Medical Drug Clinical Criteria

Subject:	Tzield (teplizumab-mzwv)		
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Overview

This document addresses the use of Tzield (teplizumab-mzwv), a CD3-directed antibody approved by the Food and Drug Administration (FDA) to delay the onset of stage 3 type 1 diabetes in adults and pediatric individuals aged 8 years and older with stage 2 type 1 diabetes. Prior to initiating therapy, stage 2 type 1 diabetes must be confirmed by documenting at least two positive pancreatic islet cell autoantibodies as well as dysglycemia without overt hyperglycemia using an oral glucose tolerance test. If an oral glucose tolerance test is not available, an alternative method for diagnosing dysglycemia may be appropriate. It is also important to ensure the clinical history does not suggest type 2 diabetes.

The efficacy of Tzield was studied in a randomized, double-blind, placebo-controlled phase 2 trial in 76 individuals 8 years of age or older. All participants were at risk for development of type 1 diabetes defined by having a relative with type 1 diabetes, presence of at least two diabetes autoantibodies in two samples and evidence of dysglycemia during an oral glucose tolerance test. Tzield was administered as a two week course of daily intravenous therapy. The median time to the diagnosis of type 1 diabetes was 48.4 months in the Tzield group and 24.4 months in the placebo group (95% confidence interval, 0.22 to 0.78; P = 0.006).

The American Diabetes Association (ADA) states the use of Tzield to delay the onset of symptomatic type 1 diabetes (stage 3) should be discussed with select individuals age 8 and older with stage 2 type 1 diabetes. ADA diagnostic criteria for stage 2 includes the presence of multiple islet autoantibodies and dysglycemia defined as a fasting plasma glucose of 100 to 125 mg/dL, a 2-hour postprandial plasma glucose of 140 mg/dL to 199 mg/dL or an A1c of 5.7% to 6.4% or greater than or equal to 10% increase in A1c.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Tzield (teplizumab-mzwv)

Initial requests for Tzield (teplizumab-mzwv) may be approved if the following criteria are met:

I. Individual is 8 years of age or older; **AND**
II. Documentation is provided that individual has stage 2 type 1 diabetes verified by (ADA 2025):
    A. Presence of two or more of the following pancreatic islet cell autoantibodies:
        1. Glutamic acid decarboxylase 65 (GAD) autoantibodies;
        2. Insulin autoantibody (IAA);
        3. Insulinoma-associated antigen 2 autoantibody (IA-2A);
        4. Zinc transporter 8 autoantibody (ZnT8A);
        5. Islet cell autoantibody (ICA);

    AND

    A. Dysglycemia without overt hyperglycemia verified by:
        1. Fasting plasma glucose of 100 to 125 mg/dL; **OR**
        2. 2-hour postprandial plasma glucose of 140 mg/dL to 199 mg/dL; **OR**
        3. Postprandial plasma glucose at 30, 60 or 90 minutes of greater than or equal to 200 mg/dL; **OR**
        4. A1C of 5.7% to 6.4% OR greater than or equal to 10% increase in A1C.

Tzield (teplizumab-mzwv) requests may not be approved for the following:

I. Individual with stage 3 type 1 diabetes; **OR**
II. Individual with clinical history consistent with type 2 diabetes; **OR**

III. Individual with an active serious infection or chronic infection, including but not limited to Epstein-Barr virus or cytomegalovirus; **OR**
IV. May not be approved when the above criteria are not met and for all other indications.

Approval Duration: one 14-day treatment course per lifetime

Quantity Limits

Tzield (teplizumab-mzwv) Quantity Limit

Drug	Treatment Day	Dose
Tzield (teplizumab-mzwv) 2 mg/2 mL vial	Day 1	65 mcg/m^2
	Day 2	125 mcg/m^2
	Day 3	250 mcg/m^2
	Day 4	500 mcg/m^2
	Day 5 - 14	1030 mcg/m^2

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J9381	Injection, teplizumab-mzwv, 5 mcg [Tzield] (teplizumab-mzwv))

ICD-10 Diagnosis

E10.10-E10.9	Type 1 diabetes mellitus

Document History

Revised: 5/16/2025
Document History:

- 5/16/2025 – Annual Review: Revise criteria for stage 2 type 1 diabetes. Coding Reviewed: No changes.
- 5/17/2024 – Annual Review: No changes. Coding Reviewed: No changes.
- 5/19/2023 – Annual Review: Clarify dysglycemia criteria. Wording and formatting changes. Coding Reviewed: Added HCPCS J9381. Removed HCPCS J3490, J3590, C9149. Added ICD-10-CM E10.10-E10.9.
- 11/22/2022 – Select Review: Add new clinical criteria and quantity limit for Tzield. Coding Reviewed: Added HCPCS J3490, J3590. All diagnoses pend. Effective 4/1/2023 Added HCPCS C9149.

References

1. American Diabetes Association (ADA) Professional Practice Committee. 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes—2025. *Diabetes Care.* 2025;48:S27–S49.
2. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: April 13, 2025.
3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
4. Greenbaum CJ, Lord S, Speake C. Type 1 diabetes mellitus: Disease prediction and screening. Last updated: March 25, 2025. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Accessed: April 13, 2025.
5. Herold KC, Bundy BN, Long SA, et al; Type 1 Diabetes TrialNet Study Group. An Anti-CD3 Antibody, Teplizumab, in Relatives at Risk for Type 1 Diabetes. *N Engl J Med*. 2019 Aug 15;381(7):603-613. Available at: https://www.nejm.org/doi/10.1056/NEJMoa1902226. Accessed: April 12, 2025.
6. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc. Updated periodically.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.