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of the Blue Cross and Blue Shield Association

Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

Effective Date: 06/08/2023

Tepezza™ (teprotumumab-trbw)

HCPCS: J3241

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

- A. Coverage of the requested drug is provided when all the following are met:
 - a. FDA approved indication
 - b. FDA approved age
 - c. Prescribed by or in consultation with an endocrinologist or ophthalmologist
 - d. Must have treated thyroid disease defined as:
 - i. Euthyroid function with free triiodothyronine (T3) and thyroxine (T4) within the normal limits for the range of the laboratory
OR
 - ii. Thyroid function is normalizing with both T3 and T4 levels being less than 50% above or 50% below the normal limits for the range of the laboratory
 - e. Treatment with an adequate course of oral or intravenous (IV) corticosteroids (for example 30 mg/day prednisone for 4 weeks) has been ineffective, not tolerated, or is contraindicated
 - f. Physician attestation a discussion has been had with the member to stop smoking if they are a current smoker
 - g. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in BCBSM/BCN's medical utilization management drug list

- B. Quantity Limitations, Authorization Period and Renewal Criteria
 - a. Quantity Limits: Align with FDA recommended dosing
 - b. Authorization Period: 6 months
 - c. Renewal Criteria: Not applicable as no further authorization will be provided.

***Note: Coverage may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at <http://www.cms.hhs.gov/>. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

This policy and any information contained herein is the property of Blue Cross Blue Shield of Michigan and its subsidiaries, is strictly confidential, and its use is intended for the P&T committee, its members and BCBSM employees for the purpose of coverage determinations.

Background Information

- Thyroid eye disease is a complex orbital inflammatory disease, which can be sight threatening, debilitating, and disfiguring. It is caused by antibodies directed against receptors in the thyroid cells and also on the surface of the cells behind the eyes. Muscles and fatty tissues behind the eye become inflamed leading to proptosis (eye bulging), strabismus (misalignment of the eyes), and diplopia (double vision) and in some cases can lead to blindness. Risk factors for the disease include female gender, middle age, and smoking. Active TED lasts for up to three years with the disease only responding to pharmacotherapy while it is active and inflammation is ongoing.
- Tepezza is an insulin-like growth factor-1 receptor antagonist indicated for the treatment of thyroid eye disease (TED).
- Goals of treatment in thyroid disease consists of achieving a euthyroid state and symptom management. The majority of patients with thyroid eye disease have mild to moderate disease and require primarily supportive care with ocular lubrication, topical cyclosporine, and lifestyle modification, such as, smoking cessation, sodium restriction, and sunglasses.
- The current mainstay of treatment for moderate to severe thyroid eye disease is oral or intravenous corticosteroids. Treatment can be initiated at doses of oral prednisone 30 mg daily for four weeks or methylprednisolone 500 mg once weekly for weeks 1 to 6, then 250 mg once weekly for weeks 7 to 12 with cumulative dose 4.5 to 5 g over 12 weeks. The European Thyroid Association recommends initial treatment with IV glucocorticoids for moderate-to-severe, active orbitopathy, citing several studies that suggest it is more efficacious and associated with fewer side effects than oral therapy. Similar trials have not been performed in the United States, where initiation with oral glucocorticoids remains the most common first-line treatment. Treatment for thyroid eye disease should start in the early months of the active inflammatory phase, as treatment becomes less effective as the disease progresses.
- There are no clinical head to head studies that compare steroids and Tepezza for the treatment TED. The 2021 European Group on Graves' orbitopathy (EUGOGO) clinical practice guidelines for the medical management of Graves' orbitopathy state Tepezza's incorporation into routine clinical practice is currently limited by the lack of comprehensive long-term efficacy and safety data and the absence of head-to-head comparison trials with intravenous glucocorticoids.
- Safety and efficacy were evaluated in the OPTIC trials, two multicenter, randomized, double-masked, placebo-controlled trials of 171 patients with thyroid eye disease. Patients were required to have active, moderate to severe thyroid eye disease with significant symptoms, including at least one of the following: lid retraction of greater than or equal to 2 mm, moderate or severe soft-tissue involvement, proptosis of greater than or equal to 3 mm, and periodic or constant diplopia. Patients were also required to have a clinical activity score (CAS) greater than or equal to 4 and symptoms less than 9 months from the onset of thyroid eye disease. All patients were euthyroid or with mild hypothyroidism or hyperthyroidism, defined as free thyroxine (T4) and free triiodothyronine (T3) levels less than 50% above or below the normal limits for the testing laboratory. Patients with previous orbital irradiation or surgery for thyroid eye disease were not allowed. The primary endpoint in the first trial was a composite endpoint of reduction of greater than or equal to 2 points in the CAS and a reduction of greater than or equal to 2 mm in proptosis. The primary endpoint in the second trial was a reduction in proptosis of greater than or equal to 2 mm. In both trials, significantly more patients treated with teprotumumab demonstrated less symptoms of thyroid eye disease than patients treated with placebo.
- In 2023, results from a randomized, double-masked, placebo-controlled, phase 4 clinical trial evaluating Tepezza for the treatment of adults with chronic TED and low CAS scores became available. The phase 4 trial evaluated patients with an initial diagnosis of TED between two to 10 years (mean duration of 5.2 years; SD 1.77) and low levels of disease activity (mean CAS of 0.4; SD 0.49), whereas the prior pivotal trials that formed the basis of the original FDA approval of Tepezza evaluated patients with disease duration of nine months or less and higher levels of disease

