BlueCross BlueShield of North Carolina

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Corporate Medical Policy

Teprotumumab-trbw (Tepezza™)

File Name:	teprotumumab_tepezza
Origination:	4/2020
Last CAP Review:	6/2020
Next CAP Review:	6/2021
Last Review:	6/2020

Description of Procedure or Service

Teprotumumab-trbw (Tepezza) is an insulin-like growth factor-1 receptor inhibitor that is indicated for the treatment of thyroid eye disease (TED).

TED, also known as thyroid-associated orbitopathy or Graves' ophthalmopathy, is a rare and debilitating inflammatory eye disease that develops in the orbit in relation to autoimmune thyroid disorders, with the majority of cases occurring in patients with current or past Graves' disease. The clinical features of TED include periorbital edema, eyelid retraction, proptosis (protrusion of the eye from the orbital rim), strabismus, exposure keratopathy, and compressive neuropathy. The course of disease transitions from an active inflammatory progressive period for 1-3 years to a stable fibrotic period, and more severe disease can lead to potential vision loss. In patients with TED, treating the underlying hyperthyroidism should be the mainstay of treatment with a goal of restoring euthyroidism. However, patients with moderate-to-severe disease typically require immunomodulatory therapy with glucocorticoids (oral or intravenous) being the standard treatment, and those at risk for sight loss usually require orbital decompression surgical treatment.

Teprotumumab-trbw (Tepezza) is a humanized monoclonal antibody approved by the U.S. Food and Drug Administration (FDA) in January 2020 for the treatment of TED. Its mechanism of action in patients with TED has not been fully characterized; however, teprotumumab-trbw binds to insulin-like growth factor-1 receptor (IGF-1R) and blocks its activation and signaling.

******Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

Policy

BCBSNC will provide coverage for teprotumumab-trbw (Tepezza) when it is determined to be medically necessary because the medical criteria and guidelines noted below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

Teprotumumab-trbw (Tepezza™)

When Teprotumumab-trbw (Tepezza) is covered

Teprotumumab-trbw (Tepezza) may be considered **medically necessary** for the treatment of thyroid eye disease (TED) in adult patients (≥ 18 years of age) when the following criteria are met:

1. The patient has a diagnosis of Graves' disease; and
2. The patient has a confirmed diagnosis of active, moderate-to-severe TED related to Graves' disease (i.e., Graves' orbitopathy); and
3. The patient has a Clinical Activity Score (CAS) ≥ 4 in the more severely affected eye(s) or as scored by a comparable objective scoring system (see Policy Guidelines); and
4. The patient is euthyroid OR has mild hypo- or hyperthyroidism (see Policy Guidelines); and
5. The patient has not had prior surgical treatment or orbital irradiation for TED and is not planning on surgical treatment or orbital irradiation for TED during teprotumumab treatment; and
6. The patient has had an inadequate response with, or has a contraindication or intolerance to, corticosteroids used for the treatment of TED (e.g., prednisone, methylprednisolone, dexamethasone); and
7. Teprotumumab is prescribed by or in consultation with a specialist in the treatment of Graves' disease associated with TED (e.g., endocrinologist, ophthalmologist); and
8. The patient has not had a decrease in best corrected visual acuity due to optic neuropathy within the previous 6 months (i.e., a decrease in vision of 2 lines on the Snellen chart, new visual field defect, or color defect secondary to optic nerve involvement); and
9. The patient does not have corneal decompensation unresponsive to medical management

Length of authorization: One treatment course of 8 infusions per lifetime

When Teprotumumab-trbw (Tepezza) is not covered

Teprotumumab-trbw (Tepezza) is considered **investigational** and therefore not covered when the above criteria are not met.

Continuation of teprotumumab-trbw (Tepezza) treatment beyond eight (8) infusions is considered **investigational**.

Policy Guidelines

The recommended dose for Tepezza is 10 mg/kg administered as an intravenous infusion for the initial dose, followed by a dose of 20 mg/kg administered intravenously every three weeks for 7 additional infusions (8 infusions total).

According to the manufacturer's safety information for Tepezza, the most common adverse reactions (> 5% incidence) include muscle spasm, nausea, hair loss, diarrhea, fatigue, hyperglycemia, hearing impairment, dry skin, altered sense of taste, and headache. Other more clinically significant adverse reactions include infusion reactions, exacerbation of preexisting inflammatory bowel disease (IBD), and hyperglycemia.

The active, inflammatory phase of thyroid eye disease (TED) is best evaluated using the Clinical Activity Score (CAS), which is a 7-point scale scoring system assessing presence of the following signs/symptoms: painful feeling behind the globe over the last 4 weeks, pain with eye movement during the last 4 weeks, redness of the eyelids, redness of the conjunctiva, swelling of the eyelids, chemosis (edema of the conjunctiva), and swollen caruncle (flesh body at medial angle of the eye). CAS score can predict response to anti-inflammatory therapies. **Note: A score of 3 or greater is indicative of active thyroid-associated ophthalmopathy in patients.

