Tepezza™ (teprotumumab-trbw) is considered medically necessary when ALL of the following criteria are met:

- Individual is 18 years of age or older
- For the treatment of thyroid eye disease
- Documentation of active thyroid eye disease confirmed by a clinical active score (CAS) of 3 or greater
- Individual has moderate to severe thyroid eye disease confirmed by at least ONE of the following:
  - Lid retraction of 2 or more millimeters
  - Significant soft tissue involvement
  - Proptosis of 3 millimeters or more
  - Presentation of diplopia
  - Corneal exposure
- Prescribed by or in consultation with an ophthalmologist, endocrinologist, or a physician who specializes in thyroid eye disease

Authorization is for a single course of therapy (8 infusions).
When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Tepezza (teprotumumab-trbw) is considered experimental, investigational or unproven for ANY other use.

Note: Receipt of sample product does not satisfy any criteria requirements for coverage.

**FDA Approved Indications**

**FDA Approved Indication**
Tepezza is an insulin-like growth factor-1 receptor inhibitor indicated for the treatment of Thyroid Eye Disease.

**Recommended Dosing**

**FDA Recommended Dosing**
The recommended dose of Tepezza is an intravenous infusion of 10 mg/kg for the initial dose followed by an intravenous infusion of 20 mg/kg every three weeks for 7 additional infusions.

**General Background**

**Disease Overview**
Thyroid eye disease is a progressive, vision-threatening autoimmune inflammatory disease of the eye and orbital tissues with predominant features of fibrosis and adipogenesis. It is also recognized in literature as Graves’ ophthalmopathy, Graves’ orbitopathy, thyroid-associated ophthalmopathy, and thyroid orbitopathy. Thyroid eye disease is most commonly related with Graves’ disease; however, it can also develop in patients with other thyroid diseases (e.g., Hashimoto’s thyroiditis). The incidence is 1.9 cases per 10,000 population per year. Orbital fibroblasts appear responsible for soft tissue enlargement by expressing potential pathogenic autoantigens, such as thyrotropin receptor and IGF-1R. Activation of orbital fibroblasts leads to increased hyaluronic acid production, proinflammatory cytokine synthesis, and enhanced differentiation into either myofibroblasts or adipocytes. These processes result in inflammation, enlargement of extraocular muscles and expansion of orbital tissue and fat, which in turn cause forward displacement of the eye, resulting in proptosis and inflammation. Other symptoms can include increased lacrimation, local irritation, eyelid retraction, and diplopia. The disease can be categorized as mild, moderate to severe, or sight-threatening. Various quantitative assessments are made (e.g., evaluation of lid aperture width, proptosis measurement, diplopia score, degrees of abduction in eye muscle movement, examination of the cornea for evidence of exposure keratitis or ulceration, and assessment of optic nerve function). (Bartley, 1996; Douglas, 2020; Horizon, 2019; Shan, 2014; Stan, 2012)

**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. Based on the mechanism of action, Tepezza is theorized to decrease inflammation and tissue growth, thus reducing the signs and symptoms of thyroid eye disease. (Douglas, 2019; Wang, 2014)

**Professional Societies/Organizations**
European Thyroid Association and the European Group on Graves’ Orbitopathy (EUGOGO) guidelines for the management of thyroid eye disease state treatment depends on assessment of the activity and severity and the impact on the quality of life of the patient. Measures for smoking cessation and euthyroidism are strongly recommended for all patients to slow the progression of thyroid eye disease. Along with watchful monitoring, local measures such as artificial tears, ointments, sunglasses and selenium supplementation, are used to manage mild symptoms of thyroid eye disease. High-dose systemic glucocorticoids (preferably IV administration)
are first-line treatment for active, moderate to severe thyroid eye disease. The optimal cumulative dose of IV methylprednisolone (over 12 weeks) appears to be 4.5 to 5 g, but higher doses (8 g) can be used for more severe forms. If there is a partial, inadequate response, or reoccurrence after use of IV glucocorticoids alternative therapies are endorsed. Second-line treatments options include a second course of IV glucocorticoids, orbital radiotherapy plus oral glucocorticoids, cyclosporine with oral glucocorticoids, or rituximab. Evidence of efficacy for alternative treatments are exploratory, limited, and sometimes conflicting. During inactive, moderate to severe thyroid eye disease, orbital surgeries (decompression surgery, strabismus surgery, lid lengthening and cosmetic periorbital surgeries) can be done depending on the degree of disfigurement and/or functional impairment that persists. Tepezza is not addressed in the guidelines. (Bartalena, 2014)

The American Board of Internal Medicine’s (ABIM) Foundation Choosing Wisely® Initiative:
No recommendations are available for Thyroid Eye Disease.

Centers for Medicare & Medicaid Services - National Coverage Determinations (NCDs)
There are no CMS National Coverage Determinations for Tepezza.

Other Covered Uses
AHFS Drug Information 2020 Edition does not support any off-label uses of Tepezza.

Experimental, Investigational, Unproven Uses
Compendia and other published clinical studies do not currently support any uses other than the FDA indication. Criteria will be updated as new published data are available.

Coding/Billing Information

Note: 1) This list of codes may not be all-inclusive.
    2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C9399</td>
<td>Unclassified drugs or biologicals</td>
</tr>
<tr>
<td>J3490</td>
<td>Unclassified drugs</td>
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References