

teprotumumab-trbw (Tepezza™)

Medicare Advantage Medical Policy #MNG-060

Original Effective Date: 02/01/2025

Current Effective Date: 02/01/2025

Applies to all products administered or underwritten by the Health Plan, unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Health Plan may consider teprotumumab-trbw (Tepezza™) for the treatment of Thyroid Eye Disease to be **eligible for coverage**.**

Patient Selection Criteria

Coverage eligibility for teprotumumab-trbw (Tepezza) will be considered when the following criteria are met:

- Patient has a diagnosis of Thyroid Eye Disease; AND
- Patient is 18 years of age or older; AND
- Tepezza is dosed as 10 mg/kg for the first infusion, followed by 20 mg/kg every 3 weeks for 7 additional infusions (8 infusions total); AND
- Patient has NOT received a prior course of Tepezza in their lifetime; AND
- Patient's Thyroid Eye Disease is classified as moderate to severe thyroid eye disease (having at least one of the following):
 - Lid retraction of ≥ 2 mm; OR
 - Moderate or severe tissue involvement; OR
 - Proptosis of ≥ 3 mm above the normal values for race and sex; OR
 - Periodic or constant diplopia; AND
- Patient is euthyroid OR patient has mild hypothyroidism or mild hyperthyroidism [e.g., free thyroxine (FT4) and free triiodothyronine (FT3) levels less than 50% above or below the normal limits]; AND
- Patient has NOT had prior surgical treatment or orbital irradiation for Thyroid Eye Disease and is NOT planning on surgical treatment or orbital irradiation for Thyroid Eye Disease during treatment with Tepezza; AND
- Patient does NOT have corneal decompensation that is unresponsive to medical management; AND
- Patient has NOT had a decrease in best corrected visual acuity due to optic neuropathy within the previous 6 months (e.g., a decrease in vision of 2 lines on the Snellen chart, new visual field defect, or color defect secondary to optic nerve involvement).

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When Services Are Considered Not Medically Necessary

Based on review of available data, the Health Plan considers the use of teprotumumab-trbw (Tepezza) when the patient's Thyroid Eye Disease is NOT classified as moderate to severe to be **not medically necessary.****

Based on review of available data, the Health Plan considers the use of teprotumumab-trbw (Tepezza) when the patient is NOT euthyroid OR when the patient does NOT have mild hypothyroidism or mild hyperthyroidism to be **not medically necessary.****

Based on review of available data, the Health Plan considers the use of teprotumumab-trbw (Tepezza) when the patient has had prior surgical treatment or orbital irradiation for Thyroid Eye Disease OR when there is planned surgical treatment or orbital irradiation for Thyroid Eye Disease during treatment with teprotumumab-trbw (Tepezza) to be **not medically necessary.****

Based on review of available data, the Health Plan considers the use of teprotumumab-trbw (Tepezza) when the patient has corneal decompensation that is unresponsive to medical management to be **not medically necessary.****

Based on review of available data, the Health Plan considers the use of teprotumumab-trbw (Tepezza) when the patient has had a decrease in best corrected visual acuity due to optic neuropathy within the previous 6 months (e.g., a decrease in vision of 2 lines on the Snellen chart, new visual field defect, or color defect secondary to optic nerve involvement) to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Health Plan considers the use of teprotumumab-trbw (Tepezza) for a non-FDA approved indication OR in patients younger than 18 years of age OR for a non-FDA approved dose to be **investigational.***

Based on review of available data, the Health Plan considers the use of nine or more doses of teprotumumab-trbw (Tepezza) to be **investigational.***

Based on review of available data, the Health Plan considers the use of more than one series of teprotumumab-trbw (Tepezza) per lifetime to be **investigational.***

Background/Overview

Tepezza is an insulin-like growth factor-1 receptor inhibitor indicated for the treatment of Thyroid Eye Disease (TED) regardless of TED activity or duration. The mechanism of action for Tepezza in this condition has not been fully characterized. Tepezza is provided as 500 mg lyophilized powder

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in a single dose vial for reconstitution. Initial dosing for Tepezza is 10 mg/kg for the first infusion, followed by 20 mg/kg every three weeks for 7 additional infusions. No more than 8 infusions are approved by the FDA.

