Medical Drug Clinical Criteria

Subject:	Tepezza (teprotumumab-trbw)		
Document #:	CC-0162	**Publish Date:**	~~06/20/2023~~07/01/2024
Status:	~~Reviewed~~Revised	**Last Review Date:**	~~05/19/2023~~05/17/2024

Table of Contents

Overview

This document addresses the use of Tepezza (teprotumumab-trbw). Tepezza is a fully human immunoglobulin G1 (IgG1) monoclonal antibody that competitively inhibits the insulin-like growth factor-1 receptor (IGF-1R). It is used to treat Thyroid Eye Disease (TED), otherwise known as Graves' Orbitopathy or Graves' Ophthalmopathy.

Thyroid Eye Disease is a rare vision-threatening autoimmune disease. It is associated with dry or irritated eyes, outward bulging of eyes (proptosis), double vision (diplopia), and optic nerve compression. TED is often associated with Graves' disease, the most common cause of hyperthyroidism and develops concurrently in roughly 40% of patients with Graves' disease. There is no disease marker for thyroid eye disease, but eye involvement occurs in the setting of current or past Graves' hyperthyroidism (low TSH, high free thyroxine [T4] and/or triiodothyronine [T3]). However, hyperthyroidism is not directly linked to TED; and about 10% of TED patients have a normally functioning thyroid. This "euthyroid" Graves' disease is still characterized by high serum thyroid autoantibody concentrations, which contribute to the development of TED. The natural history of the disease is variable and may include a period of active disease progression at varying rates followed by stabilization, or individuals may experience exacerbations and remissions, known as the chronic phase. Most patients have self-limiting mild forms of the disease where lifestyle modifications (smoking cessation, local therapies such as artificial tears, and elevating the head of the bed to decrease swelling) are warranted.

The 2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis recommend that euthyroidism be achieved and maintained in hyperthyroid patients with TED or risk factors for the development of orbitopathy. Surgery and antithyroid medications are the preferred treatments for Graves' Disease; no recommendation is provided for the treatment of TED itself. The 2022 consensus statement by the American Thyroid Association and European Thyroid Association states that Tepezza is the preferred therapy, if available, in patients with active moderate-to-severe TED with significant proptosis and/or diplopia. Elective surgery to correct proptosis, strabismus, eyelid malposition, and fat pockets can be initiated in inactive TED, but no specific treatments are recommended in this stage of disease. The consensus statement was published prior to the expanded approval of Tepezza in both active and inactive disease.

Tepezza is the first FDA approved agent to treat TED and its mechanism of action is not fully known. Signaling by overexpressed IGF-1R leads to hyaluronan accumulation and cytokine expression resulting in inflammation and extraocular tissue expansion. Tepezza was evaluated in two trials of similar design (Smith 2017, Douglas 2019 [OPTIC]). Trials required participants to have Graves' disease with active TED with a clinical activity score ≥ 4 (see table below). Patients were also required to be euthyroid or have mild hypo- or hyperthyroidism. Diabetes, if present, was well controlled with HbA1C < 9.0%. Participants had moderate-to-severe disease as shown by clinical parameters including the degree of proptosis (see table below). There were more responders in the Tepezza group versus the placebo group, based on both proptosis (defined as ≥2 mm reduction from Baseline in proptosis in the study eye, without deterioration (≥2 mm increase) of proptosis in the fellow eye at Week 24; 92.9% vs 9.5% respectively, p<0.001) and CAS (defined as participants with a reduction in clinical activity score (CAS) of ≥ 2 points, and a reduction in proptosis of ≥ 2 mm in the study eye, and no deterioration in the non-study eye; 78% vs 7.1% respectively, p<0.001). The most recent phase 4 trial (Douglas 2023) evaluated Tepezza in individuals with long-duration TED and low disease activity (CAS less than or equal to 1) over 24 weeks. All participants had at least moderate disease based on proptosis (defined as greater than or equal to 3-mm increase from before diagnosis of TED; or greater than or equal to 3-mm above normal values for race and sex). The participants received 8 infusions of either Tepezza or placebo every 3 weeks. The least squares mean change in proptosis from baseline was -2.41 mm compared to -0.92 mm in the Tepezza and placebo group, respectively, p=0.0004.

