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Policy Number: 043.001

Title: Coverage Determination Policy for Tepezza (Teprotumumab-trbw)

Regions: ☒ **Texas** ☐ **Florida** ☐ **Indiana** ☐ **New Jersey** ☒ **New Mexico**

Impacted Areas:

- ☒ Network Management/Provider Services
- ☐ Member services
- ☐ Quality Management
- ☐ Credentialing
- ☐ IT
- ☐ Administration
- ☐ Compliance/delegation
- ☒ Utilization Management
- ☐ Case management
- ☐ Disease management
- ☒ Claims
- ☐ Human resources
- ☐ Finance
- ☒ Pharmacy
- ☐ ALL

Available LCD/NCD/LCA: None

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Coverage Policy Number: 043.001

Line of Business: Medicare Part B

Policy Type: Prior Authorization

Coverage Determination:

(Initial/New Requests)

Tepezza is proven for the treatment of **Thyroid Eye Disease**. Tepezza is medically necessary when **ALL** of the following criteria are met:

A. Diagnosis of Graves' disease associated with active thyroid eye disease (TED) with a Clinical Activity Score (CAS) ≥ 4 in the most severely affected eye

B. Presence of moderately to severely active TED, associated with at least **ONE** of the following:

   i. Lid retraction ≥ 2 mm

   ii. Moderate or severe soft tissue involvement

   iii. Exophthalmos ≥ 3 mm above normal for race and gender

   iv. Diplopia

C. History of intolerance, failure, or contraindication to intravenous glucocorticoids (e.g., methylprednisolone)

D. **ONE** of the following:

   i. Patient is euthyroid [defined as free triiodothyronine (T3) and thyroxine (T4) levels within the normal limits

   ii. Presence of mild hypo- or hyperthyroidism [defined as free T3 and T4 levels less than 50% above or below the normal limits] and patient is undergoing treatment to correct the mild hypo- or hyperthyroidism to maintain a euthyroid state

E. Tepezza will not be used in combination with another biologic immunomodulator [e.g., rituximab (Rituxan, Ruxience, Truxima, Riabni), Actemra (tocilizumab), Kevzara (sarilumab)

F. Dosing is in accordance with the United States Food and Drug Administration approved labeling

G. Authorization will be issued for a maximum of 8 doses per lifetime.

(Renewal/Continuation of Therapy Requests)

Tepezza is unproven and not medically necessary for continued use beyond 8 infusions.
The clinical benefit of Tepezza has not been demonstrated beyond 8 infusions in phase 3 clinical trials.

FDA Approved Dose and Indication

FDA Approved Indication	FDA Approved Dose
Treatment of Thyroid Eye Disease	• **Initial dose:** 10 mg/kg IV infusion • **Maintenance dose(s):** 20mg/kg IV infusion every 3 weeks for 7 additional doses (8 total doses including initial dose)

General Background

Thyroid eye disease (TED) also known as thyroid associated orbitopathy (TAO) and Grave's orbitopathy (GO). This disease is a progressive, vision-threatening autoimmune inflammatory condition affecting the orbit and ocular adnexa of the eye. TED is most commonly related with Grave's disease; however, it can also develop in patients with other thyroid diseases (e.g., Hashimoto's thyroiditis). In Graves' disease, the main autoantigen is the thyroid-stimulating hormone (TSH) receptor (TSHR), which is expressed primarily in the thyroid but is also expressed in adipocytes, fibroblasts, and a variety of additional sites and appears to be closely aligned with the insulin-like growth factor 1 (IGF-1) receptor. TSHR antibodies and activated T cells also play an important role in the pathogenesis of Graves' orbitopathy by activating retroocular fibroblast and adipocyte TSHR and IGF-1 receptors and initiating a retro-orbital inflammatory environment. TED is associated with distinct clinical features, including upper eyelid retraction, restrictive strabismus, and proptosis. TED can threaten vision through compressive optic neuropathy or corneal decompensation from exposure keratopathy.[4,5]

The evaluation of a patient with TED includes laboratory assessment (if not already available), examination of the eyes, and assessment of disease activity and severity. Thyroid function tests will have already been obtained in most patients. If not available, recommendation is to measure: TSH, Free T4, Total T3 and TSH receptor (TSHR) antibodies. Disease activity is commonly assessed using a seven-point clinical activity score (CAS):

Elements	Each visit	Comparison with 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

Patients with a score of 3 or more are classified as having active disease and are therefore more likely to respond to immunomodulatory therapy, such as corticosteroids. 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 (≥2 mm), Decreased eye movements (≥5 degrees) and Decreased visual acuity (≥1 line on the Snellen eye chart). Severity is determined by a different assessment:[6]

Grade	Lid retraction	Soft tissues	Proptosis	Diplopia	Corneal exposure	Optic nerve status
Mild	<2 mm	Mild involvement	<3 mm	Transient or absent	Absent	Normal
Moderate	≥2 mm	Moderate involvement	≥3 mm	Inconstant	Mild	Normal
Severe	≥2 mm	Severe involvement	≥3 mm	Constant	Mild	Normal
Sight threatening	-	-	-	-	Severe	Compression