TED is an autoimmune condition typically associated with Graves' disease; however it should be noted that not everyone with TED has Graves' disease. The annual incidence rate of TED is estimated to be 16 cases per 100,000 for women and 2.9 cases per 100,000 for men, however men typically experience more severe disease. TED is associated with orbital fibroblast activation and proliferation, which leads to enlargement of the extraocular muscles, cellular infiltration of interstitial tissues, and an increase in orbital fat and connective tissue. Signs and symptoms of TED include swelling, redness, and discomfort of the lids and ocular surface, increased lacrimation, thickening, and retracting of the eyelids, bulging of the eyes, misalignment of the eyes, and diplopia. The acute inflammatory phase is typically self-limiting within 18 to 24 months. This condition can potentially threaten sight if there is compression of the optic nerve (3-5% of cases). Treatment for TED is currently only symptomatic (prior to the approval of Tepezza) and includes systemic corticosteroids in combination with orbital radiotherapy in moderate to severe cases. The 2016 European Thyroid Association/European Group on Graves' Orbitopathy Guidelines for the Management of Graves' Orbitopathy recommends methylprednisolone intravenously 4.5 gm (500 mg once weekly for 6 weeks, followed by 250 mg once weekly for the remaining 6 weeks) in most cases of moderate to severe Thyroid Eye Disease. It should be noted that Bartalena et al. showed that those who deteriorate after 6 weeks of the intravenous steroid regimen are unlikely to benefit from continuing the intravenous steroids beyond that point. Other treatment options include orbital decompression surgeries once TED is out of the active stage. In December of 2022, the American Thyroid Association and European Thyroid Association collaborated on the "Management of Thyroid Eye Disease: A Consensus Statement by the American Thyroid Association and European Thyroid Association" to provide an updated overview of the management of TED. More specifically, experts concluded that treatment with systemic corticosteroids is preferred in those who have moderate to severe disease in the absence of significant diplopia and/or proptosis. For those who do have moderate to severe disease when significant diplopia and/or proptosis are present, Tepezza is a preferred treatment option. Currently, Tepezza is the first and only drug approved by the FDA for the treatment of TED.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Tepezza was approved for the treatment of Thyroid Eye Disease in January of 2020.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration

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approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Tepezza was evaluated in 2 randomized, double-masked, placebo-controlled studies in 171 patients with Thyroid Eye Disease: Study 1 and Study 2. Patients were randomized to receive Tepezza or placebo in a 1:1 ratio. Patients were given intravenous infusions (10 mg/kg for 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 symptoms and were euthyroid or had thyroxine and free triiodothyronine levels less than 50% above or below normal limits. Prior surgical treatment or orbital irradiation for TED was not permitted. Other trial exclusions include subjects with corneal decompensation that is unresponsive to medical management as well as subjects that had a loss of visual acuity due to optic neuropathy. Proptosis ranged from 16 to 33 mm and 125 patients (73%) had diplopia at baseline.

A total of 84 patients were randomized to Tepezza and 87 patients were randomized to placebo. The primary outcome was the proptosis responder rate at week 24. 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, the proptosis responder rate was 71% in the Tepezza group vs. 20% in the placebo group. In Study 2, the proptosis responder rate was 83% in the Tepezza group vs. 10% in the placebo group. The average change from baseline in proptosis at 24 weeks was -2.5 mm in Study 1 and -2.8 mm in Study 2. 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. The diplopia responder rate was also higher in the Tepezza group. Sixty-seven percent of patients (12 of 18) who were diplopiareponders at week 24 maintained diplopia response 51 weeks after the last Tepezza infusion.

