Clinical Policy: Teprotumumab (Tepezza)

Reference Number: PA.CP.PHAR.465
Effective Date: 04/2020
Last Review Date: 01/2023

Coding Implications
Revision Log

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 PA Health & Wellness® 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. 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;
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 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

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

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

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
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 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.
7. **Approval duration: 6 months (up to 8 total lifetime infusions)**

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

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 – PA.CP.PMN.53

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).

- 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:

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 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.; October 2021. Available at: https://www.hzndocs.com/TEPEZZA-Prescribing-Information.pdf. Accessed September 19, 2022.
2. NCT03298867 in ClinicalTrials.gov. NIH U.S. National Library of Medicine. Accessed October 7, 2021.
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. Smith TJ, Kahaly GJ, Ezra DG, et al. Teprotumumab for Thyroid-Associated Ophthalmopoathy. NEJM 2017; 376 (18): 1748-1761.

8. 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.
9. 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.	04/2020	
Added requirement that member has not had previous surgical intervention for TED consistent with clinical trial exclusion criteria.	07/2020	
1Q 2021 annual review: corrected erroneous criterion for continued therapy to read "Member does not require surgical ophthalmological intervention"; references reviewed and updated.	01/2021	
1Q 2022 annual review: references reviewed and updated.	01/2022	
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.	01/2023	