Degree of Proptosis: Upper limit of Normal for Race/Sex		
	Female	Male
African American	23 mm	24 mm
White	19 mm	21 mm
Asian	16 mm (Thai) 16 mm (Chinese)	17 mm (Thai) 18.6 mm (Chinese)

Clinical Activity Score	
Item	Description
1	Spontaneous orbital pain
2	Gaze evoked orbital pain
3	Eyelid swelling that is considered to be due to active (inflammatory phase) TED/GO
4	Eyelid erythema
5	Conjunctival redness that is considered to be due to active (inflammatory phase) TED/GO
6	Chemosis (swelling of the conjunctiva)
7	Inflammation of caruncle (red prominence at the inner corner of the eye) or plica (crescent fold in the medial conjunctive lying lateral to the caruncle)
Scoring: Each item is scored (1= present; 0= absent) and scores for each are summed for total score	

TED= Thyroid Eye Disease; GO= Graves' Orbitopathy

Tepezza has primarily been studied as a one-course therapeutic option. The OpticX trial (an open label extension of the OPTIC trial) evaluated Tepezza in individuals unresponsive or who experienced a disease flare after treatment with Tepezza (n=14) or placebo (n=37) (Douglas 2022). Both Tepezza nonresponders (n=5) and responders who experienced a disease flare (n=8) were retreated with a second course. Of nonresponders, 2 subsequently responded, 1 showed a proptosis reduction of 1.5 mm from OPTIC baseline, and 2 discontinued treatments early. In relapsed individuals, 5 of 8 patients (62.5%) responded when re-treated (mean proptosis reduction, 1.9 ± 1.2 mm from OPTIC-X baseline and 3.3 ± 0.7 mm from OPTIC baseline). Tepezza's duration of response and the efficacy of subsequent courses are still not fully understood as OpticX provided limited data regarding the retreatment of Tepezza..

Tepezza has a warning for exacerbation of preexisting inflammatory bowel disease. Individuals should be monitored for IBD flare and should be considered for discontinuation if this occurs. Tepezza also has a warning for hyperglycemia as 10% of patients experienced this adverse effect in clinical trials. Hyperglycemia events should be closely monitored and controlled. Individuals with pre-existing diabetes should be well controlled prior to starting Tepezza. Lastly, Tepezza has a warning for hearing impairment including hearing loss. Assess individuals' hearing before, during and after treatment with Tepezza.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Tepezza (teprotumumab-trbw)

Requests for one course* of Tepezza (teprotumumab-trbw) may be approved if the following criteria are met ~~(Douglas 2020)~~:

I. Individual has a diagnosis of Thyroid Eye Disease; **AND**
II. Tepezza (teprotumumab-trbw) is prescribed by, or in consultation with an endocrinologist AND an ophthalmologist; **AND**
~~II.~~III. Documentation is provided that individual has ~~symptomatic~~ moderate to severe disease, as defined by ~~one or more of~~ the following:
  A. For individuals with symptomatic, active disease, one of the following (Douglas 2020):
    ~~A.~~i. Lid retraction ≥ 2 mm; **OR**
    ~~B.~~ii. Moderate or severe soft tissue involvement**; OR**
    ~~C.~~iii. Proptosis ≥ 3 mm above normal values for race and ~~gender~~sex; **OR**
    iv. Intermittent or constant diplopia; **AND**
  B. For individuals with stable, chronic (inactive) TED, one of the following (Douglas 2023):
    i. Greater than or equal to 3 mm increase in proptosis from before diagnosis of TED; **OR**
    ii. Proptosis ≥ 3 mm above normal values for race and sex;
~~D.~~ **AND**
~~III. Documentation is provided that individual has a clinical activity score (CAS) greater than or equal to 4 in the more severely affected eye; **AND**~~
IV. Documentation is provided that one of the following applies:
  A. Thyroid function tests are provided and are within normal limits as defined by laboratory standard (i.e. individual is euthyroid); **OR**
  B. Thyroid function tests show free thyroxine (T4) and free triiodothyronine (T3) levels less than 50% above or below normal limits as defined by laboratory standard.

