PART B DRUG MEDICAL/PHARMACY	ASPIRE HEALTH	Effective Date May 1, 2024	
	TEPEZZA (TEPROTUMUMAB-TRBW)	Policy # Tepezza (teprotumumab-trbw)	
		Review Date 02/27/2024	Applicable to: ☑ Medicare Advantage ☐ Commercial ☐ Elevance Health HMO ☐ Blue Shield Trio
	Approver's Name & Title QI & UM Drug Subcommittee		

Aspire Health Plan applies medical drug clinical criteria as a reference for medical policy information only. Federal and state laws or requirements, contract language, and Plan benefit may take precedence over the application of these clinical criteria. Please consult the applicable certificate or contract for benefit details. This policy is subject to revision at the discretion of the Plan and is therefore subject to change. Refer to the disclaimer section below for more information.

POLICY

This policy addresses the coverage of Tepezza (teprotumumab-trbw) for the treatment of thyroid eye disease.

APPLICABLE HCPCS

J3241 Injection, teprotumumab-trbw, 10 mg

Available as:

- Single-dose vial: 500 mg

CLINICAL CRITERIA

I. INITIAL CRITERIA

Tepezza (teprotumumab-trbw) may be authorized when **ALL** of the following have been met with *documentation.

*Medical record documentation by the Prescriber / administering physician should substantiate the medical necessity for the use of Tepezza (teprotumumab-trbw) by clearly indicating the relevant clinical signs and symptoms related to the medical condition for which this drug is indicated. The documentation must also include all prior treatment regimens and the member's response to that therapy.

1. Prescribed by, or in conjunction with, an endocrinologist, ophthalmologist, or ocular surgeon specializing in the treatment of thyroid eye disease; **AND**

2. Diagnosis of Graves' disease with associated TED (i.e., Graves' ophthalmopathy, Graves' orbitopathy); **AND**

3. Documentation of active disease, defined as a Clinical Activity Score (CAS) of at least four (the Graves' orbitopathy CAS elements below are each assigned a score of 1):
   - Pain
     - Pain/pressure in a periorbital or retroorbital distribution
     - Pain on attempted up, side or down gaze during the last 4 weeks
   - Redness
     - Redness of eyelids
     - Redness of conjunctiva
   - Swelling
     - Swelling of eyelids
     - Chemosis
     - Inflammation of caruncle or plica
     - Increase in measured proptosis ≥ 2mm assessed over 3 months
   - Impaired function
     - Decrease in eye movement ≥ 8° assessed over 3 months
     - Decrease in visual acuity (2 Snellen chart lines) assessed over 3 months

AND

4. Documentation of at least ONE of the following (labs must be within the last 30 days):

   a. Member is euthyroid [defined as free thyroxine (FT4) and total triiodothyronine (T3) or free T3 (FT3) levels within the laboratory defined reference range]; **or**

   b. Member has mild hypo- or hyperthyroidism [free thyroxine (FT4) and total triiodothyronine (T3) or free T3 (FT3) levels less than 50% above or below the laboratory defined reference range and is undergoing treatment to correct the mild hypo- or hyperthyroidism to maintain a euthyroid state.

AND

5. Documentation of intolerance, contraindication to or failed treatment with oral or intravenous glucocorticoid therapy (e.g., prednisone, methylprednisolone) for at least 4 weeks; **AND**

6. Tepezza will not be used in combination with another biologic immunomodulator [e.g., rituximab (Rituxan®, Ruxience®, Truxima®, Riabni™), Actemra® (tocilizumab), Kevzara® (sarilumab)]; **AND**

7. Member has not received ≥ 8 Tepezza infusions (including the initial 10 mg/kg first infusion).

II. REAUTHORIZATION / CONTINUATION OF THERAPY CRITERIA

Tepezza will not be authorized for continuation of therapy. The clinical benefit of Tepezza has not been demonstrated beyond 8 infusions in phase 3 clinical trials. The continued use of Tepezza beyond 8 infusions in the patient's lifetime is unproven and not medically necessary.

STEP THERAPY

Step therapy not applicable.

DOSAGE AND AUTHORIZATION TIMEFRAMES

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.

1. Recommended Dosage: Treatment includes a total of 8 IV infusions, with an initial infusion dose of 10 mg/kg and then 20 mg/kg every 3 weeks for 7 additional infusions.

2. Quantity: Maximum of 8 doses per lifetime

3. Authorization Period: May authorized for 6 months for a total of up to eight infusions

4. Reauthorization: Not applicable. Continuation of Tepezza beyond eight infusions is considered experimental/investigational and not medically necessary.

DRUG INFORMATION

PHARMACOLOGIC CATEGORY: Insulin-Like Growth Factor-1 Receptor (IGF-1R) Antagonist; Monoclonal Antibody

PRODUCTS: Teprotumumab

ROUTE OF ADMINISTRATION: Intravenous Infusion

FDA-APPROVED INDICATIONS:

Thyroid eye disease (TED): Treatment of thyroid eye disease regardless of thyroid eye disease activity or duration.

COMPENDIAL APPROVED (OFF-LABELED) USES: None

CONTRAINDICATIONS: There are no contraindications listed in the manufacturer's labeling.

OTHER CONSIDERATIONS:

In clinical trials, treatment with teprotumumab-trbw resulted in decreased proptosis and diplopia. Common adverse reactions include muscle spasm, nausea, alopecia, diarrhea, fatigue, hyperglycemia, hearing impairment, dry skin, dysgeusia, and headache.

