

Medical Policy Manual **Approved Rev: Do Not Implement until 12/31/26**

Teplizumab-mzwv (TzielTM)

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the medical policy and a health plan or government program (e.g., TennCare), the express terms of the health plan or government program will govern.

POLICY

INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication

Tziel is indicated to:

- Delay the onset of Stage 3 type 1 diabetes (T1D) in adults and pediatric patients 1 year of age and older with Stage 2 type 1 diabetes.
- Delay the decline in endogenous insulin production in pediatric patients aged 8 to 17 years recently diagnosed with Stage 3 T1D. This indication is approved under accelerated approval based on evidence of reduced C-peptide decline. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

Limitations of Use

- There is limited evidence of safety and effectiveness in patients aged 45 years and older with Stage 2 T1D.
- Tziel is not effective as a disease modifying therapy in non-autoimmune dysglycemic conditions.

All other indications are considered experimental/investigational and not medically necessary.

DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

Delay of stage 3 type 1 diabetes:

- Presence of two or more pancreatic islet cell autoantibodies
- Chart notes or laboratory test results documenting dysglycemia within the past 2 months.

Delay the decline in endogenous insulin production in Stage 3 type 1 diabetes:

- Presence of one or more pancreatic islet cell autoantibodies.
- Chart notes or laboratory test results demonstrating a peak stimulated C-peptide ≥ 0.2 pmol/mL on a mixed meal tolerance test or alternative method if appropriate (e.g., oral glucose tolerance test [OGTT], fasting C-peptide).
- Chart notes or laboratory test results documenting recently diagnosed Stage 3 type 1 diabetes.

PRESCRIBER SPECIALTIES



Medical Policy Manual **Approved Rev: Do Not Implement until 12/31/26**

This medication must be prescribed by or in consultation with an endocrinologist.

COVERAGE CRITERIA

Delay of Stage 3 Type 1 Diabetes

Authorization of 1 month may be granted for members with Stage 2 type 1 diabetes to delay the onset of Stage 3 type 1 diabetes when all of the following criteria are met:

- Member is **1 to less than 45** years of age.
- Member **is positive** for two or more of the following pancreatic islet cell autoantibodies **on two separate occasions**:
 - Glutamic acid decarboxylase 65 (GAD) autoantibodies
 - Insulin autoantibody (IAA)
 - Insulinoma-associated antigen 2 autoantibody (IA-2A)
 - Zinc transporter 8 autoantibody (ZnT8A)
 - Islet cell autoantibody (ICA)
- Member has dysglycemia **confirmed by** any of the following **in the past 2 months**:
 - Fasting blood glucose level of 100 to 125 mg/dL (5.6 to 6.9 mmol/L).
 - 2-hour postprandial plasma glucose level of at least 140 mg/dL (7.8 mmol/L) and less than 200 mg/dL (11.1 mmol/L).
 - **A1C ≥ 5.7 and $< 6.5\%$ (39–47 mmol/mol) or $\geq 10\%$ increase in A1C.**
- Member does not have symptoms associated with type 1 diabetes (e.g., increased urination, excessive thirst, weight loss).
- **Member does not have type 2 diabetes or other forms of diabetes (e.g., genetic forms of diabetes, maturity-onset diabetes of the young (MODY), latent autoimmune diabetes in adults (LADA), or diabetes secondary to medications or surgery).**
- Member will not exceed a one-time 14-day treatment course consisting of the following dosing schedule:
 - Day 1: 65 mcg/m²
 - Day 2: 125 mcg/m²
 - Day 3: 250 mcg/m²
 - Day 4: 500 mcg/m²
 - Days 5 through 14: 1,030 mcg/m²

Delay the Decline in Endogenous Insulin Production in Stage 3 Type 1 Diabetes

Authorization of 12 months may be granted for members with recently diagnosed Stage 3 type 1 diabetes when all of the following criteria are met:

- Member is **8 to 17 years of age.**
- Member is **positive** for one or more of the following pancreatic islet cell autoantibodies:
 - Glutamic acid decarboxylase 65 (GAD) autoantibodies
 - Insulin autoantibody (IAA)
 - Insulinoma-associated antigen 2 autoantibody (IA-2A)
 - Zinc transporter 8 autoantibody (ZnT8A)
 - Islet cell autoantibody (ICA)
- Member has a peak stimulated C-peptide **≥ 0.2 pmol/mL** on a mixed meal tolerance test or alternative method if appropriate (e.g., oral glucose tolerance test [OGTT], fasting C-peptide).
- Member is **recently diagnosed** within the past 6 weeks with Stage 3 type 1 diabetes as confirmed by one of the following:
 - **A1C $\geq 6.5\%$ (≥ 48 mmol/mol).**

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- Fasting blood glucose level ≥ 126 mg/dL (≥ 7.0 mmol/L).
- 2-hour postprandial plasma glucose level ≥ 200 mg/dL (≥ 11.1 mmol/L) during oral glucose tolerance test.
- In members with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥ 200 mg/dL (≥ 11.1 mmol/L). Random is any time of the day without regard to time since previous meal.
- Provider attests that the medication will be administered as soon as possible following the diagnosis of Stage 3 type 1 diabetes but no later than 8 weeks from diagnosis.
- Member will not exceed two 12-day treatment courses (second course should be administered 6 months after the first) consisting of the following dosing schedule:
 - Day 1: 106 mcg/m²
 - Day 2: 425 mcg/m²
 - Days 3 through 12: 850 mcg/m²

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

REFERENCES

1. Tzield [package insert]. Red Bank, NJ: Provention Bio, Inc.; **June 2026**.
2. Herold KC, Bundy BN, Long SA, et al. An Anti-CD3 Antibody, Teplizumab, in Relatives at Risk for Type 1 Diabetes. *N Engl J Med* 2019; 381(7):603-613. doi:10.1056/NEJMoa1902226.
3. American Diabetes Association Professional Practice Committee; 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes-2026. *Diabetes Care* 2026; 49 (Supplement_1): S27–S49.
4. Ramos EL, Dayan CM, Chatenoud L, et al. Teplizumab and β -cell function in newly diagnosed type 1 diabetes. *N Engl J Med* 2023; 389(23):2151-2161.

EFFECTIVE DATE 12/31/2026

ID_CHS_56782026_1026