Original Effective Date: 03/10/2023
Current Effective Date: 06/28/2025
Last P&T Approval/Version: 04/30/2025
Next Review Due By: 04/2026
Policy Number: C24729-A

Tzield (teplizumab-mzwv)

PRODUCTS AFFECTED

Tzield (teplizumab-mzwv)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Stage 2 type 1 diabetes

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. DELAY ONSET OF STAGE 3 TYPE 1 DIABETES:
   1. Documentation of Stage 2 Type 1 diabetes confirmed by TWO positive pancreatic islet auto antibodies [DOCUMENTATION REQUIRED]
      NOTE: Glutamic acid decarboxylase 65 (GAD) autoantibodies, Insulin autoantibody (IAA), Insulinoma-associated antigen 2 autoantibody (IA-2A), Zinc transporter 8 autoantibody (ZnT8A),

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Islet cell autoantibody (ICA)
AND

2. Documentation of member having dysglycemia without overt hyperglycemia using an oral glucose tolerance test within the last 60 days (if an oral glucose tolerance test is not available, an alternative method for diagnosing dysglycemia without overt hyperglycemia may be appropriate) [DOCUMENTATION REQUIRED]
   NOTE: Dysglycemia defined as a fasting glucose level of 110 to 125 mg/dL (6.1 to 6.9 mmol/L), a 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), or an intervening postprandial glucose level at 30, 60, or 90 minutes of greater than 200 mg/dL on two occasions.
   AND
3. The member's clinical history does not suggest type 2 diabetes

CONTINUATION OF THERAPY:
NA

DURATION OF APPROVAL:
Initial authorization: 3 months (One course of 14 days per member lifetime), Continuation of therapy: NA

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with a board-certified endocrinologist [If prescribed in consultation, consultation notes must be submitted with initial request]

AGE RESTRICTIONS:
8 years of age and older

QUANTITY:
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

PLACE OF ADMINISTRATION:
The recommendation is that infused medications in this policy will be for pharmacy or medical benefit coverage administered in a place of service that is a non-hospital facility-based location as per the Molina Health Care Site of Care program.

Note: Site of Care Utilization Management Policy applies for Tzield (teplizumab-mzwv). For information on site of care, see Specialty Medication Administration Site of Care Coverage Criteria (molinamarketplace.com)

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Intravenous

DRUG CLASS:
Antidiabetic-Anti-CD3 Antibodies

FDA-APPROVED USES:
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

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COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
Over 1.8 million Americans have Type 1 diabetes (T1D), an autoimmune disease caused by the destruction of beta cells. Diagnosis of T1D usually occurs in children and young adults, but it can happen at any age after symptoms appear when a person cannot make enough insulin.
According to the Centers for Disease Control and Prevention (CDC), about 5%–10% of people with diabetes have type 1, which usually develops in children, teenagers, and young adults, but could happen at any age.
Patients who have a genetic susceptibility to developing T1D progress through stages before developing overt hyperglycemia requiring insulin treatment.
• Stage 1 is defined by the appearance of autoantibodies.
• Stage 2 involves dysglycemia
• At Stage 3, autoimmune destruction of beta cells has occurred, so blood glucose is elevated and patients are symptomatic and require insulin treatment.
Eventually, all patients with T1D have to monitor blood sugar levels and are at risk of the same complications as patients with type 2 diabetes (T2D).
The American Diabetes Association (ADA) recommends screening for autoantibodies in patients with first-degree relatives with T1D. The peak age of T1D diagnosis is around 13–14 years, but people can be diagnosed much younger or older. Currently, broad-population screening for T1D does not occur.
Interventions at Stage 1 or Stage 2 may delay the progression to Stage 3 T1D. While islet cell transplantation has been used, this treatment requires lifelong immunosuppression.
However, T1D starts in the body long before any symptoms appear and can be detected at this pre-symptomatic stage through a blood test. The psychological impact of T1D is hard to quantify, but a diagnosis is life-altering, and regular monitoring and maintenance can be extremely stressful. T1D typically takes more than a decade off a person's life, and life expectancy is reduced by 16 years on average for people diagnosed before the age of 10.
Insulin therapy and glucose monitoring are currently the standard of care for treating clinical-stage, or Stage 3 T1D, and are necessary to keep T1D patients alive. The constant monitoring and administration of insulin represents a significant life-long burden for patients.
TZIELD (teplizumab-mzwv) is a CD3-directed antibody indicated to delay the onset of Stage 3 T1D in adults and pediatric patients aged 8 years and older with Stage 2 T1D. TZIELD injection is supplied as a sterile, preservative-free, clear and colorless solution in a 2 mg/2 mL (1 mg/mL) single-dose vial for intravenous use. TZIELD should be administered by intravenous infusion (over a minimum of 30 minutes) once daily for 14 days.

