

## Clinical Policy: Teplizumab-mzwv (Tzielid)

Reference Number: PA.CP.PHAR.492

Effective Date: 01/2023

Last Review Date: 01/2026

### Description

Teplizumab-mzwv (Tzielid<sup>®</sup>) is a CD3-directed antibody.

### FDA Approved Indication(s)

Tzielid 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<sup>®</sup> that Tzielid 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, zinc transporter 8 autoantibody (ZnT8A), insulinoma-associated antigen 2 autoantibody (IA-2A);
  - 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  $\geq 110$  mg/dL, and  $< 126$  mg/dL;
    - ii. 2 hour plasma glucose  $\geq 140$  mg/dL, and  $< 200$  mg/dL;
    - iii. 30, 60, or 90 minute value on OGTT  $\geq 200$  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  $\geq 8$  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.PHARM.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

IA-2A: insulinoma-associated antigen  
2 autoantibody

ICA: islet cell antibodies

mIAA: anti-insulin autoantibodies

OGTT: oral glucose tolerance test

T1D: type 1 diabetes

ZnT8A: zinc transporter 8  
autoantibody

### *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: single or transient single diabetes-related autoantibodies, normoglycemia, presymptomatic
  - Stage 2:  $\geq 2$  diabetes-related autoantibodies, dysglycemia, presymptomatic
  - Stage 3:  $\geq 1$  diabetes-related autoantibodies, hyperglycemia, symptomatic
  - Stage 4: longstanding T1D
- Treatment of 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.
- A new phase 3 study for the treatment of early-onset T1D in children and adolescents with newly diagnosed disease (PROTECT, NCT03875729) was completed in 2023. Teplizumab met the primary end point of preservation of  $\beta$ -cell function as measured by stimulated C-peptide levels, but this did not translate to benefit with regard to the clinical outcomes; there were no significant differences compared to placebo for the secondary end points of insulin doses that were required to meet glycemic goals, glycosylated hemoglobin levels, time in the target glucose range, and clinically important hypoglycemic events.

**V. Dosage and Administration**

Indication	Dosing Regimen	Maximum Dose
Delayed onset of Stage 3 T1D	14 day treatment course administered IV QD: <ul style="list-style-type: none"> <li>• Day 1: 65 mcg/m<sup>2</sup></li> <li>• Day 2: 125 mcg/m<sup>2</sup></li> <li>• Day 3: 250 mcg/m<sup>2</sup></li> <li>• Day 4: 500 mcg/m<sup>2</sup></li> </ul> Days 5-14: 1,030 mcg/m <sup>2</sup>	11,240 mcg/m <sup>2</sup> / treatment course

**VI. Product Availability**

Single-dose vial: 2 mg/2 mL

**VII. References**

1. Tzielid Prescribing Information. Red Bank, NJ: Provention Bio, Inc; April 2025. Available at: <https://www.tzielid.com>. Accessed October 21, 2025.
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.
4. Mehta S, Ryabets-Lienhard A, Patel N, et al. Pediatric Endocrine Society statement on considerations for use of teplizumab (Tzielid™) in clinical practice. *Horm Res Paediatr*. Published online April 30, 2024. DOI: 10.1159/000538775
5. Philip M, Achenbach P, Addala A, et al. Consensus guidance for monitoring individuals with islet autoantibody-positive pre-stage 3 type 1 diabetes. *Diabetes Care*. 2024; 47(8): 1276-1298.

*Prevention of T1DM*

6. 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.
7. Provention Bio, Inc. Teplizumab for prevention of type 1 diabetes in relatives "at-risk". Available at: <https://clinicaltrials.gov/ct2/show/NCT01030861>. Accessed November 6, 2024.
8. 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*

9. 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.
10. 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.
11. 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.
12. 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.
13. 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.
14. Ramos EL, Dayan CM, Chatenoud L, et al. Teplizumab and  $\beta$ -cell function in newly diagnosed type 1 diabetes. *N Engl J Med.* 2023; 289: 2151-2161.

**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-mzvw, 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
1Q 2025 annual review: added ZnT8A and IA-2A as additional diabetes-related autoantibody options per pivotal study design and specialist feedback; added information about PROTECT trial to Appendix D; references reviewed and updated.	01/2025

<b>Reviews, Revisions, and Approvals</b>	<b>Date</b>
1Q 2026 annual review: no significant changes; references reviewed and updated	01/2026