or storm
E05.90	Thyrotoxicosis, unspecified without thyrotoxic crisis or storm
H05.831	Thyroid orbitopathy, right orbit

HCPCS Level II Code Number(s)

J3241 Injection, teprotumumab-trbw, 10 mg

Revenue Code Number(s)

N/A

Policy History

Revisions From MA08.115c:

12/15/2025	This policy will become effective on 12/15/2025. The following ICD-10 code has been added to the policy: H05.831 Thyroid orbitopathy, right orbit

	H05.832 Thyroid orbitopathy, left orbit H05.833 Thyroid orbitopathy, bilateral

Revisions From MA08.115b:

03/28/2025	This version of the policy will become effective 03/28/2025. This policy has been updated to clarify the criteria coverage for teprotumumab-trbw (Tepezza) for thyroid eye disease (TED). The policy has been expanded to include both symptomatic, active and inactive moderate- to- severe TED, in accordance with FDA and peer-reviewed literature. The Clinical Activity Score was removed. Additional criteria for planned surgical ophthalmological intervention has been added. Language regarding cosmetic use has been added. The following ICD-10 CM codes have been added to this policy as Medically Necessary: E05.10 Thyrotoxicosis with toxic single thyroid nodule without thyrotoxic crisis or storm E05.20 Thyrotoxicosis with toxic multinodular goiter without thyrotoxic crisis or storm E05.30 Thyrotoxicosis from ectopic thyroid tissue without thyrotoxic crisis or storm E05.80 Other thyrotoxicosis without thyrotoxic crisis or storm E05.90 Thyrotoxicosis, unspecified without thyrotoxic crisis or storm H05.89 Other disorders of orbit

Revisions From MA08.115a:

05/07/2024	This policy has been reissued in accordance with the Company's annual review process.
06/06/2022	This version of the policy will become effective 06/06/2022. This policy has been updated to communicate the coverage criteria for teprotumumab-trbw (Tepezza), consistent with its clinical trials for FDA-approval, as well as prevailing community standards. Additionally, teprotumumab-trbw (Tepezza) is considered experimental/investigational for its use in chronic/inactive/stable disease and subsequent treatment/retreatment.

Revisions From MA08.115:

05/24/2021	This version of the policy will become effective 05/24/2021. The following new policy has been developed to communicate Company's coverage criteria for Teprotumumab (Tepezza™) intravenous infusion.

Version Effective Date:
12/15/2025
Version Issued Date:
12/15/2025
Version Reissued Date:
N/A