TED severity can be categorized by three main gradations (mild, moderate-to-severe, and sight threatening) based on objective assessments of lid retraction, soft-tissue involvement, proptosis compared to the upper limit of normal, diplopia, presence/absence of corneal exposure, and optic nerve status. Active moderate-to-severe disease can be defined as the patient having at least one of the following: lid retraction of ≥ 2 mm, moderate or severe soft-tissue involvement, proptosis of ≥ 3 mm above normal value, and/or periodic or constant diplopia. Moderate-to-severe TED includes patients without sight-threatening disease whose eye disease has enough impact on daily life to justify the risks of immunosuppression in active disease or surgical intervention in inactive disease.

Mild hypo- or hyperthyroidism was defined in the pivotal clinical trials as free thyroxine (FT4) and free triiodothyronine (FT3) levels less than 50% above or below normal limits, with every effort made to promptly correct the mild hypo- or hyperthyroidism.

Clinical Trial Evidence

The efficacy of teprotumumab-trbw was evaluated in two randomized, double-masked, placebo-controlled clinical trials assessing 171 patients with moderate-to-severe thyroid eye disease (TED): Study 1 (NCT01868997) and Study 2 (OPTIC; NCT03298867). In both trials, patients were randomized 1:1 to receive teprotumumab (n=84) or placebo (n=87) as an intravenous infusion (10 mg/kg for the first infusion and 20 mg/kg for the remaining 7 infusions) every three weeks for a total of 8 infusions. Patients included in the trials had a clinical diagnosis of TED with presence of symptoms and were euthyroid or had thyroxine and free triiodothyronine levels less than 50% above or below normal limits. Patients included in the trials also had a Clinical Activity Score (CAS) of 4 or more on a 7-point scale (with a score of ≥3 indicating active thyroid-associated ophthalmopathy) in the more severely affected (study) eye. Patients who had prior surgical treatment for TED were excluded. At baseline, proptosis ranged from 16 to 33 mm and 73% of patients had diplopia.

The primary endpoint was proptosis response rate at week 24, defined as the percentage of patients with reduction in proptosis of 2 mm or greater from baseline in the study eye, without deterioration in proptosis in the non-study eye (≥2 mm increase). In Study 1, definition of response included a reduction of 2 points or more in the CAS (range, 0 to 7). In Study 1, 69% in the teprotumumab group demonstrated a response at week 24 compared with 20% in the placebo group ($p<0.001$), and improvement in proptosis from baseline was observed as early as week 6 in 43% of patients in the teprotumumab group versus 4% in the placebo group ($p<0.001$). In Study 2, the percentage of patients with a proptosis response was 83% in the teprotumumab group vs 10% in the placebo group ($p<0.001$) with a number needed to treat of 1.36. The median time to response with teprotumumab in Study 2 was 6.4 weeks, and the mean proptosis change from baseline was greater with teprotumumab versus placebo at all time points. Following treatment discontinuation in Study 1, 53% of patients who were proptosis responders at week 24 maintained proptosis response 51 weeks after the final teprotumumab infusion. Teprotumumab-trbw compared with placebo significantly improved responses at 24 weeks in both randomized trials of patients with moderate-to-severe ophthalmopathy.

An ongoing open-label extension study of patients enrolled in Study 2 is currently being conducted with results of the study still pending. (OPTIC-X; NCT03298867)

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: *J3241*

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

Horizon Therapeutics, Inc. Tepezza (teprotumumab-trbw) for injection, for intravenous use. Highlights of prescribing information. January 2020. Available at: https://www.hzndocs.com/TEPEZZA-Prescribing-Information.pdf. Last accessed April 2020.

U.S. Food and Drug Administration. FDA approves first treatment for thyroid eye disease. January 2020. Available at: https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-thyroid-eye-disease. Last accessed April 2020.

Smith TJ, Kahaly GJ, Ezra DG, et al. Teprotumumab for thyroid-associated ophthalmopathy. N Engl J Med 2017;376(18):1748-61.

Douglas RS, Kahaly GJ, Patel A, et al. Teprotumumab for the treatment of active thyroid eye disease. N Engl J Med 2020;382:341-52.

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(10):1343-1421.

Wang Y, Smith TJ. Current concepts in the molecular pathogenesis of thyroid-associated ophthalmopathy. Invest Ophthalmol Vis Sci 2014;55(3):1735-48.

Medical Director review 4/2020

Specialty Matched Consultant Advisory Panel review 6/2020

Policy Implementation/Update Information

4/14/20 New policy developed. Teprotumumab-trbw (Tepezza) may be considered medically necessary for the treatment of thyroid eye disease (TED) in adult patients (≥ 18 years of age) when specified medical criteria and guidelines are met. Added HCPCS codes C9399, J3490, and J3590 to Billing/Coding section. References added. Medical Director review 4/2020. (krc)

4/28/20 Under "When Covered" section, the following typographical clarification made to criterion #9: "compensation" updated to "decompensation". (krc)

6/30/20 Added HCPCS code C9061 to Billing/Coding section effective 7/1/2020. Specialty Matched Consultant Advisory Panel review 6/17/2020. No change to policy statements. (krc)

10/1/20 Added HCPCS code J3241 to Billing/Coding section effective 10/1/2020 and deleted codes C9061, C9399, J3490, J3590 termed 9/30/2020. (krc)