STATE OF IOWA DEPARTMENT OF
Health AND Human
SERVICES

Tzield (teplizumab-mzwv)
PAM–082

Iowa Medicaid Program:	Prior Authorization	**Effective Date:**	04/01/2023
Revision Number:	1	**Last Rev Date:**	07/19/2024
Reviewed By:	Medicaid Medical Director	**Next Rev Date:**	04/18/2025
Approved By:	Medicaid Clinical Advisory Committee	**Approved Date:**	07/19/2024

Overview

Medication:[1]	teplizumab-mzwv
Brand Name:	Tzield®
Pharmacologic Category:	Antidiabetic agent; CD3-directed antibody
FDA-Approved Indication(s):	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
How Supplied:	• Single-dose vial, 2 mg/2 mL (1 mg/mL) • Supplied in carton with either 1, 10, or 14 vials
Dosage and Administration:	Administer by IV infusion once daily for 14 consecutive days (body surface area-based dose) • 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 through 14: 1,030 mcg/m^2
Benefit Category:	Medical

Descriptive Narrative

Type 1 diabetes (T1D) is caused by immune-mediated destruction and dysfunction of insulin-producing pancreatic beta cells. Over time, overt insulin insufficiency develops, requiring exogenous insulin therapy. Type 1 diabetes develops on a background of genetic risk, but most individuals with genetic risk never develop type 1 diabetes. In contrast, virtually all individuals with ≥2 diabetes-related autoantibodies eventually develop clinical type 1 diabetes.

Screening for diabetes-related autoantibodies, if followed by appropriate metabolic monitoring, reduces the likelihood of severe hyperglycemia or diabetic ketoacidosis at the time of clinical type 1 diabetes diagnosis. In the clinical setting, most efforts focus on providing diabetes-related autoantibody screening to first- and second-degree relatives of individuals with type 1 diabetes. Autoantibody testing is most critical during early childhood, as the rate of progression from multiple autoantibodies to clinical disease is more rapid in younger individuals. Consequently,

although type 1 diabetes can occur at any age, most research studies have focused on the optimal timing of autoantibody screening in children.[2]

Type 1 diabetes (T1D) has a long preclinical period during which endogenous insulin secretion remains relatively stable, followed by a peridiagnostic period when secretion declines more rapidly. This long preclinical period comprises well-defined stages of disease progression, affording an opportunity to intervene with disease-modifying therapies.

1. **Stage 1 diabetes –** an asymptomatic period defined by seroconversion with the presence of at least two diabetes-related autoantibodies but preserved normoglycemia. This is considered the onset of type 1 diabetes.
2. **Stage 2 diabetes –** characterized by asymptomatic progression to dysglycemia.
3. **Stage 3 diabetes –** onset of clinical disease and is defined by glycemic criteria. Individuals with stage 3 diabetes usually but not uniformly have hyperglycemia-related symptoms.

In individuals with preclinical (stage 1 or stage 2) type 1 diabetes, the goal of disease-modifying therapies is to prevent or delay the onset of clinical disease. In individuals with clinical (stage 3) type 1 diabetes, the goal of disease-modifying therapy is to preserve beta cell function and insulin secretion.[3]

Guidelines

The American Diabetes Association® published updates to the *Standards of Care in Diabetes – 2023* (Standards of Care) on the use of Tzield® in delaying the onset of type 1 diabetes. A grading system developed by the ADA and modeled after existing methods is used to clarify and codify the evidence that forms the basis for the recommendations in the Standards of Care.[4]

Section 2 – Classification and Diagnosis of Diabetes [5]
Updated to refine the diagnostic criteria for type 1 diabetes (T1D) screening in presymptomatic individuals. Individuals testing positive for autoantibodies may meet criteria for intervention with teplizumab in order to delay development of diabetes. • **Recommendation 2.6** – Screening for presymptomatic T1D may be done by detection of autoantibodies to insulin, glutamic acid decarboxylase (GAD), islet antigen 2 (IA-2), or zinc transporter 8 (ZnT8). ➢ Level of evidence: **B** • **Recommendation 2.7** – Having multiple confirmed islet antibodies is a risk factor for clinical diabetes. Testing for dysglycemia may be used to further forecast near-term risk. When multiple islet autoantibodies are identified, referral to a specialized center for further evaluation and/or consideration of a clinical trial or approved therapy to potentially delay development of clinical diabetes should be considered. ➢ Level of evidence: **B** • **Recommendation 2.8** – Standardized islet autoantibody tests are recommended for classification of diabetes in adults who have phenotypic risk factors that overlap with those for type 1 diabetes (e.g., younger age at diagnosis, unintentional weight loss, ketoacidosis, or short time to insulin treatment). ➢ Level of evidence: **E**