Monitoring Parameters:

- Monitor patients for elevated blood glucose and symptoms of hyperglycemia while on treatment with teprotumumab-trbw, especially patients with preexisting diabetes.
- Preexisting inflammatory bowel disease (IBD) may be exacerbated with teprotumumab-trbw therapy. Patients with IBD should be monitored for disease flares, and if IBD exacerbation is suspected, discontinuation of teprotumumab-trbw therapy may be needed.

CLINICAL SUMMARY / APPENDIX

Tepezza (teprotumumab-trbw) is an insulin-like growth factor-1 receptor inhibitor indicated for the treatment of Thyroid Eye Disease (TED), also known as thyroid associated orbitopathy (TAO) and Grave's orbitopathy (GO). This disease is an autoimmune inflammatory condition affecting the orbit and ocular adnexa of the eye. 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.

The mechanism of action of teprotumumab-trbw has not been fully characterized, but may be due to binding to the IGF-1 receptor and blocking of its activation and signaling. Tepezza was approved based on evidence from two clinical trials (Trial 1/ NCT01868997 and Trial 2/ NCT03298867) consisting of a total of 170 adults with Graves' disease and active moderate to severe TED were randomized to receive Tepezza or placebo every 3 weeks for 8 doses. Of the patients who were administered Tepezza, 71% in Study 1 and 83% in Study 2 demonstrated a greater than 2 millimeter reduction in proptosis (eye protrusion) as compared to 20% and 10% of subjects who received placebo, respectively.

The European Group on Graves' Orbitopathy (EUGOGO) defines mild TED disease as the presence of mild lid retraction (< 2 mm), 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.

EUGOGO (2021) clinical practice guidelines for the medical management of Graves' orbitopathy supports the use of systemic corticosteroids in TED:

- A combination of IV methylprednisolone and mycophenolate sodium is recommended as first-line treatment.
- If response to primary treatment is poor and Graves' ophthalmopathy (GO) is still moderate-to-severe and active, teprotumumab is considered a second-line option as longer-term data, availability, affordability, costs, and need for subsequent rehabilitative surgery are pending.

Clinical Activity Score (CAS)

Graves' orbitopathy is considered active in patients with a CAS of ≥ 3 (Ross et al., 2016 American Thyroid Association Guidelines). The Phase 3 clinical trial evaluating teprotumumab enrolled patients with a CAS of ≥ 4 (Smith et al. 2017).

REFERENCES

Government Agency

Centers for Medicare and Medicaid Services (CMS). Medicare coverage database (search: Tepezza**;** teprotumumab-Trbw). Available from CMS. No National Coverage Determination (NCD), Local Coverage Determinations (LCDs) and Local Coverage Articles (LCAs) or identified.

Prescribing Information

Tepezza (teprotumumab) [prescribing information]. Deerfield, IL: Horizon Therapeutics USA Inc; July 2023.

Peer Reviewed Literature, Guidelines

1. Bartalena L, Kahaly GJ, 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: 27 August 2021; 185 (4): G43-G67.
2. Douglas RS, Kahaly GJ, Patel A, et al. Teprotumumab for the treatment of active thyroid eye disease. *N Engl J Med*. 2020;382(4):341-352. [PubMed 31971679]
3. 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.
4. Smith TJ, Kahaly GJ, Ezra DG, et al. Teprotumumab for thyroid-associated ophthalmopathy. *N Engl J Med*. 2017;376(18):1748-1761.[PubMed 28467880]10.1056/NEJMoa1614949.

IMPORTANT REMINDER

This Medicare Part B Step Therapy Medical Necessity Guideline is provided for informational purposes only and neither constitutes nor replaces professional medical advice. Physicians, hospitals, and other providers are expected to administer or use drugs/biologicals in the most effective and clinically appropriate manner. Treating physicians and other health care providers are solely responsible for all medical care decisions. In accordance with the member's Evidence of Coverage (EOC), every benefit plan has its own coverage

provisions, limitations, and exclusions. In the event of a conflict between this policy and the member's EOC, the member's EOC provisions will take precedence.

Aspire Health Plan (AHP) adheres to Medicare guidelines, including National Coverage Determination (NCD), Local Coverage Determinations (LCDs), Local Coverage Articles (LCAs), and other relevant Medicare manuals established by CMS. Compliance with these guidelines is required when applicable. Refer to the CMS website at http://www.cms.hhs.gov. For the most up-to-date Medicare policies and coverage, please search the Medicare Coverage Database. All LCDS are the same for each state within a Jurisdiction. Medicare Part B Administrative Contractor (MAC) for CA [Jurisdiction E (1)]: Active LCDs - JE Part B – Noridian (noridianmedicare.com). In the event of a discrepancy between this policy and the Medicare NCD or LCD, the Medicare NCD/LCD will govern.

This policy is utilized by AHP to determine coverage in the absence of applicable CMS Medicare guidelines. Please refer to the links provided in the References section below to access the Medicare source materials that were used for developing this resource document. This document does not serve as a substitute for the official Medicare source materials that provide detailed information on Medicare coverage requirements. In the event of a conflict between this document and Medicare source materials, the Medicare source materials will take precedence.

The inclusion of a code in this policy does not imply that the health service it describes is covered or not covered. Benefit coverage for health services is determined by the member-specific plan document and applicable laws that may mandate coverage for a particular service. Inclusion of a code does not imply or guarantee reimbursement or payment of a claim. Other Policies and Standards may also apply. Providers are expected to retain or have access to the necessary documentation when requested in order to support coverage.

The use of physician samples or manufacturer discounts does not guarantee later coverage under the provisions of the medical certificate and/or pharmacy benefit. All criteria must be met in order to obtain coverage of the listed drug product

POLICY HISTORY

Version	Committee Approval Date	Revision Author/Title	Summary of Changes
1	02/27/2024		New Policy