teprotumumab-trbw (Tepezza™)

Policy # 00708
Original Effective Date: 08/10/2020
Current Effective Date: 08/10/2020

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider teprotumumab-trbw (Tepezza™‡) for the treatment of Thyroid Eye Disease to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for teprotumumab-trbw (Tepezza) will be considered when the following criteria are met:

- Patient has a diagnosis of Thyroid Eye Disease; AND
- Patient is 18 years of age or older; AND
- Tepezza is dosed as 10 mg/kg for the first infusion, followed by 20 mg/kg every 3 weeks for 7 additional infusions (8 infusions total); AND
- Patient has NOT received a prior course of Tepezza in their lifetime; AND
- Patient's Thyroid Eye Disease is classified as moderate to severe thyroid eye disease (having at least one of the following):
    - Lid retraction of ≥ 2 mm; OR
    - Moderate or severe tissue involvement; OR
    - Proptosis of ≥ 3 mm above the normal values for race and sex; OR
    - Periodic or constant diplopia; AND

  *(Note: The above severity requirement is an additional Company requirement, based on clinical trials, for coverage eligibility and will be denied as not medically necessary** if not met)*
- Patient has a Clinical Activity Score of at least 4 (defined as the presence of at least 4 of the following 7 items), which indicates ACTIVE disease process:

- Spontaneous retrobulbar (behind the eyeball) pain
- Pain on attempted eye movements (upward, side to side, or downward gaze)
- Conjunctival redness
- Redness of the eyelids
- Chemosis (swelling of the conjunctiva)
- Swelling of the caruncle or plica
- Swelling of the eyelids; AND

*(Note: The above Clinical Activity Score requirement is an additional Company requirement, based on clinical trials, for coverage eligibility and will be denied as not medically necessary** if not met)*

- Patient is euthyroid OR patient has mild hypothyroidism or mild hyperthyroidism [e.g., free thyroxine (FT4) and free triiodothyronine (FT3) levels less than 50% above or below the normal limits]; AND
  *(Note: The above criterion is an additional Company requirement, based on clinical trials, for coverage eligibility and will be denied as not medically necessary** if not met)*
- Patient has NOT had prior surgical treatment or orbital irradiation for Thyroid Eye Disease and is NOT planning on surgical treatment or orbital irradiation for Thyroid Eye Disease during treatment with Tepezza; AND
  *(Note: The above criterion is an additional Company requirement, based on clinical trials, for coverage eligibility and will be denied as not medically necessary** if not met)*
- Patient does NOT have corneal decompensation that is unresponsive to medical management; AND
  *(Note: The above criterion is an additional Company requirement, based on clinical trials, for coverage eligibility and will be denied as not medically necessary** if not met)*
- Patient has NOT had a decrease in best corrected visual acuity due to optic neuropathy within the previous 6 months (e.g., a decrease in vision of 2 lines on the Snellen chart, new visual field defect, or color defect secondary to optic nerve involvement); AND
  *(Note: The above criterion is an additional Company requirement, based on clinical trials, for coverage eligibility and will be denied as not medically necessary** if not met)*
- Patient has tried and failed (e.g., intolerance, inadequate response, deterioration) an intravenous methylprednisolone regimen, which includes at least 4.5 grams over at least a 12 week period for the treatment of Thyroid Eye Disease, unless there is clinical evidence or patient history that suggests the use of this medication regimen will be ineffective or cause

an adverse reaction to the patient OR the patient experienced deterioration after 6 weeks of therapy with the above mentioned intravenous methylprednisolone regimen.
*(Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of teprotumumab-trbw (Tepezza) when the patient's Thyroid Eye Disease is NOT classified as moderate to severe to be **not medically necessary.****

Based on review of available data, the Company considers the use of teprotumumab-trbw (Tepezza) when the patient does NOT have a Clinical Activity Score of at least 4 to be **not medically necessary.****

Based on review of available data, the Company considers the use of teprotumumab-trbw (Tepezza) when the patient is NOT euthyroid OR when the patient does NOT have mild hypothyroidism or mild hyperthyroidism to be **not medically necessary.****

Based on review of available data, the Company considers the use of teprotumumab-trbw (Tepezza) when the patient has had prior surgical treatment or orbital irradiation for Thyroid Eye Disease OR when there is planned surgical treatment or orbital irradiation for Thyroid Eye Disease during treatment with teprotumumab-trbw (Tepezza) to be **not medically necessary.****

Based on review of available data, the Company considers the use of teprotumumab-trbw (Tepezza) when the patient has corneal decompensation that is unresponsive to medical management to be **not medically necessary.****

Based on review of available data, the Company considers the use of teprotumumab-trbw (Tepezza) when the patient has had a decrease in best corrected visual acuity due to optic neuropathy within the previous 6 months (e.g., a decrease in vision of 2 lines on the Snellen chart, new visual field defect, or color defect secondary to optic nerve involvement) to be **not medically necessary.****

