Tzield® (Teplizumab-Mzwv) (for Pennsylvania Only)

Policy Number: CSPA2026D00117E
Effective Date: May 1, 2026

➲ Instructions for Use

Table of Contents **Page**

Related Policies
None

Application

This Medical Benefit Drug Policy only applies to the state of Pennsylvania.

Coverage Rationale

Tzield, administered as a one-time 14-day course of therapy, is proven and medically necessary to delay the onset of stage 3 type 1 diabetes in pediatric and adult patients when all of the following criteria are met:

- Patient is 8 years of age and older; **and**
- Diagnosis of stage 2 type 1 diabetes confirmed by **all** of the following:
  - Presence of at least **two** of the following pancreatic islet 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)

    and
  - Presence of dysglycemia without overt hyperglycemia defined by **one** of the following:
    - Fasting plasma glucose ≥ 100mg/dL and < 126 mg/dL; **or**
    - 2-hour post-prandial plasma glucose level ≥ 140 mg/dL and < 200 mg/dL; **or**
    - A1C ≥ 5.7 and < 6.5% or ≥ 10% increase in A1C

    and
  - Patient does not have symptoms associated with stage 3 type 1 diabetes (e.g., increased urination, excessive thirst, weight loss); **and**
  - Diagnosis of type 2 diabetes has been ruled out

  and
- Prescribed by or in consultation with an endocrinologist; **and**
- Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
- Patient has not been previously treated with Tzield; **and**
- Authorization will be issued for no more than one treatment course (i.e., 14 doses) per lifetime

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state, or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J9381	Injection, teplizumab-mzwv, 5 mcg

Diagnosis Code	Description
E10.8	Type 1 diabetes mellitus with unspecified complications
E10.9	Type 1 diabetes mellitus without complications

Background

Type 1 diabetes (T1D) is a chronic autoimmune disease that leads to destruction of insulin-producing beta cells and dependence on exogenous insulin for survival. Approximately 1 to 1.5 million Americans have TD1, which is one of the most common diseases of childhood. Although it can appear at any age, TD1 is usually diagnosed in children and young adults. A person is at higher risk for T1D if they have a parent, brother, or sister with T1D, although most patients do not have a family history. Type 1 diabetes progresses through asymptomatic stages before the development of overt hyperglycemia. These stages are characterized by the appearance of autoantibodies (stage 1) and then dysglycemia (stage 2). In stage 2, metabolic responses to a glucose load are impaired but the level of glycosylated hemoglobin remains normal. Insulin therapy and glucose monitoring are currently the standard of care for treating the clinical stage, Stage 3 T1D.

Teplizumab-mzwv is a CD3-directed monoclonal antibody which binds CD3 on the surface of T lymphocytes. Teplizumab-mzwv may deactivate the T lymphocytes that attack pancreatic insulin-producing beta cells, while increasing the proportion of regulatory T lymphocytes that help moderate the immune response.

Clinical Evidence

Proven

Teplizumab-mzwv 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.

The efficacy of teplizumab-mzwv was established in a randomized double-blind, event-driven, placebo-controlled study in 76 patients, 8 to 49 years of age with Stage 2 T1D. Patients were randomized to receive teplizumab-mzwv or placebo once daily by intravenous (IV) infusion for 14 days. The primary efficacy endpoint was the time from randomization to development of Stage 3 T1D was diagnosed in 20 (45%) of the teplizumab-treated patients and in 23 (72%) of the placebo-treated patients. A Cox proportional hazards model, stratified by age and oral glucose tolerance test status at randomization, demonstrated that the median time from randomization to Stage 3 T1D diagnosis was 50 months in the teplizumab-mzwv group and 25 months in the placebo group, for a difference of 25 months. With a median follow-up time of 51 months, therapy with Tzield resulted in a statistically significant delay in the development of Stage 3 T1D (hazard ratio 0.41, 95% CI: 0.22, 0.78; $p = 0.0066$). The most common adverse reactions (> 10%) with teplizumab-mzwv use were lymphopenia, rash, leukopenia, and headache.

Lymphocyte count decreased to a nadir on day 5 (total decrease, 72.3%; interquartile range, 82.1 to 68.4; $p < 0.001$.) and resolved by day 45 in all participants except one; in that participant, the lymphocyte counts returned to the normal range on day 105. A spontaneously resolving rash occurred in 16 (36%) of participants who received teplizumab-mzwv.

Professional Societies

American Diabetes Association (ADA)

In 2026, the ADA published “Standards of Care in Diabetes-2026” which includes current clinical practice recommendations and is intended to provide the components of diabetes care, general treatment goals and guidelines,

and tools to evaluate quality of care. The ADA differentiates type 1 diabetes from type 2 diabetes through clinical presentation and laboratory findings as summarized below:

- Type 1 diabetes is due to autoimmune b-cell destruction, usually leading to absolute insulin deficiency, including latent autoimmune diabetes of adulthood while type 2 diabetes is due to a non-autoimmune progressive loss of adequate b-cell insulin secretion frequently on the background of insulin resistance
- Children with type 1 diabetes often present with the hallmark symptoms of polyuria/polydipsia, and approximately half present with diabetic ketoacidosis (DKA)
- The onset of type 1 diabetes may be more variable in adults; they may not present with the classic symptoms seen in children and may progress to insulin replacement more slowly
- The features most useful in determination of type 1 diabetes include younger age at diagnosis (< 35 years) with lower BMI (< 25 kg/m^2), unintentional weight loss, ketoacidosis, and plasma glucose > 360 mg/dL at presentation
- Three distinct stages of type 1 diabetes have been identified:
  - Stage 1
    - Characteristics: Autoimmunity, normoglycemia, presymptomatic
    - Diagnostic Criteria: Multiple islet autoantibodies, no dysglycemia
  - Stage 2
    - Characteristics: Autoimmunity, dysglycemia, presymptomatic
    - Diagnostic Criteria:
      - Islet autoantibodies (usually multiple)
      - Dysglycemia
        - Fasting plasma glucose 100–125 mg/dL
        - 2-hour post prandial plasma glucose 140–199 mg/dL
        - A1C 5.7–6.4% or ≥ 10% increase in A1C
  - Stage 3
    - Characteristics: Autoimmunity, overt hyperglycemia, symptomatic
    - Diagnostic Criteria: Autoantibodies may become absent, diabetes by standard criteria

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Teplizumab-mzwv is a CD3-directed antibody 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.

References

1. Tzield® [package insert]. Morristown, NJ: Provention Bio Inc.; April 2025.
2. Herold KC, Bundy BN, Long SA, et al. An Anti-CD3 Antibody, Teplizumab, in Relatives at Risk for Type 1 Diabetes [published correction appears in N Engl J Med. 2020 Feb 6;382(6):586]. *N Engl J Med*. 2019;381(7):603-613. doi:10.1056/NEJMoa1902226.
3. American Diabetes Association Professional Practice Committee for Diabetes. 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes-2026. *Diabetes Care*. 2026;49(Supplement_1):S27-S49.

Policy History/Revision Information

Date	Summary of Changes
05/01/2026	**Supporting Information** • Updated *Clinical Evidence*, *FDA*, and *References* sections to reflect the most current information • Archived previous policy version CSPA2025D00117D

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state or contractual requirements for benefit plan coverage govern. Before using this

policy, check the federal, state or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. The UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.