Clinical Policy: Teprotumumab (Tepezza)

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 free triiodothyronine (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
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.PHAR.21 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.PHAR.21 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
   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.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>prednisone</td>
<td>30 mg/day PO</td>
<td>30 mg/day</td>
</tr>
<tr>
<td>methylprednisolone (SOLU-Medrol®)</td>
<td>500 mg IV once weekly for weeks 1 to 6, then 250 mg IV once weekly for weeks 7-12</td>
<td>500 mg/week</td>
</tr>
</tbody>
</table>
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).
  o Painful feeling behind the globe over last four weeks
  o Pain with eye movement during last four weeks
  o Redness of the eyelids
  o Redness of the conjunctiva
  o Swelling of the eyelids
  o Chemosis (edema of the conjunctiva)
  o Swollen caruncle (flesh body at medial angle of eye)
  o Increase in proptosis ≥ 2 mm
  o Decreased eye movements ≥ 5° any direction
  o Decreased visual acuity ≥ 1 line on Snellen chart

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>TED</td>
<td>Initial: 10 mg/kg IV one time dose</td>
<td>See dosing regimen</td>
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<tr>
<td></td>
<td>Maintenance: 20 mg/kg IV every 3 weeks for seven infusions</td>
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</tbody>
</table>

VI. Product Availability
Single-dose vial: 500 mg

VII. References
Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Description</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Policy created pre-emptively.</td>
<td>01.21.20</td>
<td>02.20</td>
</tr>
<tr>
<td>Drug is now FDA approved - criteria updated per FDA labeling: modified</td>
<td>02.19.20</td>
<td>05.20</td>
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<tr>
<td>criteria to require member be euthyroid, clarified systemic corticosteroid</td>
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<tr>
<td>trial required, clarified 8 total infusions allowed and included requirement</td>
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<tr>
<td>in initial approval criteria; for continued therapy added additional</td>
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<td></td>
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<tr>
<td>response criteria requiring ≥ 2 mm reduction in proptosis, removed</td>
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<tr>
<td>requirement that TED remain active to allow completion of treatment</td>
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<tr>
<td>course in members responding positively to therapy; for continued therapy</td>
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<td></td>
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<tr>
<td>added requirement to validate member does not require surgical</td>
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<tr>
<td>ophthalmological intervention; references reviewed and updated.</td>
<td></td>
<td></td>
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<tr>
<td>Added requirement that member has not had previous surgical intervention</td>
<td>05.12.20</td>
<td>08.20</td>
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<tr>
<td>for TED consistent with clinical trial exclusion criteria.</td>
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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.

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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.

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