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
TN-10 Study
TZIELD was investigated in the TN-10 Study, a pivotal randomized, double-blind, event driven, placebo controlled clinical trial which evaluated TZIELD for the delay of T1D (Stage 3, or clinical T1D) in Stage 2 T1D patients, defined by the presence of two or more T1D-related autoantibodies and dysglycemia. Seventy-six patients (TZIELD N=44, placebo N=32) were enrolled ages 8 to 49, with 72% under the age of 18, and randomized to receive a single 14-day course of either teplizumab or placebo by IV infusion. The

HIGH RISK ALERT

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primary efficacy endpoint in this study was the time from randomization to development of Stage 3 T1D diagnosis.

In Study TN-10, Stage 3 T1D was diagnosed in 20 (45%) of the TZIELD-treated patients and in 23 (72%) of the placebo-treated patients. A Cox proportional hazards model was used to analyze the time to Stage 3 T1D diagnosis, stratified by age and oral glucose tolerance test status at randomization. The median time from randomization to Stage 3 T1D diagnosis was 50 months in the TZIELD 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 to 0.78; p=0.0066).

The most common adverse reactions (>10%) that occurred during treatment and through 28 days after the last study drug administration from the TN-10 study were lymphopenia (73% TZIELD, 6% Placebo), rash (TZIELD 36%, Placebo 0%), leukopenia (TZIELD 21%, Placebo 0%) and headache (TZIELD 11%, Placebo 6%).

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Tzield (teplizumab-mzwv) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Tzield (teplizumab-mzwv) include: No labeled contraindications.

Exclusions/Discontinuation:
Avoid use of Tzield during pregnancy and at least 30 days prior to planned pregnancy.
Advise patient to receive all age-appropriate vaccinations prior to starting Tzield and avoid concurrent use of live, inactivated, and mRNA vaccines with Tzield.
Use of Tzield is not recommended in patients with certain laboratory abnormalities:

- Lymphocyte count less than 1,000 lymphocytes/mcL
- Hemoglobin less than 10 g/ dL
- Platelet count less than 150,000 platelets/mcL
- Absolute neutrophil count less than 1,500 neutrophils/mcL
- Elevated ALT or AST greater than 2 times the upper limit of normal (ULN)
- Bilirubin greater than 1.5 times ULN

Use of Tzield is not recommended in patients with Laboratory or clinical evidence of acute infection with Epstein-Barr virus (EBV) or cytomegalovirus (CMV)
Use of Tzield is not recommended in patients with Active serious infection or chronic active infection other than localized skin infections

OTHER SPECIAL CONSIDERATIONS:
Do not administer two doses on the same day. If a planned Tzield infusion is missed, resume dosing by administering all remaining doses on consecutive days to complete the 14-day treatment course.

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical*

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Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.

HCPCS CODE	DESCRIPTION
J9381	Injection, teplizumab-mzwv, 5 mcg

AVAILABLE DOSAGE FORMS:
Tzield SOLN 2 mg/2 mL single dose vial

REFERENCES

1. Tzield (teplizumab-mzwv) injection, for intravenous use [prescribing information]. Red Bank, NJ: Provention Bio Inc; December 2023.
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SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Duration of Approval Contraindications/Exclusions/ Discontinuation References	Q2 2025
REVISION- Notable revisions: Required Medical Information Place of Administration Other Special Considerations Coding/Billing Information Available Dosage Forms References	Q2 2024
NEW CRITERIA	QUARTER 1 2023

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