STATE OF IOWA DEPARTMENT OF
Health AND Human
SERVICES

Tepezza (teprotumumab-trbw)
PAM–022

Iowa Medicaid Program:	Prior Authorization	**Effective Date:**	01/01/2021
Revision Number:	3	**Last Rev Date:**	04/21/2023
Reviewed By:	Medicaid Medical Director	**Next Rev Date:**	04/19/2024
Approved By:	Medicaid Clinical Advisory Committee	**Approved Date:**	04/16/2021

Overview

Medication:[1]	teprotumumab-trbw
Brand Name:	Tepezza®
Pharmacologic Category:	Insulin-like growth factor 1 receptor (IGF-1R) inhibitor
FDA-Approved Indication(s):	Treatment of thyroid eye disease (TED)
How Supplied:	500 mg lyophilized powder in a single-dose vial for reconstitution
Dosage and Administration:	10 mg/kg intravenous (IV) one-time dose, followed by 20 mg/kg IV once every 3 weeks for 7 infusions (total of 8 infusions is a complete course of therapy)
Benefit Category:	Medical

Descriptive Narrative

Thyroid eye disease (TED) is an autoimmune disease of the orbit and retro-ocular tissues occurring primarily in patients with Graves' disease and rarely in patients with Hashimoto's thyroiditis. It is characterized by outward bulging of eyes (proptosis), excessive tearing, and periorbital edema, and is often accompanied by pain and diplopia associated with optic nerve compression.

About 90 percent of patients with thyroid eye disease have Graves' disease, the most common cause of hyperthyroidism (TED is also referred to as Graves' orbitopathy). Graves' disease affects approximately 1 to 2 percent of the adult population, with about 40 percent of those patients subsequently developing TED over the course of their lifetime. Factors which may increase the risk of orbitopathy in patients with Graves' disease include genetics, gender (more common in females than in males), smoking (cigarette smoking is a confirmed risk factor for Graves' orbitopathy), and radioiodine therapy. Other possible risk factors include advancing age, stress, and poorly controlled thyroid function. Although about 10 percent of TED patients are labeled as having "euthyroid" Graves' disease, most cases of TED occur in the setting of current or past Graves' hyperthyroidism.[2]

Treatment of patients with thyroid eye disease includes:

- Reversal of hyperthyroidism, if present;
- Monitoring for and prompt treatment of hypothyroidism, occurring as a consequence of treating hyperthyroidism;
- Cessation of smoking, if applicable;
- Local measures to reduce ocular surface tension; and
- Treatment of inflammation and swelling in the periorbital tissues.

Patients should be treated according to the severity of their disease, keeping in mind its natural history. The natural history of TED is variable and may include a period of rapid deterioration followed by stabilization, or individuals may experience exacerbations and remissions. Disease activity is commonly assessed using a seven-point clinical activity score (CAS). Patients with a score of 3 or more are classified as having active disease and are therefore more likely to respond to immunomodulatory therapy.[3] The Phase 3 clinical trial evaluating teprotumumab-trbw enrolled patients with a CAS of $\geq$ 4.[4]

Clinical Activity Score (CAS) for Measuring TED

Elements*	Each Visit	Comparison to Previous Visit	Score
Painful feeling behind the globe over last four weeks	X		1
Pain with eye movement during last four weeks	X		1
Redness of the eyelids	X		1
Redness of the conjunctiva	X		1
Swelling of the eyelids	X		1
Chemosis (edema of the conjunctiva)	X		1
Swollen caruncle (flesh body at medial angle of eye)	X		1
Increase in proptosis ≥ 2 mm		X	1
Decreased eye movements ≥ 5° any direction		X	1
Decreased visual acuity ≥ 1 line on Snellen chart		X	1

* A seven-point scale (excluding the last 3 elements) is used when no previous assessment is available.

The CAS is also used to monitor response to therapy and is included in most clinical trials. The CAS can also be extended to include change over time by adding the following three criteria: increase in proptosis ($\geq$ 2 mm), decreased eye movements ($\geq$ 5 degrees), and decreased visual acuity ($\geq$ 1 line on the Snellen eye chart).[5]

While most patients have self-limiting mild disease, moderate-to-severe and sight-threatening thyroid eye disease occur in about 6 percent and 0.5 percent of patients with Graves' disease, respectively. Patients who have self-limiting mild disease, with no progression during follow-up, are often successfully treated with local measures alone. Patients with moderate-to-severe orbitopathy, however, may require immunomodulatory therapy, and those with sight-threatening orbitopathy frequently require surgical rehabilitation.[6]

Guidelines

In 2016, the American Thyroid Association published guidelines for the diagnosis and management of hyperthyroidism and other causes of thyrotoxicosis. Tepezza® was FDA-approved in 2020 and so is not yet included in those guidelines.