activity. At week 24, the primary endpoint was met and patients treated with Tepezza achieved a statistically significant reduction in proptosis from baseline compared to those receiving placebo.

References:

1. Tepezza [prescribing information]. Lake Forest, IL: Horizon Therapeutics USA, Inc.; April 2023.
2. 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.
3. Bartalena L, Baldeschi L, Boboridis K, et al. The 2016 european thyroid association/european group on graves' orbitopathy guidelines for the management of graves' orbitopathy. *Eur Thyroid J*. 2016 Mar; 5 (1): 9 - 26.
4. Smith TJ, Kahaly GJ, Ezra DG, et al. Teprotumumab for thyroid-associated ophthalmopathy. *NEJM*. 2017 May 4; 376 (18): 1748 – 61.
5. Douglas RS. Teprotumumab, an insulin-like growth factor-1 receptor antagonist antibody, in the treatment of active thyroid eye disease: a focus on proptosis. *Eye*. 2019; 33: 183- 90.
6. Douglas RS, Kahaly GJ, Patel A, et al. Teprotumumab for the treatment of active thyroid eye disease. *NEJM*. 2020 Jan 23; 382: 341 – 52.
7. McAlinden C. An overview of thyroid eye disease. *Eye and Vision*. 2014; 1: 9 – 12.
8. Bartalena L, Kahaly GJ, Baldeschi L, at al. The 2021 european group on graves' orbitopathy (EUGOGO) clinical practice guidelines for the medical management of graves' orbitopathy. *Eur J Endocrinol*. 2021 Aug 27; 185 (4): G43 - G67.
9. Horizon Therapeutics. Horizon Therapeutics plc announces positive topline data from Tepezza (teprotumumab-trbw) phase 4 clinical trial in patients with chronic/low clinical activity score (CAS) Thyroid eye disease (TED). 2023 April 10. Available at: <https://ir.horizontherapeutics.com/news-releases/news-release-details/horizon-therapeutics-plc-announces-positive-topline-data>. Accessed on May 4, 2023.

Policy History												
#	Date	Change Description										
1.8	Effective Date: 06/08/2023	Updated to remove criteria specific to disease activity in support of the updated FDA indication										
1.7	Effective Date: 12/01/2022	Annual review of criteria was performed, no changes were made										
1.6	Effective Date: 12/09/2021	Annual review of criteria was performed, no changes were made										
1.5	Effective Date: 12/03/2020	Updated to include requirement patients be euthyroid and updated steroid requirement to only allow for oral or IV steroids.										
1.4	Effective Date: 06/01/2020	UM medical management system update for MAPPO and BCNA <table border="1" data-bbox="485 548 1365 758"> <thead> <tr> <th>Line of Business</th> <th>PA Required in Medical Management System (Yes/No)</th> </tr> </thead> <tbody> <tr> <td>BCBS</td> <td>Yes</td> </tr> <tr> <td>BCN</td> <td>Yes</td> </tr> <tr> <td>MAPPO</td> <td>Yes</td> </tr> <tr> <td>BCNA</td> <td>Yes</td> </tr> </tbody> </table>	Line of Business	PA Required in Medical Management System (Yes/No)	BCBS	Yes	BCN	Yes	MAPPO	Yes	BCNA	Yes
Line of Business	PA Required in Medical Management System (Yes/No)											
BCBS	Yes											
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1.3	Effective Date: 05/01/2020	UM medical management system update for BCBS <table border="1" data-bbox="485 842 1365 1052"> <thead> <tr> <th>Line of Business</th> <th>PA Required in Medical Management System (Yes/No)</th> </tr> </thead> <tbody> <tr> <td>BCBS</td> <td>Yes</td> </tr> <tr> <td>BCN</td> <td>Yes</td> </tr> <tr> <td>MAPPO</td> <td>No</td> </tr> <tr> <td>BCNA</td> <td>No</td> </tr> </tbody> </table>	Line of Business	PA Required in Medical Management System (Yes/No)	BCBS	Yes	BCN	Yes	MAPPO	No	BCNA	No
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BCBS	Yes											
BCN	Yes											
MAPPO	No											
BCNA	No											
1.2	Effective Date: 04/16/2020	New full drug review										
1.1	Effective Date: 03/01/2020	UM medical management system update for BCN <table border="1" data-bbox="485 1220 1365 1430"> <thead> <tr> <th>Line of Business</th> <th>PA Required in Medical Management System (Yes/No)</th> </tr> </thead> <tbody> <tr> <td>BCBS</td> <td>No</td> </tr> <tr> <td>BCN</td> <td>Yes</td> </tr> <tr> <td>MAPPO</td> <td>No</td> </tr> <tr> <td>BCNA</td> <td>No</td> </tr> </tbody> </table>	Line of Business	PA Required in Medical Management System (Yes/No)	BCBS	No	BCN	Yes	MAPPO	No	BCNA	No
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BCBS	No											
BCN	Yes											
MAPPO	No											
BCNA	No											
1.0	Effective Date: 02/06/2020	Preliminary review										

