# Clinical Policy: Teprotumumab (Tepezza)

Reference Number: CP.PHAR.465
Effective Date: 01.21.20
Last Review Date: 02.24
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) regardless of TED activity or duration.

## 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. Prescribed by or in consultation with an ophthalmologist;
3. Age ≥ 18 years;
4. One of the following (a or b):
   a. 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;
   b. Member has a recent (within the last 30 days) free thyroxine (FT4) and total triiodothyronine (T3) or free T3 (FT3) levels less than 50% above or below the laboratory defined reference range and is undergoing treatment to correct the mild hypo- or hyperthyroidism to maintain a euthyroid state;
5. Member has not had previous surgical intervention for TED;
6. Member does not require surgical ophthalmological intervention;
7. Failure of a 4-week trial of a systemic corticosteroid (at up to maximally indicated doses), unless one of the following (a, b, or c):
   a. Clinically significant adverse effects are experienced or all are contraindicated;
   b. Member has significant proptosis (examples may include but are not limited to proptosis ≥ 3 mm above the upper limit for race and sex, or proptosis that impacts activities of daily life [e.g., reading, driving, computer work, and watching television]);

c. Member has diplopia;
8. Member has not received ≥ 8 Tepezza infusions (including the initial 10 mg/kg first infusion);
9. Dose does not exceed both of the following (a and b):
   a. A single 10 mg/kg dose followed by seven 20 mg/kg infusions given every 3 weeks (*see Appendix E for vial rounding recommendations*);
   b. Vial quantity as identified by the online dose calculator using the member's weight (see *Appendix D*) or as recommended in *Appendix E* for vial rounding.

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

**B. Other diagnoses/indications** (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member has not had previous surgical intervention for TED;
3. Member does not require surgical ophthalmological intervention;
4. Member has not received ≥ 8 Tepezza infusions (including the initial 10 mg/kg first infusion);
5. If request is for a dose increase, new dose does not exceed both of the following (a and b):
   a. A total of seven 20 mg/kg infusions given every 3 weeks (*see Appendix E for vial rounding recommendations*);
   b. Vial quantity as identified by the online dose calculator using the member's weight (see *Appendix D*) or as recommended in *Appendix E* for vial rounding.

**Approval duration: 1 month (up to 8 total lifetime infusions)**

**B. Other diagnoses/indications** (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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*
- 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).
- The following link will provide the dose and appropriate vial quantity based on the member's weight (note this does not account for dose rounding recommendations found in *Appendix E* below): https://www.tepezzahcp.com/starting-patients/dosing-and-administration

*Appendix E: Vial Rounding Recommendations (40 to 170 kg)*

| Weight Range (kg) | Initial Dose (1 dose) Vial Quantity Recommendation | Maintenance (7 doses total) Vial Quantity Recommendation |
|---|---|---|
| 40 – 52.5 | 1 | 14 (2 vials per dose) |
| 52.6 – 55 | 1 | 21 (3 vials per dose) |
| 55.1 – 77.5 | 2 | 21 (3 vials per dose) |
| 77.6 – 102.5 | 2 | 28 (4 vials per dose) |
| 102.6 – 105 | 2 | 35 (5 vials per dose) |
| 105.1 – 127.5 | 3 | 35 (5 vials per dose) |
| 127.6 – 152.5 | 3 | 42 (6 vials per dose) |
| 152.6 – 155 | 3 | 49 (7 vials per dose) |
| 155.1 – 170 | 4 | 49 (7 vials per dose) |

## V. Dosage and Administration

| Indication | Dosing Regimen | Maximum Dose |
|---|---|---|
| TED | Initial: 10 mg/kg IV one time dose<br>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. Deerfield, IL: Horizon Therapeutics USA, Inc.; July 2023. Available at: https://www.hzndocs.com/TEPEZZA-Prescribing-Information.pdf. Accessed October 6, 2023.
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 12, 2023.
3. Douglas RS, Kahaly GJ, Patel A, et al. Teprotumumab for the Treatment of Active Thyroid Eye Disease. N Engl J Med. 2020 Jan 23;382(4):341-352.
4. Smith TJ, Kahaly GJ, Ezra DG, et al. Teprotumumab for Thyroid-Associated Ophthalmopathy. N Engl J Med. 2017 May 4;376(18):1748-1761.
5. 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.
6. 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.
7. 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.
8. 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.
9. 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). Press Release; Horizon Therapeutics. April 10, 2023. Available at: https://finance.yahoo.com/news/horizon-therapeutics-plc-announces-positive-120000335.html. Accessed October 12, 2023.
10. Burch HB, Perros P, Bednarczuk T, et al. Management of Thyroid Eye Disease: A Consensus Statement by the American Thyroid Association and the European Thyroid Association. Thyroid: 12 Dec 2022. 32 (12): 1439-1470.

## 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 |

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| Drug is now FDA approved - criteria updated per FDA labeling: modified criteria to require member be euthyroid, clarified systemic 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. | 02.19.20 | 05.20 |
| 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 |
| Template changes applied to other diagnoses/indications and continued therapy section. | 09.28.22 | |
| 1Q 2023 annual review: Added dosing requirements for vial quantity using the online dose calculator or dose rounding recommendations based on newly added *Appendix E*; per prescribing information added the following option for thyroid lab assessment: "Member has a recent (within the last 30 days) free thyroxine (FT4) and total triiodothyronine (T3) or free T3 (FT3) levels less than 50% above or below the laboratory defined reference range and is undergoing treatment to correct the mild hypo- or hyperthyroidism to maintain a euthyroid state"; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section. | 09.15.22 | 02.23 |
| RT4: updated indication extension for TED treatment regardless of TED activity or duration, removed the initial therapy CAS criterion, removed positive response criteria of proptosis and CAS reduction from continued therapy as full lifetime course of therapy is within 6 month authorization and proptosis/CAS reduction are endpoints assessed at 24 weeks (after full duration of therapy). | 04.28.23 | |
| 1Q 2024 annual review: for corticosteroid redirection added additional bypass for significant proptosis and diplopia consistent with 2022 ATA recommendations; for continuation of therapy reduced approval duration to 1 month; references reviewed and updated. | 10.06.23 | 02.24 |

**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.