American Thyroid Association - Guidelines

Recommendations for thyroid eye disease (from 2016 guidelines):

- *Strong recommendation, moderate-quality evidence:*
  - Euthyroidism should be expeditiously achieved and maintained in hyperthyroid patients with Graves' orbitopathy (GO) or risk factors for the development of orbitopathy.
  - We recommend clinicians advise patients with Graves' disease (GD) to stop smoking and refer them to a structured smoking cessation program. As both firsthand and secondhand smoking increase GO risk, patients exposed to secondhand smoke should be identified and advised of its negative impact.
  - In nonsmoking patients with GD without apparent GO, radioactive iodine (RAI) therapy (without concurrent steroids), antithyroid drugs (ATDs), or thyroidectomy should be considered equally acceptable therapeutic options in regard to risk of GO.
  - In patients with Graves' hyperthyroidism who have mild active ophthalmopathy and no risk factors for deterioration of their eye disease, RAI therapy, ATDs, and thyroidectomy should be considered equally acceptable therapeutic options.
  - In GD patients with mild GO who are treated with RAI we recommend steroid coverage if there are concomitant risk factors for GO deterioration.[7]

American Thyroid Association/European Thyroid Association – Joint Consensus Statement

A joint consensus statement was issued by the American Thyroid Association and the European Thyroid Association in 2022. It includes the following recommendations:

Regarding diagnosis and assessment of thyroid eye disease (TED):

- Endocrinologists managing patients with Graves' disease should identify referral pathways that ensure patient access to TED specialty care.
- Ophthalmologists are the key to management of TED and should always be involved in the care of patients with moderate-to-severe and sight-threatening TED.

Regarding the management of moderate-to-severe thyroid eye disease (TED):

- Intravenous glucocorticoids (IVGC)
  - IVGC therapy is a preferred treatment for active moderate-to-severe TED when disease activity is the prominent feature (in the absence of either significant proptosis* or diplopia).

- Standard dosing consists of IV methylprednisolone (IVMP) at cumulative doses of 4.5 grams over approximately 3 months (0.5 g weekly for 6 weeks, followed by 0.25 g weekly for an additional 6 weeks).
- Poor response to IVMP at 6 weeks should prompt consideration for treatment withdrawal and evaluation of other therapies. Clinicians should be alerted for worsening diplopia or onset of dysthyroid optic neuropathy (DON) that have occurred even while on IVMP therapy.
- A cumulative dose of IVMP > 8 g should be avoided.

- Therapies for patients with moderate-to severe TED unresponsive or intolerance to IVGC
  - Rituximab (RTX) and tocilizumab (TCZ) may be considered for TED inactivation in glucocorticoid-resistant patients with active moderate-to-severe TED.
    - Teprotumumab (Tepezza®) has not been evaluated in this setting.
    - RTX therapy is acceptable in patients with moderate-to-severe TED and prominent soft tissue involvement.
    - TCZ is an acceptable treatment for TED inactivation in glucocorticoid-resistant patients with active moderate-to-severe disease.
  - Radiotherapy (RT) is a preferred treatment in patients with active moderate-to-severe TED whose principle feature is progressive diplopia.
    - RT should be used cautiously in diabetic patients to avoid possible retinopathy. It is relatively contraindicated for those younger than 35 years of age to avoid a theoretical lifetime risk of tumors developing in the radiation field.
  - Teprotumumab (Tepezza®) is a preferred therapy, if available, in patients with active moderate-to-severe TED with significant proptosis* and/or diplopia.

- Surgical intervention for inactive moderate-to-severe TED
  - Surgery for moderate-to-severe TED should be performed by an orbital surgeon experienced with these procedures and their complications.
  - Rehabilitative surgery for moderate-to-severe TED should only be performed when the disease is inactive and euthyroidism has been achieved and maintained.
  - The specific surgical approach should be tailored to the indication (DON, proptosis), type of orbitopathy (muscle or fat predominant congestive disease), and desired reduction in proptosis.
  - In patients with diplopia and inactive TED, binocular single vision in the primary position of gaze may be restored with strabismus surgery or permanent prisms ground into the spectacle lenses.[8]

* For therapies selected to reduce proptosis, the task force elected to use the term "significant proptosis" rather than a numerical threshold. In keeping with the definition of moderate-to-severe TED, a degree of proptosis $\geq$ 3mm above the upper limit for race and sex would be regarded as "significant proptosis."

Criteria

Prior authorization is required.

Tepezza® is considered medically necessary when **ALL** of the following are met:

1. Diagnosis of thyroid eye disease (TED); **AND**
2. Member has active disease, with a clinical activity score (CAS) ≥ 4 in the more severely affected eye; **AND**
3. Member has symptomatic moderate-to-severe disease, as defined by **AT LEAST ONE** of the following:
    a. Lid retraction ≥ 2 mm; and/or
    b. Moderate or severe soft tissue involvement**;** and/or
    c. Proptosis ≥ 3 mm above normal for race and gender; and/or
    d. Intermittent or constant diplopia; **AND**
4. Member is 18 years of age or older; **AND**
5. Thyroid function tests [free thyroxine (FT4) and free triiodothyronine (FT3)] within the past 30 days meet **ONE** of the following:
    a. Results are within the laboratory-defined reference range (i.e., member is euthyroid); **OR**
    b. Results document mild hypo- or hyperthyroidism (i.e., FT4 and FT3 levels are less than 50 percent above or below the laboratory defined reference range) and member is undergoing treatment to achieve and maintain a euthyroid state; **AND**
6. Member has failed a clinical trial of corticosteroids unless clinically significant adverse effects are experienced or therapy is contraindicated; **AND**
7. Member does not have **ANY** of the following:
    a. Previous surgical intervention for TED; **AND**
    b. Require surgical ophthalmological intervention; **AND**
    c. Hyperglycemia (note: Members with hyperglycemia or pre-existing diabetes should be under appropriate glycemic control before and while receiving Tepezza®); **AND**
8. Prescribed by, or in consultation with an ophthalmologist; **AND**
9. Dose prescribed does not exceed 10 mg/kg for the first infusion, followed by 20 mg/kg every 3 weeks for an additional 7 infusions; **AND**
10. Member has received less than 8 infusions of Tepezza® in their lifetime.

Tepezza® is considered medically necessary for continuation of therapy when **ALL** of the following are met:

1. Member is currently receiving medication through the Iowa Medicaid benefit or has previously met initial approval criteria; **AND**
2. Prescribed by, or in consultation with, an ophthalmologist; **AND**
3. Member has received less than 8 infusions of Tepezza® (authorization may only be granted up to a total of 8 infusions per lifetime).

Approval Duration and Quantity Limits

Initial Authorization	Subsequent Authorization(s)
Approval Duration: 6 months	Only applicable if member has not received a lifetime total of 8 infusions **and** meets criteria for continued therapy. May authorize for 20 mg/kg IV every 3 weeks until a total of 8 lifetime infusions is met.**
Quantity Limits: 8 total infusions (one 10 mg/kg IV dose, followed by 20 mg/kg IV once every 3 weeks for 7 additional infusions)	

** Ongoing clinical trials to reassess retreatment have limited results available so far. Data not sufficient to justify approving retreatment at this time.

Coding and Product Information

The following list(s) of codes and product information are provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS code is inappropriate.

HCPCS	Description
J3241	Injection, teprotumumab-trbw, 10 mg

ICD-10	Description
E05.00	Thyrotoxicosis with diffuse goiter without thyrotoxic crisis or storm
E05.01	Thyrotoxicosis with diffuse goiter with thyrotoxic crisis or storm
E05.55	Thyroid eye disease (TED); Graves' orbitopathy
H05.89	Other disorders of orbit

NDC	Labeler	Dosage	Pkg Size	Pkg Qty	Units/Pkg
75987-0130-15	Horizon Therapeutics USA, Inc.	10 mg	1	1	50

Compliance

1. Should conflict exist between this policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual or as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. Medical necessity guidelines are developed for selected physician-administered medications found to be safe and proven to be effective in a limited, defined population or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

References

[1] Tepezza prescribing information (12/2022). Horizon Therapeutics USA, Inc.: Deerfield, IL. Available online at www.tepezzahcp.com. Accessed February 17, 2023.

[2] Davies TF, Burch HB. Clinical features and diagnosis of thyroid eye disease. Mulder JE, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed February 17, 2023.

[3] Davies TF, Burch HB. Treatment of thyroid eye disease. Mulder JE, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed February 17, 2023.

[4] Treatment of Graves' Orbitopathy (Thyroid Eye Disease) to Reduce Proptosis With Teprotumumab Infusions in a Randomized, Placebo-Controlled, Clinical Study (OPTIC). ClinicalTrials.gov identifier: NCT03298867. Updated February 7, 2022. clinicaltrials.gov/ct2/show/NCT03298867. Accessed February 17, 2023.

[5] Reference above citation: Davies TF: Clinical features and diagnosis of thyroid eye disease.

[6] Burch HB, Perros P, 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. Epub 2022 Dec 8. PMID: 36480280.

[8] Reference above citation: Burch HB: Management of Thyroid Eye Disease: A Consensus Statement by the American Thyroid Association and the European Thyroid Association.

Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

Criteria Change History

Change Date	Changed By	Description of Change	Version

Signature

Change Date	Changed By	Description of Change	Version
04/21/2023	CAC	Annual review. Updated references. Added criterion "Members with hyperglycemia or pre-existing diabetes should be under appropriate glycemic control before and while receiving Tepezza®" in response to recent warning and precaution added to Tepezza® prescribing information regarding the incidence of hyperglycemia in treated patients. Added dosing information into criteria. Added recommendations from 2022 Joint Consensus Statement (ATA and ETA). Added statement regarding retreatment to Approval Duration/Quantity Limits: "Ongoing clinical trials to reassess retreatment have limited results available so far. Data not sufficient to justify approving retreatment at this time."	3

Signature
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Change Date	Changed By	Description of Change	Version
04/15/2022	CAC	Annual review.	2

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Change Date	Changed By	Description of Change	Version
04/16/2021	CAC	Criteria implementation.	1

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CAC = Medicaid Clinical Advisory Committee