Clinical Policy: Teprotumumab (Tepezza)

Reference Number: CP.PHAR.465
Effective Date: 01.21.20
Last Review Date: 02.22
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Teprotumumab (Tepezza™) is an insulin-like growth factor 1 receptor (IGF-1R) inhibitor.

FDA Approved Indication(s)

Tepezza is indicated for the treatment of thyroid eye disease (TED).

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Tepezza is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Thyroid Eye Disease (must meet all)**:**

1. Diagnosis of Graves' disease with associated TED (i.e., Graves' ophthalmopathy, Graves' orbitopathy);
2. Member has active TED with a clinical activity score (CAS) of ≥ 4 (see *Appendix D*);
3. Prescribed by or in consultation with an ophthalmologist;
4. Age ≥ 18 years;
5. Member is euthyroid with documentation of a recent (within the last 30 days) free thyroxine (FT4) and total triiodothyronine (T3) or free T3 (FT3) levels within the laboratory defined reference range;
6. Member has not had previous surgical intervention for TED;
7. Member does not require surgical ophthalmological intervention;
8. Failure of a 4-week trial of a systemic corticosteroid (at up to maximally indicated doses), unless clinically significant adverse effects are experienced or all are contraindicated;
9. Member has not received ≥ 8 Tepezza infusions (including the initial 10 mg/kg first infusion);
10. Dose does not exceed a single 10 mg/kg dose followed by seven 20 mg/kg infusions given every 3 weeks.

Approval duration: 6 months (up to 8 total lifetime infusions)

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Thyroid Eye Disease (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by both of the following (a and b):
   a. Reduction in proptosis ≥ 2 mm;
   b. Reduction in CAS from baseline of ≥ 2 points;
3. Member has not had previous surgical intervention for TED;
4. Member does not require surgical ophthalmological intervention;
5. Member has not received ≥ 8 Tepezza infusions (including the initial 10 mg/kg first infusion);
6. If request is for a dose increase, new dose does not exceed a total of seven 20 mg/kg infusions given every 3 weeks.

Approval duration: 6 months (up to 8 total lifetime infusions)

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
CAS: clinical activity score
FDA: Food and Drug Administration
GO: Graves' ophthalmopathy
TED: thyroid eye disease

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
prednisone	30 mg/day PO	30 mg/day
methylprednisolone (SOLU-Medrol®)	500 mg IV once weekly for weeks 1 to 6, then 250 mg IV once weekly for weeks 7-12	500 mg/week

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: General Information
- The Graves' orbitopathy CAS elements below are each assigned a score of 1. 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).
  - Painful feeling behind the globe over last four weeks
  - Pain with eye movement during last four weeks
  - Redness of the eyelids
  - Redness of the conjunctiva
  - Swelling of the eyelids
  - Chemosis (edema of the conjunctiva)
  - Swollen caruncle (flesh body at medial angle of eye)
  - Increase in proptosis ≥ 2 mm
  - Decreased eye movements ≥ 5° any direction
  - Decreased visual acuity ≥ 1 line on Snellen chart
- Use of systemic corticosteroids in TED is supported by the following treatment guidelines:
  - 2021 European Group on Graves' orbitopathy (EUGOGO) clinical practice guidelines for the medical management of Graves' orbitopathy: 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.
  - 2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis: In the absence of any strong contraindication to GC, consider for coverage of mild active GO who are treated with RAI, even in the absence of risk factors for GO deterioration (weak recommendation, low-quality evidence). Additionally in mild GO patients who are treated with RAI, steroid coverage is recommended if there are concomitant risk factors for GO deterioration (strong recommendation, moderate-quality evidence).

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
TED	Initial: 10 mg/kg IV one time dose Maintenance: 20 mg/kg IV every 3 weeks for seven infusions	See dosing regimen

VI. Product Availability

Single-dose vial: 500 mg

VII. References

1. Tepezza Prescribing Information. Lake Forest, IL: Horizon Therapeutics USA, Inc.; January 2020. Available at: https://www.hzndocs.com/TEPEZZA-Prescribing-Information.pdf. Accessed October 7, 2021.
2. NCT03298867 in ClinicalTrials.gov. NIH U.S. National Library of Medicine. Available at: https://clinicaltrials.gov/ct2/show/NCT03298867?term=NCT03298867&draw=2&rank=1. Accessed October 7, 2021.
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. Mourits MP, Prummel MF, Wiersinga WM, Koornneef L. Clinical activity score as a guide in the management of patients with Graves' ophthalmopathy. Clin Endocrinol (Oxf) 1997; 47:9.
5. Smith TJ, Kahaly GJ, Ezra DG, et al. Teprotumumab for Thyroid-Associated Ophthalmopoathy. NEJM 2017; 376 (18): 1748-1761.
6. Patel KN, Yip L, Lubitz CC, et al. The American Association of Endocrine Surgeons Guidelines for the Definitive Surgical Management of Thyroid Disease in Adults. Annals of Surgery: March 2020; 271 (3): e21-e93.
7. 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.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J3241	Injection, teprotumumab-trbw, 10 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively.	01.21.20	02.20
Drug is now FDA approved - criteria updated per FDA labeling: modified criteria to require member be euthyroid, clarified systemic	02.19.20	05.20

Reviews, Revisions, and Approvals	Date	P&T Approval Date
corticosteroid trial required, clarified 8 total infusions allowed and included requirement in initial approval criteria; for continued therapy added additional response criteria requiring ≥ 2 mm reduction in proptosis, removed requirement that TED remain active to allow completion of treatment course in members responding positively to therapy; for continued therapy added requirement to validate member does not require surgical ophthalmological intervention; references reviewed and updated.		
Added requirement that member has not had previous surgical intervention for TED consistent with clinical trial exclusion criteria.	05.12.20	08.20
1Q 2021 annual review: no significant changes; references to HIM.PHAR.21 revised to HIM.PA.154; updated HCPCS code; references reviewed and updated.	11.04.20	02.21
1Q 2022 annual review: added additional option for total T3 or free T3 (FT3) to determine member is euthyroid per 2016 ATA guidelines; references reviewed and updated.	10.07.21	02.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan

retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.