References

1. Tepezza [package insert]. Horizon Therapeutics USA, Inc. Lake Forest, Illinois. Updated July 2023.
2. Smith TJ, Kahayl GJ, Ezra DG, et al. Teprotumumab for Thyroid-Associated Ophthalmology. *N Engl J Med* 2017; 376:1748-1761.
3. Bartley, G. (1994). The epidemiological characteristics and clinical course of ophthalmology associated with autoimmune thyroid disease in Olmsted Country, Minnesota. *Trans Am Ophthalmol Soc*, 92:477-588.
4. Edsel, I., & al, e. (2011, April 29). Thyroid Associated Orbitopathy. Retrieved June 7, 2011, from Medscape Reference: <http://emedicine.medscape.com/article/1218444-overview#a1>.
5. Prummel, M., & Wiersinga, W. (1993). Smoking and risk of Graves' disease. *JAMA*, 269 (4):479-82.

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6. Wiersinga, W., & al, e. (2006). Clinical Assessment of patients with Graves' orbitopathy: the European Group on Graves' Orbitopathy recommendations. *Eur J Endocrinol*, 155:387-389.
7. Mallika, P., & et al. (2009). Thyroid Associated Ophthalmopathy - A Review. *Malaysian Family Physician*, 4 (1):1985-2274.
8. Bartalena, L., et al. (2008). Consensus statement of the European Group on Graves' orbitopathy (EUGOGO) on management of GO. *Eur J Endocrinol*, 158:273-285.
9. Bartalena L, Baldeschi L, Boboridis K, 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.
10. Kahaly G.J. Randomized, single blind trial of intravenous versus oral steroid monotherapy in Graves' orbitopathy. *J. Clin. Endocrinol. Metab.* 2005;90(9):5234–5240.
11. Bartalena L, Veronesi G, Krassas GE, et al. Does early response to intravenous glucocorticoids predict the final outcome in patients with moderate-to-severe and active Graves' orbitopathy?. *J Endocrinol Invest* 2017; 40: 547-553.
12. Task Force Members: Henry B. Burch, Petros Perros, Tomasz Bednarczuk, David S. Cooper, Peter J. Dolman, Angela M. Leung, Ilse Mombaerts, Mario Salvi, and Marius N. Stan. Management of Thyroid Eye Disease: A Consensus Statement by the American Thyroid Association and the European Thyroid Association. *Thyroid@.Dec* 2022.1439-1470.<http://doi.org/10.1089/thy.2022.0251>

Policy History

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11/19/2024 UM Committee review. New policy.

Next Scheduled Review Date: 11/2025

Coding

The five character codes included in the Health Plan Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2023 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of the Health Plan Medical Policy Coverage Guidelines is with the Health Plan and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in the Health Plan Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability

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for data contained or not contained herein. Any use of CPT outside of the Health Plan Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	J3241
ICD-10 Diagnosis	All related diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
 1. Consultation with technology evaluation center(s);
 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 3. Reference to federal regulations.

**Medically Necessary (or “Medical Necessity”) - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services

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at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient’s health insurance contract contains language that differs from the Health Plan Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Health Plan recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

Medicare Advantage Members

Established coverage criteria for Medicare Advantage members can be found in Medicare coverage guidelines in statutes, regulations, National Coverage Determinations (NCD)s, and Local Coverage Determinations (LCD)s. To determine if a National or Local Coverage Determination addresses coverage for a specific service, refer to the Medicare Coverage Database at the following link: <https://www.cms.gov/medicare-coverage-database/search.aspx>. You may wish to review the Guide to the MCD Search here: <https://www.cms.gov/medicare-coverage-database/help/mcd-bene-help.aspx>.

When coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs, internal coverage criteria may be developed. This policy is to serve as the summary of evidence, a list of resources and an explanation of the rationale that supports the adoption of this internal coverage criteria.