Section 3 – Prevention or Delay of Type 2 Diabetes and Associated Comorbidities [6]
Updated to reflect the addition of teplizumab to delay type 1 diabetes (T1D) in certain adults and children at high risk for developing the disease. • **Recommendation 3.2** – In people with preclinical T1D, monitor for disease progression using A1C approximately every 6 months and 75-g oral glucose tolerance test (i.e., fasting and 2-h plasma glucose) annually; modify frequency of monitoring based on individual risk assessment based on age, number and type of autoantibodies, and glycemic metrics. ➢ Level of Evidence: **E** • **Recommendation 3.15** – Teplizumab-mzwv infusion to delay the onset of symptomatic T1D (stage 3) should be considered in selected individuals aged ≥ 8 years with stage 2 T1D. Management should be in a specialized setting with appropriately trained personnel. ➢ Level of Evidence: **B**

ADA evidence-grading system for "Standards of Care in Diabetes"	
A grading system developed by the American Diabetes Association® (ADA) and modeled after existing methods is used to clarify and codify the evidence that forms the basis for the recommendations in the Standards of Care. All of the recommendations in the Standards of Care are critical to comprehensive care regardless of rating. ADA recommendations are assigned ratings of **A**, **B**, or **C**, depending on the quality of the evidence in support of the recommendation. Expert opinion **E** is a separate category for recommendations in which there is no evidence from clinical trials, clinical trials may be impractical, or there is conflicting evidence. Recommendations assigned an **E** level of evidence are informed by key opinion leaders in the field of diabetes (members of the PPC) and cover important elements of clinical care.	
Level of Evidence	Description
A	Clear evidence from well-conducted, generalizable randomized controlled trials that are adequately powered, including: • Evidence from a well-conducted multicenter trial • Evidence from a meta-analysis that incorporated quality ratings in the analysis Supportive evidence from well-conducted randomized controlled trials that are adequately powered, including: • Evidence from a well-conducted trial at one or more institutions • Evidence from a meta-analysis that incorporated quality ratings in the analysis
B	Level of evidence B: Supportive evidence from well-conducted cohort studies, including: • Evidence from a well-conducted prospective cohort study or registry • Evidence from a well-conducted meta-analysis of cohort studies Supportive evidence from a well-conducted case-control study
C	Supportive evidence from poorly controlled or uncontrolled studies, including: • Evidence from randomized clinical trials with one or more major or three or more minor methodological flaws that could invalidate the results • Evidence from observational studies with high potential for bias (such as case series with comparison with historical controls) • Evidence from case series or case reports Conflicting evidence with the weight of evidence supporting the recommendation
E	Expert consensus or clinical experience

Criteria

Prior authorization is required.

Tzield® is considered medically necessary when **ALL** of the following are met:

