Clinical Criteria

Subject:	Tepezza (teprotumumab-trbw)		
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Overview

This document addresses the use of Tepezza (teprotumumab-trbw). Tepezza is a fully human insulin-like growth factor-1 (IgG1) monoclonal antibody that competitively inhibits the IgG1 receptor. 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), diplopia, and optic nerve compression. It is linked to Graves' disease which is the most common cause of hyperthyroidism. TED develops in about 40% of patients with Graves' disease. Therefore, classic findings would include orbitopathy 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 rapid deterioration followed by stabilization, or individuals may experience exacerbations and remissions. Most patients have self-limiting mild disease. Lifestyle modifications include smoking cessation, local therapies such as artificial tears, and elevating the head of the bed to decrease swelling.

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 2016 European Thyroid Association/European Group on Graves' Orbitopathy Guidelines for the Management of Graves' Orbitopathy recommends high-dose intravenous glucocorticoids be considered as first-line therapy for moderate-to-severe and active GO. Both guidelines precede FDA approval of Tepezza. Tepezza has not been directly compared to corticosteroid therapy in the treatment of TED.

Tepezza is the first FDA approved agent to treat TED and its mechanism of action is not fully known. Signaling by overexpressed Insulin-like growth factor 1 receptors (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 with 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 degree of proptosis (see table below). Tepezza has only been studied as one course of therapy, and the duration of response is not fully known. The ongoing OpticX trial (NCT03461211) is studying expanded treatment with Tepezza. Patients previously part of the OPTIC study (NCT03298867) who were proptosis non responders at week 24, or meet criteria for retreatment due to relapse during follow up will be treated with an additional course of Tepezza. Estimated study completion date is March 2022.

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)	17 mm (Thai)
	16 mm (Chinese)	18.6 mm (Chinese)

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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 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 experiences 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.

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. Individual has symptomatic moderate to severe disease, as defined by one or more of the following:
   A. Lid retraction ≥ 2 mm; OR
   B. Moderate or severe soft tissue involvement; OR
   C. Proptosis ≥ 3 mm above normal for race and gender; OR
   D. Intermittent or constant diplopia; AND
III. Individual has a clinical activity score (CAS) greater than or equal to 4 in the more severely affected eye; AND
IV. Thyroid function tests are provided which show a 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 has had prior orbital irradiation or surgery for TED; OR
III. Individual shows evidence of optic neuropathy (including but not limited to decrease in vision of 2 lines on the Snellen chart, new visual field defect, or color defect); OR
IV. Individual has unresponsive corneal decompensation; OR
V. 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) over 21 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

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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

J3590	Unclassified biologics (when specified as [Tepezza])
J3490	Unclassified drugs (when specified as [Tepezza])
C9061	Injection, teprotumumab-trbw, 10 mg (Tepezza) (Effective 7/1/2020) (Hospital Outpatient Only)

ICD-10 Diagnosis

All Diagnosis	When using NOC (unspecified) HCPCS codes
E05.00	Thyrotoxicosis with diffuse goiter without thyrotoxic crisis or storm

Document History

New: 05/15/2020
Document History:

- 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

References

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7. 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.
8. 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: 9-26.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

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