* The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or <http://dailymed.nlm.nih.gov/dailymed/index.cfm>.

Blue Cross Blue Shield/Blue Care Network of Michigan
Medication Authorization Request Form
Tepezza™ (teprotumumab-trbw) HCPCS CODE: J3241



Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

This form is to be used by participating physicians to obtain coverage for Tepezza™. For commercial members only, please complete this form and submit via fax to 1-877-325-5979. If you have any questions regarding this process, please contact BCBSM Provider Relations and Servicing or the Medical Drug Helpdesk at 1-800-437-3803 for assistance.

PATIENT INFORMATION	PHYSICIAN INFORMATION
Name	Name
ID Number	Specialty
D.O.B. <input type="checkbox"/> Male <input type="checkbox"/> Female	Address
Patient weight (in kg) Date recorded: _____	City /State/Zip
Diagnosis	Phone/Fax: P: () - F: () -
Drug Name	NPI
Dose and Quantity	Contact Person
Directions	Contact Person Phone / Ext.
Date of Service(s)	

STEP 1: DISEASE STATE INFORMATION

1. Initiation or Continuation of treatment? Initiation Continuation *Date patient started therapy:* _____
2. Site of administration? Provider office/Home infusion Other: _____
 Hospital outpatient facility (go to #3) *Reason for Hospital Outpatient:* _____
3. Please specify location of administration if hospital outpatient infusion: _____
4. Please provide the NPI number for the place of administration: _____
5. **Initiation AND Continuation of Therapy:**
 - a. Please check the patient's diagnosis: Thyroid eye disease Other: _____
 - b. What is the clinical activity score (CAS) in the most severely affected eye? _____ Date: _____
 - c. Patient's active thyroid eye disease is defined by:
 - Decrease in color vision
 - Moderate or severe soft tissue involvement
 - Exophthalmos greater than or equal to 3 mm above normal for race and gender.
Please list millimeter: _____
 - Inconstant diplopia
 - Constant diplopia
 - d. Please provide T3 and T4 level:
 - Free triiodothyronine (T3) level: _____, Lab range: _____, Date: _____
 - Thyroxine (T4) level: _____, Lab range: _____, Date: _____
 - e. Has the patient tried and failed an adequate course of oral or intravenous (IV) corticosteroids (for example 30 mg/day Prednisone for 4 weeks)? Yes No Comment: _____
 - f. Has the physician discussed with the patient to stop smoking if they are a current smoker?
 Yes No Comment: _____ Not a current smoker
6. **Continuation Request-** *Please include rationale for continuation of therapy* _____

Please add any other supporting medical information necessary for our review

Coverage will not be provided if the prescribing physician's signature and date are not reflected on this document.

Request for expedited review: I certify that applying the standard review time frame may seriously jeopardize the life or health of the member or the member's ability to regain maximum function

Physician's Name	Physician Signature	Date
Step 2: Checklist	<input type="checkbox"/> Form Completely Filled Out <input type="checkbox"/> Attached Chart Notes	<input type="checkbox"/> Concurrent Medical Problems <input type="checkbox"/> Prior Therapies
Step 3: Submit	By Fax: BCBSM Specialty Pharmacy Mailbox 1-877-325-5979	By Mail: BCBSM Specialty Pharmacy Program P.O. Box 312320, Detroit, MI 48231-2320

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