1. Diagnosis of type 1 diabetes (T1D), stage 2, as confirmed by **ALL** of the following (a, b, and c):
    a. Presence of **TWO** or more of the following pancreatic islet autoantibodies:
        i. Glutamic acid decarboxylase 65 (GAD) autoantibodies; and/or
        ii. Insulin autoantibody (IAA); and/or
        iii. Insulinoma-associated antigen 2 autoantibody (IA-2A); and/or
        iv. Zinc transporter 8 autoantibody (ZnT8A); and/or
        v. Islet cell autoantibody (ICA); **AND**
    b. Abnormal glucose tolerance during an oral glucose-tolerance test (OGTT) within the past 60 days (or alternative glycemic test if an oral glucose-tolerance test is not available) (i, ii, or iii):
        i. Fasting plasma glucose level of 110 to 125 mg/dL (6.1 to 6.9 mmol/L); or
        ii. 2-hour plasma glucose level of 140 to 199 mg/dL (7.8 to 11.1 mmol/L); or
        iii. Postprandial plasma glucose level at 30, 60, or 90 minutes of greater than 200 mg/dL; **AND**
    c. Member does not have symptoms of diabetes (e.g., polyuria, polydipsia, polyphagia); **AND**
2. Member is 8 years of age or older; **AND**
3. Member does **NOT** have a diagnosis of Stage 3 T1D or type 2 diabetes; **AND**
4. Member has not received a previous 14-day course of Tzield®; **AND**
5. Prescribed by, or in consultation with, an endocrinologist; **AND**
6. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed a 14-day course at the following doses:
        i. Day 1: 65 mcg/m^2
        ii. Day 2: 125 mcg/m^2
        iii. Day 3: 250 mcg/m^2
        iv. Day 4: 500 mcg/m^2
        v. Days 5 through 14: 1,030 mcg/m^2 per day; or
    b. Regimen is supported by clinical practice guidelines. Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Tzield® is **NOT** considered medically necessary for continuation of therapy, as it is indicated to be administered as a one-time treatment course only.

Approval Duration and Quantity Limits

Approval Duration	Maximum Dose (based on body surface area of member)
30 days (to allow for 14 total days of treatment)	Not to exceed 14 days of therapy; dose per day as follows: • 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 through 14: 1,030 mcg/m^2 per day

Coding and Product Information

The following list(s) of codes and product information are provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS code is inappropriate.

HCPCS	Description
~~C9149~~	~~Injection, teplizumab-mzwv, 5 mcg~~ *(effective 4-1-23 to 6-30-23)*
J9381	Injection, teplizumab-mzwv, 5 mcg *(effective 7-1-2023)*

ICD-10	Description
E10.1 – E10.9	Type 1 diabetes mellitus

NDC (2 mg/2 mL single-dose vial) (# of SDVs per carton)	Labeler	Dosage	Pkg Size	Pkg Qty	Units/Pkg
73650-0316-01 (1 SDV)	Provention Bio, Inc. (73650)	5 mcg	1	EA	400
73650-0316-10 (10 SDV)	Provention Bio, Inc. (73650)	5 mcg	1	EA	4,000
73650-0316-14 (14 SDV)	Provention Bio, Inc. (73650)	5 mcg	1	EA	5,600

Compliance

1. Should conflict exist between this policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual or as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. Medical necessity guidelines are developed for selected physician-administered medications found to be safe and proven to be effective in a limited, defined population or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

References

[1] Tzield® prescribing information (12/2023). Provention Bio, Inc.: Red Bank, NJ. Available online at: www.tzieldhcp.com. Accessed May 22, 2024.

[2] Greenbaum CJ, Lord S, Speake C. Type 1 diabetes mellitus: Disease prediction and screening. Rubinow K, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed May 30, 2024.

[3] Greenbaum CJ, Lord S, Speake C. Type 1 diabetes mellitus: Prevention and disease-modifying therapy. Rubinow K, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed May 30, 2024.

[4] American Diabetes Association Professional Practice Committee. Introduction and Methodology: Standards of Care in Diabetes-2024. Diabetes Care. 2024 Jan 1;47(Supplement_1):S1-S4. PMID: 38078587.

[5] American Diabetes Association Professional Practice Committee. 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes-2024. Diabetes Care. 2024 Jan 1;47(Suppl 1):S20-S42. PMID: 38078589.

[6] American Diabetes Association Professional Practice Committee. 3. Prevention or Delay of Diabetes and Associated Comorbidities: Standards of Care in Diabetes-2024. Diabetes Care. 2024 Jan 1;47(Suppl 1):S43-S51. PMID: 38078581.

Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

Criteria Change History

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		
Signature			

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		
Signature			

Change Date	Changed By	Description of Change	Version
07/19/2024	CAC	Criteria implementation.	1
Signature William (Bill) Jagiello, DO			

CAC = Medicaid Clinical Advisory Committee