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Based on review of available data, the Company considers the use of teprotumumab-trbw (Tepezza) when the patient has NOT tried and failed intravenous methylprednisolone (at least 4.5 grams over at least a 12 week period) OR if the patient has NOT experienced deterioration after 6 weeks of the above mentioned intravenous methylprednisolone regimen for the treatment of Thyroid Eye Disease to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of teprotumumab-trbw (Tepezza) for a non-FDA approved indication OR in patients younger than 18 years of age OR for a non-FDA approved dose to be **investigational.***

Based on review of available data, the Company considers the use of nine or more doses of teprotumumab-trbw (Tepezza) to be **investigational.***

Based on review of available data, the Company considers the use of more than one series of teprotumumab-trbw (Tepezza) per lifetime to be **investigational.***

Background/Overview

Tepezza is an insulin-like growth factor-1 receptor inhibitor indicated for the treatment of Thyroid Eye Disease (TED). The mechanism of action for Tepezza in this condition has not been fully characterized. Tepezza is provided as 500 mg lyophilized powder in a single dose vial for reconstitution. Initial dosing for Tepezza is 10 mg/kg for the first infusion, followed by 20 mg/kg every three weeks for 7 additional infusions. No more than 8 infusions are approved by the FDA.

TED is an autoimmune condition typically associated with Graves' disease; however it should be noted that not everyone with TED has Graves' disease. The annual incidence rate of TED is estimated to be 16 cases per 100,000 for women and 2.9 cases per 100,000 for men, however men typically experience more severe disease. TED is associated with orbital fibroblast activation and proliferation, which leads to enlargement of the extraocular muscles, cellular infiltration of interstitial tissues, and an increase in orbital fat and connective tissue. Signs and symptoms of TED

include swelling, redness, and discomfort of the lids and ocular surface, increased lacrimation, thickening, and retracting of the eyelids, bulging of the eyes, misalignment of the eyes, and diplopia. The acute inflammatory phase is typically self-limiting within 18 to 24 months. This condition can potentially threaten sight if there is compression of the optic nerve (3-5% of cases). Treatment for TED is currently only symptomatic (prior to the approval of Tepezza) and includes systemic corticosteroids in combination with orbital radiotherapy in moderate to severe cases. The 2016 European Thyroid Association/European Group on Graves' Orbitopathy Guidelines for the Management of Graves' Orbitopathy recommends methylprednisolone intravenously 4.5 gm (500 mg once weekly for 6 weeks, followed by 250 mg once weekly for the remaining 6 weeks) in most cases of moderate to severe Thyroid Eye Disease. It should be noted that Bartalena et al. showed that those who deteriorate after 6 weeks of the intravenous steroid regimen are unlikely to benefit from continuing the intravenous steroids beyond that point. Other treatment options include orbital decompression surgeries once TED is out of the active stage. Currently, Tepezza is the first and only drug approved by the FDA for the treatment of TED.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Tepezza was approved for the treatment of Thyroid Eye Disease in January of 2020.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, Blue Cross and Blue Shield Association technology assessment program (TEC) and other non-affiliated technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Tepezza was evaluated in 2 randomized, double-masked, placebo-controlled studies in 171 patients with Thyroid Eye Disease: Study 1 and Study 2. Patients were randomized to receive Tepezza or placebo in a 1:1 ratio. Patients were given intravenous infusions (10 mg/kg for first infusion and 20 mg/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 levels less than 50% above or below normal limits. Prior surgical treatment or orbital irradiation for

TED was not permitted. Other trial exclusions include subjects with corneal decompensation that is unresponsive to medical management as well as subjects that had a loss of visual acuity due to optic neuropathy. Proptosis ranged from 16 to 33 mm and 125 patients (73%) had diplopia at baseline.

A total of 84 patients were randomized to Tepezza and 87 patients were randomized to placebo. The primary outcome was the proptosis responder rate at week 24. 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 TED including pain, gaze evoked orbital pain, swelling, eyelid erythema, redness, chemosis, inflammation, clinical activity score and assessments of functional vision and patient appearance. In Study 1, the proptosis responder rate was 71% in the Tepezza group vs. 20% in the placebo group. In Study 2, the proptosis responder rate was 83% in the Tepezza group vs. 10% in the placebo group. The average change from baseline in proptosis at 24 weeks was -2.5 mm in Study 1 and -2.8 mm in Study 2. Following discontinuation of treatment in Study 1, 53% of patients (16 of 30 patients) who were proptosis responders at week 24 maintained proptosis response 51 weeks after the last Tepezza infusion. The diplopia responder rate was also higher in the Tepezza group. Sixty-seven percent of patients (12 of 18) who were diplopia responders at week 24 maintained diplopia response 51 weeks after the last Tepezza infusion.

References

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Policy History

Original Effective Date: 08/10/2020
Current Effective Date: 08/10/2020
07/02/2020 Medical Policy Committee review
07/08/2020 Medical Policy Implementation Committee approval. New policy.
09/16/2020 Coding update
Next Scheduled Review Date: 07/2021

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2019 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines is with Blue Cross and Blue Shield of Louisiana and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines. Fee schedules, relative value units,

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CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	C9399, J3490, J3590 Deleted code effective 10/1/2020: C9061 Added code effective 10/1/2020: J3241
ICD-10 Diagnosis	All related diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:

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1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.