Medical Policy

Utilization Management and Clinical Medical Policy

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Teprotumumab-trbw (Tepezza®)	**MP-RX-FP-89-23**	☒ **MMM MA** ☒ **MMM MultiHealth**	**11/30/2023** **Last Review Date:** **10/21/2026**	**10/21/2026** **Frequently Revision:** **Annual**

Service Category:

- ☐ Anesthesia
- ☐ Surgery
- ☐ Radiology Procedures
- ☐ Pathology and Laboratory Procedures
- ☐ Medicine Services and Procedures
- ☐ Evaluation and Management Services
- ☐ DME/Prosthetics or Supplies
- ☒ Other: Part B Drugs

Service Description:

This document addresses the use of Teprotumumab-trbw (Tepezza®), an insulin-like growth factor-1 receptor inhibitor approved by the Food and Drug Administration (FDA) for the treatment of Thyroid Eye Disease (TED), otherwise known as Graves' Orbitopathy or Graves' Ophthalmopathy.

Background Information:

Tepezza is a fully human immunoglobulin G1 (IgG1) monoclonal antibody that competitively inhibits the insulin-like growth factor-1 receptor (IGF-1R) reducing inflammation, fibrosis, and swelling in thyroid eye disease (TED). By blocking IGF-1R activation, it alleviates proptosis, diplopia, and orbital tissue expansion. 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 in roughly 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 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

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≥ 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, pp<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 longduration 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.

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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.

Approved Indications

A. Treatment of Thyroid Eye Disease.

Other Uses

A. None.

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Medical Necessity Guidelines:

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.

Teprotumumab-trbw (Tepezza®)

A. Criteria For Initial Approval (*Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met **all** approval criteria.)*

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

i. Individual has a diagnosis of Thyroid Eye Disease regardless of disease activity or duration; **AND**

ii. Tepezza (teprotumumab-trbw) is prescribed by, or in consultation with an endocrinologist AND an ophthalmologist; **AND**

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):
  1. Lid retraction ≥ 2 mm;
  OR
  2. Moderate or severe soft tissue involvement;
  OR
  3. Proptosis ≥ 3 mm above normal for race and gender;
  OR
  4. Intermittent or constant diplopia; **AND**
- B. For individuals with stable, chronic (inactive) TED, one of the following (Douglas 2023):
  1. Greater than or equal to 3 mm increase in proptosis from before diagnosis of TED;
  OR
  2. Proptosis ≥ 3 mm above normal values for race and sex; **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.

B. Criteria For Continuation of Therapy

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Not applicable. Tepezza is approved as one course of treatment, defined as a total of 8 intravenous infusions administered every 3 weeks. Reauthorization beyond one course of treatment is not applicable.

C. Authorization Duration

i. Initial Approval Duration: One course of treatment; defined as a total of 8 intravenous infusions of Tepezza (teprotumumab) administered every 3 weeks
ii. Reauthorization Approval Duration: N/A

D. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

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
iii. When the above criteria are not met and for all other indications.

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Limits or Restrictions:

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Drug	Limit
Tepezza (teprotumumab-trbw) 500 mg vial	• **Initial dose:** 10 mg/kg IV • **Subsequent doses (infusions 2-8):** 20mg/kg IV every 3 weeks for seven infusions Dosing is based on the patient's actual body weight.
Exceptions	
N/A	

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Codes Information:

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

ICD-10 Diagnostic Codes:

Codes	Description
E05.00	Thyrotoxicosis with diffuse goiter without thyrotoxic crisis or storm
H05.241-H05.249	Constant Exophthalmos [when specified due to thyrotoxicosis]
H05.831-H05.839	Thyroid orbitopathy

HCPCS Codes:

Codes	Description
J3241	Injection, teprotumumab-trbw, 10 mg

CPT Codes:

Codes	Description

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Reference Information:

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2. 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
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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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Policy History:

Type of Review	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Annual Review	Updated background information with current guideline recommendations. Aligned clinical criteria with the current FDA Prescribing Information, including clarification that Tepezza is indicated for Thyroid Eye Disease regardless of disease activity or duration and is administered as one course of 8 intravenous infusions every 3 weeks. Removed continuation criteria and updated approval duration because Tepezza is approved as 8 infusions treatment course and reauthorization is not applicable. Updated Conditions Not Covered to remove categorical exclusions. Updated recommended dosage, including clarification that dose is based on actual body weight. Coding reviewed: added ICD-10 codes H05.831-H05.839. Updated reference list and incorporated new policy template.	10/15/2026	10/21/2026
Annual Review	Minimal changes; Word Formatting. Coding reviewed: No changes.	9/5/2025	9/16/2025
Annual Review	Update Background Information, Clinical Criteria, Limits or restrictions and References. Wording and formatting changes. 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.	3/14/2025	4/2/2025
Policy Inception	Elevance Health's Medical Policy adoption.	N/A	11/30/2023