

Tzield® (Teplizumab-Mzwv)

Policy Number: IEX00117.05

Effective Date: September 1, 2023

[U Instructions for Use](#)

Table of Contents	Page
Applicable States	1
Coverage Rationale	1
Applicable Codes	2
Background	2
Clinical Evidence	2
U.S. Food and Drug Administration	3
References	3
Policy History/Revision Information	4
Instructions for Use	4

Related Policies
None

Applicable States

This Medical Benefit Drug Policy applies to Individual Exchange benefit plans in all states except for Massachusetts, Nevada, and New York.

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 or 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 the member specific benefit plan document 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-mzww, 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-mzww is a CD3-directed monoclonal antibody which binds CD3 on the surface of T lymphocytes. Teplizumab-mzww 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-mzww is indicated to delay the onset of Stage 3 type 1 diabetes in adults and pediatric patients 8 years of age and older with Stage 2 type diabetes^{1,2}.

The efficacy of teplizumab-mzww 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-mzww 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-mzww 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-mzww 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-mzww.

Professional Societies

American Diabetes Association (ADA)

In 2023, the ADA published “Standards of Care in Diabetes” 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 care³. 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 and metabolic syndrome
- 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 experience temporary remission from the need for insulin
- The features most useful in discrimination of type 1 diabetes include younger age at diagnosis (< 35 years) with lower BMI (< 25 kg/m²), unintentional weight loss, ketoacidosis, and 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-mzww is indicated to delay the onset of Stage 3 type 1 diabetes in adults and pediatric patients 8 years of age and older with Stage 2 type diabetes.

References

1. Tzield® [package insert]. Red Bank, NJ: Provention Bio Inc.; November 2022.
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. ElSayed NA, Aleppo G, Aroda VR, et al. 2. Classification and Diagnosis of Diabetes: Standards of Care in Diabetes-2023 [published correction appears in *Diabetes Care.* 2023 Feb 01:]. *Diabetes Care.* 2023;46(Suppl 1):S19-S40. doi:10.2337/dc23-S002.

Policy History/Revision Information

Date	Summary of Changes
09/01/2023	<p>Coverage Rationale</p> <ul style="list-style-type: none">● Revised medical necessity criteria:<ul style="list-style-type: none">○ Added criterion requiring the patient does not have symptoms associated with stage 3 type 1 diabetes (e.g., increased urination, excessive thirst, weight loss)○ Removed criterion requiring the patient has a relative with type 1 diabetes○ Replaced criterion requiring:<ul style="list-style-type: none">§ “Tzield is prescribed by an endocrinologist” with “Tzield is prescribed by <i>or in consultation with an endocrinologist</i>”§ “Authorization will be issued for no more than 14 doses” with “authorization will be issued for no more than <i>one treatment course (i.e., 14 doses) per lifetime</i>” <p>Supporting Information</p> <ul style="list-style-type: none">● Archived previous policy version IEX00117.04

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard benefit plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. 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. 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.