Clinical Policy: Teplizumab-mzwv (Tzield)

Reference Number: PA.CP.PHAR.492
Effective Date: 01/2023
Last Review Date: 01/2024

Revision Log

Description
Teplizumab-mzwv (Tzield™) is a CD3-directed antibody.

FDA Approved Indication(s)
Tzield is indicated to delay the onset of Stage 3 type 1 diabetes (T1D) in adults and pediatric patients aged 8 years and older with Stage 2 T1D.

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 Tzield is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Delayed Onset of Stage 3 Type 1 Diabetes (must meet all)**:**

1. Diagnosis of Stage 2 T1D as evidenced by all of the following (a, b, and c):
   a. Presence of 2 or more diabetes-related autoantibodies detected in 2 samples obtained within the last 6 months: anti-insulin autoantibodies (mIAA), islet cell antibodies (ICA), anti-glutamic acid decarboxylase(GAD)65ab, anti-ICA512ab;
   b. Abnormal glucose tolerance during an oral glucose-tolerance test (OGTT) confirmed within the last 7 weeks (i, ii, or iii) (*two confirmatory tests are required for members age ≥ 18 years*):
      i. Fasting plasma glucose ≥ 110 mg/dL, and < 126 mg/dL;
      ii. 2 hour plasma glucose ≥ 140 mg/dL, and < 200 mg/dL;
      iii. 30, 60, or 90 minute value on OGTT ≥ 200 mg/dL;
   c. Member does not have symptoms of diabetes (e.g., polyuria, polydipsia, polyphagia);
2. Prescribed by or in consultation with an endocrinologist;
3. Age ≥ 8 years;
4. Member does not have a diagnosis of Stage 3 T1D or type 2 diabetes;
5. Documentation of member's current body surface area (BSA) (m^2);
6. Dose does not exceed a total of 11,240 mcg/m^2 administered over a 14-day treatment course (*see section V*).

Approval duration: 3 months (one 14-day treatment course only)

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. Delayed Onset of Stage 3 Type 1 Diabetes

1. Continued therapy will not be authorized as Tzield is indicated to be administered as a one-time treatment course only.

Approval duration: Not applicable

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

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.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. 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.
B. Stage 3 or 4 T1D;
C. Type 2 diabetes.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

BSA: body surface area
FDA: Food and Drug Administration
GAD: glutamic acid decarboxylase
ICA: islet cell antibodies
mIAA: anti-insulin autoantibodies
OGTT: oral glucose tolerance test
T1D: type 1 diabetes

Appendix B: Therapeutic Alternatives

Not Applicable

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: General Information

- There are 4 recognized stages of T1D:
  - Stage 1: ≥ 2 diabetes-related autoantibodies, normoglycemia, presymptomatic
  - Stage 2: ≥ 2 diabetes-related autoantibodies, dysglycemia, presymptomatic
  - Stage 3: ≥ 2 diabetes-related autoantibodies, dysglycemia, symptomatic
  - Stage 4: longstanding T1D
- In 2010, teplizumab failed to meet the primary efficacy endpoint (a composite of total daily insulin usage and HbA1c level at 12 months) in the phase 3 Protégé study, demonstrating no difference compared to placebo for the treatment of patients with early-onset T1D; as a result, clinical programs were suspended. In 2018, Provention Bio acquired teplizumab from MacroGenics/Lilly. A new phase 3 study for the treatment of

early-onset T1D was completed (PROTECT, NCT03875729). Results from this study are not yet available.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Delayed onset of Stage 3 T1D	14 day treatment course administered IV QD: • Day 1: 65 mcg/m^2 • Day 2: 125 mcg/m^2 • Day 3: 250 mcg/m^2 • Day 4: 500 mcg/m^2 Days 5-14: 1,030 mcg/m^2	11,240 mcg/m^2/ treatment course .

VI. Product Availability

Single-dose vial: 2 mg/mL

VII. References

1. Tzield Prescribing Information. Red Bank, NJ: Provention Bio, Inc; November 2022. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/761183Orig1s000lbl.pdf. Accessed October 19, 2023.
2. Insel RA, Dunne JL, Atkinson MA, et al. Staging presymptomatic type 1 diabetes: A scientific statement of JDRF, the Endocrine Society, and the American Diabetes Association. Diabetes Care. 2015; 38(10): 1964-1974.
3. Couper JJ, Haller MJ, Greenbaum CJ, et al. ISPAD clinical practice consensus guidelines 2018: Stages of type 1 diabetes in children and adolescents. Pediatric Diabetes. 2018; 19(S27): 20-27.

Prevention of T1DM

4. Herold KC et al. An anti-CD3 antibody, teplizumab, in relatives at risk for type 1 diabetes. New Engl J Med. 2019; 381(7): 603-613. doi: 10.1056/NEJMoa1902226. Epub 2019 Jun 9. Erratum in: N Engl J Med. 2020 Feb 6; 382(6): 586.
5. Provention Bio, Inc. Teplizumab for prevention of type 1 diabetes in relatives "at-risk". Available at: https://clinicaltrials.gov/ct2/show/NCT01030861. Accessed October 19, 2023.
6. Sims EK et al. Teplizumab improves and stabilizes beta cell function in antibody-positive high-risk individuals. Science Translational Medicine. 2021; 13(583): eabc8980.

Treatment of T1DM

7. Sherry N et al. Teplizumab for treatment of type 1 diabetes (Protégé study): 1-year results from a randomized, placebo-controlled trial. Lancet. 2011; 378(9790): 487-497.
8. Hagopian W et al. Teplizumab preserves C-peptide in recent-onset type 1 diabetes: two-year results from the randomized, placebo-controlled Protégé trial. Diabetes. 2013; 62(11): 3901-3908.
9. Herold KC et al. Teplizumab (anti-CD3 mAb) treatment preserves C-peptide responses in patients with new-onset type 1 diabetes in a randomized controlled trial: Metabolic and immunologic features at baseline identify a subgroup of responders. Diabetes. 2013; 62: 3766-3774.

10. Provention Bio, Inc. Recent-onset type 1 diabetes trial evaluating efficacy and safety of teplizumab (PROTECT). Available at: https://clinicaltrials.gov/ct2/show/NCT03875729. Accessed October 19, 2023.
11. Nourelden AZ et al. Safety and efficacy of teplizumab for treatment of type one diabetes mellitus: A systematic review and meta-analysis. Endocr Metab Immune Disord Drug Targets. 2021; 21(10): 1895-1904.

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
J9381	Injection, teplizumab-mzwv, 5 mcg

Reviews, Revisions, and Approvals	Date
Policy created	01/2023
1Q 2024 annual review: added HCPCS code [J9381] and deleted HCPCS code [C9399] and HCPCS code [J3590]; updated Appendix D; references reviewed and updated.	01/2024