The European Group on Graves' Orbitopathy (EUGOGO) defines mild TED disease as the presence of mild lid retraction (< 2mm), mild exophthalmos (< 3 mm), mild soft tissue involvement, and corneal exposure that is responsive to topical lubrication. Moderate to severe TAO is defined as lid retraction > 2 mm, exophthalmos > 3 mm, moderate to severe soft tissue involvement, and presence of diplopia. Sight-threatening TAO is defined as presence of direct optic neuropathy or corneal breakdown.[4]

Mechanism of Action

Teprotumumab is an insulin-like growth factor-1 receptor inhibitor (IGF-1R), a fully human IgG1 monoclonal antibody. Teprotumumab binds to IGF-1R and blocks its activation and signaling. The mechanism of action of teprotumumab in patients with thyroid eye disease has not been fully characterized but is theorized to decrease inflammation and tissue growth, thus reducing the signs and symptoms of thyroid eye disease.

Pharmacology

Tepezza is a fully human immunoglobulin G1 monoclonal antibody. The agent is produced in Chinese hamster ovary cells. Tepezza targets and binds to IGF-1R, a tyrosine kinase cell surface receptor that is overexpressed in the orbital fibroblasts of patients with thyroid eye disease. This inhibits IGF-1R autophosphorylation, decreases cell surface expression of IGF-1R, and prevents downstream signaling.

Warnings

Infusion reactions: If an infusion reaction occurs, interrupt or slow the rate of infusion and use appropriate medical management

Exacerbation of Preexisting Inflammatory Bowel Disease (IBD): Monitor patients with preexisting IBD for flare of disease; discontinue TEPEZZA if IBD worsens

Hyperglycemia: Monitor glucose levels in all patients; treat hyperglycemia with glycemic control medications

Clinical Evidence

The efficacy and safety of teprotumumab was evaluated in 2 randomized, double-masked, placebo-controlled trials in 171 patients diagnosed with thyroid eye disease. Patients were randomized to either receive teprotumumab (n=84) or placebo (n=87) in a 1:1 ratio. Patients receiving teprotumumab were infused 10mg/kg for the first infusion and 20mg/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 level less than 50% above or below normal limits. Proptosis ranged from 16 to 33mm and 125 patients (73%) had diplopia at baseline. The primary outcome was 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 Thyroid Eye Disease including pain, gaze evoked orbital pain, swelling, eyelid erythema, redness, chemosis, inflammation, clinical activity score and assessments of functional vision and patient appearance.[1]

In study 1 (NCT01868997), in the intention-to-treat population, 29 of 42 patients who received teprotumumab (69%), as compared with 9 of 45 patients who received placebo (20%), had a response at week 24 (P<0.001). Therapeutic effects were rapid; at week 6, a total of 18 of 42 patients in the teprotumumab group (43%) and 2 of 45 patients in the placebo group (4%) had a response (P<0.001). Differences between the groups increased at subsequent time points. The only drug-related adverse event was hyperglycemia in patients with diabetes; this event was controlled by adjusting medication for diabetes.[3]

In study 2 (NCT03298867), at week 24, the percentage of patients (n=83) with a proptosis response was higher with teprotumumab than with placebo (83% [34 patients] vs. 10% [4 patients], P<0.001), with a number needed to treat of 1.36. All secondary outcomes were significantly better with teprotumumab than with placebo, including overall response (78% of patients [32] vs. 7% [3]), Clinical Activity Score of 0 or 1 (59% [24] vs. 21% [9]), the mean change in proptosis (−2.82 mm vs. −0.54 mm), diplopia response (68% [19 of 28] vs. 29% [8 of 28]), and the mean change in GO-QOL overall score (13.79 points vs. 4.43 points) (P≤0.001 for all). Reductions in extraocular muscle, orbital fat volume, or both were observed in 6 patients in the teprotumumab group who underwent orbital imaging. Most adverse events were mild or moderate in severity; two serious events occurred in the teprotumumab group, of which one (an infusion reaction) led to treatment discontinuation.[2]

Among patients with active thyroid eye disease, teprotumumab resulted in better outcomes with respect to proptosis, Clinical Activity Score, diplopia, and quality of life than placebo; serious adverse events were uncommon.[2]

HCPCS Code

HCPCS Code	Description
J3241	Tepezza (Teprotumumab-trbw)

Dosage Form, Strength, and Route of Administration
500 mg lyophilized powder in a single-dose vial for reconstitution, administered intravenously (IV)

Acronyms

TED = Thyroid Eye Disease

TAO = Thyroid Associated Orbitopathy

GO = Grave's Orbitopathy

TSH = Thyroid Stimulating Hormone

TSHR = Thyroid Stimulating Hormone Receptor

IGF-1 = Insulin-like Growth Factor 1

IGF-1R = Insulin-like Growth factor receptor

CAS = Clinical Activity Score

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