Tepezza (teprotumumab-trbw) may not be approved for the following:

I. More than one course* of treatment; **OR**
II. Individual is using Tepezza to reduce proptosis for cosmetic reasons alone; **OR**
~~II.~~III. Individual has had prior orbital irradiation or eye surgery for TED; **OR**

Formatted: Font: Bold
Formatted
Formatted: Font: Not Bold
Formatted: Font: Not Bold
Formatted: Font: Not Bold
Formatted: No bullets or numbering
Formatted: No underline

~~III.~~IV. Individual has decreased best-corrected visual acuity due to optic neuropathy as defined by decrease in vision of 2 lines on the Snellen chart, new visual field defect, or color defect; **OR**
~~IV.~~V. Individual has unresponsive corneal decompensation; **OR**
~~V.~~VI. When the above criteria are not met and for all other indications.

***Approval Duration:** One course of treatment; defined as a total of 8 intravenous infusions of Tepezza (teprotumumab) administered every 3 weeks

Quantity Limits

Tepezza (teprotumumab-trbw) Quantity Limits

Drug	Limit
Tepezza (teprotumumab-trbw) 500 mg vial	**Initial dose**: One 10 mg/kg infusion **Subsequent doses**: 20mg/kg every 3 weeks for seven infusions

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J3241	Injection, teprotumumab-trbw, 10 mg

ICD-10 Diagnosis

E05.00	Thyrotoxicosis with diffuse goiter without thyrotoxic crisis or storm
H05.241-H05.249	Constant Exophthalmos [when specified due to thyrotoxicosis]

Document History

Revised: 05/17/2024
Document History:

- 05/17/2024 – Annual Review: Update criteria to include individuals with chronic, inactive TED; add requirement for specialist prescribing; add may not approve statement for cosmetic use. Coding Reviewed: Added ICD-10-CM H05.241-H05.249.
- 05/19/2023 – Annual Review: No changes. Coding Reviewed: No changes.
- 05/20/2022 – Annual Review: Clarify thyroid function test criterion to include euthyroid individuals; update may not approve section to clarify surgery and optic neuropathy exclusions from the clinical trial; clarify approval duration. Coding Reviewed: No changes.
- 08/01/2021 – Administrative update to add documentation.
- 05/21/2021 – Annual Review: No changes. Coding Reviewed: No changes.
- 05/15/2020 – Annual Review: Add new clinical criteria document for Tepezza. Coding Reviewed: Added HCPCS codes J3490, J3590, C9061 and ICD-10 dx E05.00. Effective 10/1/2020 Added HCPCS J3241. Delete 9/30/2020 HCPCS J3590, J3490, C9061

References

1. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm.
2. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
3. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2024; Updated periodically.
4. 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; 26:1343-1421. Erratum in: *Thyroid.* 2017 Nov;27(11):1462
5. Smith TJ, Kahaly GJ, Ezra DG, et al. Teprotumumab for Thyroid-Associated Ophthalmopathy. *N Engl J Med.* 2017; 376: 1748-1761.
6. Douglas RS, Kahaly GJ, Patel A, et al. Teprotumumab for the Treatment of Active Thyroid Eye Disease. *N Engl J Med.* 2020; 382: 341-352.
7. 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;129(4):438-449. doi:10.1016/j.ophtha.2021.10.017

8. 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. doi:10.1210/clinem/dgad637
9. Bartalena L, Kahaly G, Baldeschi L, et al. The 2021 European Group on Graves' orbitopathy (EUGOGO) clinical practice guidelines for the medical management of Graves' orbitopathy. European Journal of Endocrinology. 2021; 185(4), G43-G67.
10. 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 Dec;32(12):1439-1470. doi: 10.1089/thy.2022.0251.