CENTENE Corporation

Clinical Policy: Teplizumab-mzwv (Tzield)

Reference Number: CP.PHAR.492
Effective Date: 11.17.22
Last Review Date: 02.26
Line of Business: Commercial, HIM/ICHRA, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Teplizumab-mzwv (Tzield®) is a CD3-directed antibody.

FDA Approved Indication(s)

Tzield is indicated to:

- Delay the onset of Stage 3 type 1 diabetes (T1D) in adult and pediatric patients 1 year of age and older with Stage 2 T1D
- Delay the decline in endogenous insulin production in pediatric patients aged 8 to 17 years recently diagnosed with Stage 3 T1D*
  **This indication is approved under accelerated approval based on evidence of reduced C-peptide decline. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s)*

Limitation(s) of use:

- There is limited evidence of safety and effectiveness in patients aged 45 years and older with Stage 2 T1D.
- Tzield is not effective as a disease modifying therapy in non-autoimmune dysglycemic conditions.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Tzield is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Stage 2 Type 1 Diabetes (must meet all)**:**

1. Diagnosis of Stage 2 T1D as evidenced by all of the following (a, b, and c):
   a. Presence of 2 or more diabetes-related autoantibodies detected in 2 samples obtained within the last 6 months: anti-insulin autoantibodies (mIAA), islet cell antibodies (ICA), anti-glutamic acid decarboxylase(GAD)65ab, anti-ICA512ab, zinc transporter 8 autoantibody (ZnT8A), insulinoma-associated antigen 2 autoantibody (IA-2A);
   b. Abnormal glucose tolerance during an oral glucose-tolerance test (OGTT) confirmed within the last 7 weeks (i, ii, or iii) (*two confirmatory tests are required for members age ≥ 18 years*):
      i. Fasting plasma glucose ≥ 110 mg/dL, and < 126 mg/dL;

ii. 2 hour plasma glucose ≥ 140 mg/dL, and < 200 mg/dL;
iii. 30, 60, or 90 minute value on OGTT ≥ 200 mg/dL;
c. Member does not have symptoms of diabetes (e.g., polyuria, polydipsia, polyphagia);
2. Prescribed by or in consultation with an endocrinologist;
3. Age ≥ 1 year;
4. Member does not have a diagnosis of Stage 3 T1D or type 2 diabetes;
5. Documentation of member's current body surface area (BSA) (m^2);
6. Dose does not exceed a total of 11,240 mcg/m^2 administered over a 14-day treatment course (*see section V*).

Approval duration: 3 months (one 14-day treatment course only)

B. Recently Diagnosed Stage 3 Type 1 Diabetes (must meet all)**:**
1. Diagnosis of Stage 3 T1D;
2. Diagnosis was made within the last 8 weeks;
3. Diagnosis is confirmed by one of the following (a, b, c, or d):
   a. A1c ≥ 6.5% (≥ 48 mmol/mol);
   b. Fasting plasma glucose ≥ 126 mg/dL (≥ 7.0 mmol/L);
   c. 2-hour plasma glucose ≥ 200 mg/dL (≥ 11.1 mmol/L) during OGTT;
   d. Random plasma glucose ≥ 200 mg/dL (≥ 11.1 mmol/L) during classic symptoms of hyperglycemia (e.g., polyuria, polydipsia, unexplained weight loss) or hyperglycemic crisis;
4. Prescribed by or in consultation with an endocrinologist;
5. Age ≥ 8 years and ≤ 17 years;
6. Presence of at least one T1D-related autoantibody: GAD65 autoantibodies, islet antigen 2 (IA-2) autoantibodies, ZnT8A, ICA, insulin autoantibodies (if testing obtained within first 14 days of insulin treatment);
7. Peak stimulated C-peptide ≥ 0.2 pmol/mL from a 2-hour mixed meal tolerance test performed at least 6 days after diagnosis;
8. Member does not have a diagnosis of Stage 4 T1D or type 2 diabetes;
9. Member has not previously received Tzield for Stage 2 T1D to delay the onset to Stage 3 T1D;
10. Member has not previously received two 12-day treatment courses of Tzield for Stage 3 T1D;
11. Documentation of member's current BSA (m^2);
12. Dose does not exceed a total of 9 mg/m^2 per 12-day treatment course (*see section V*);
13. Request does not exceed a total of two 12-day treatment courses, administered approximately 6 months apart.

Approval duration: 12 months (total of two 12-day treatment courses only)

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of

business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Stage 2 Type 1 Diabetes

1. Continued therapy will not be authorized as Tzield is indicated to be administered as a one-time treatment course only.

Approval duration: Not applicable

B. Recently Diagnosed Stage 3 Type 1 Diabetes

1. Continued therapy will not be authorized as Tzield is indicated to be administered for a total of 2 treatment courses only.

Approval duration: Not applicable

C. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid, or evidence of coverage documents;

B. Stage 4 T1D;
C. Type 2 diabetes.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

BSA: body surface area
CMV: cytomegalovirus
EBV: Epstein-Barr virus
FDA: Food and Drug Administration
GAD: glutamic acid decarboxylase
IA-2: islet antigen 2
IA-2A: insulinoma-associated antigen 2 autoantibody
ICA: islet cell antibodies
mIAA: anti-insulin autoantibodies
OGTT: oral glucose tolerance test
T1D: type 1 diabetes
ZnT8A: zinc transporter 8 autoantibody

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): patients who are immunocompromised or have active viral infection (such as Epstein-Barr virus [EBV] or cytomegalovirus [CMV] infection)
- Boxed warning(s): viral reactivation (Tzield is not recommended in patients with laboratory or clinical evidence of active EBV and CMV infection due to reports of serious, life-threatening cases of viral reactivation)

Appendix D: General Information

- There are 4 recognized stages of T1D:
  - Stage 1: single or transient single diabetes-related autoantibodies, normoglycemia, presymptomatic
  - Stage 2: ≥ 2 diabetes-related autoantibodies, dysglycemia, presymptomatic
  - Stage 3: ≥ 1 diabetes-related autoantibodies, hyperglycemia, symptomatic
  - Stage 4: longstanding T1D
- Treatment of T1D:
  - In 2010, teplizumab failed to meet the primary efficacy endpoint (a composite of total daily insulin usage and A1c level at 12 months) in the phase 3 Protégé study, demonstrating no difference compared to placebo for the treatment of patients with early-onset T1D; however, there was a statistically significant benefit in the secondary endpoint of slowing the decline of C-peptide levels at 24 months .
  - A new phase 3 study for the treatment of early-onset T1D in children and adolescents with newly diagnosed disease (PROTECT, NCT03875729) was completed in 2023. Teplizumab met the primary end point of preservation of β-cell function as measured by stimulated C-peptide levels at 78 weeks, but this did not translate to benefit with regard to the clinical outcomes; there were no significant differences compared to placebo for the secondary end points of insulin doses that were required to meet glycemic goals, glycated hemoglobin levels, time in the target glucose range, and clinically important hypoglycemic events.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Stage 2 T1D	14 day treatment course administered IV QD: • 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 5-14: 1,030 mcg/m^2	11,240 mcg/m^2/ treatment course .
Recently diagnosed Stage 3 T1D	Two 12-day treatment courses administered IV QD approximately 6 months apart: • Day 1: 106 mcg/m^2 • Day 2: 425 mcg/m^2 • Days 3-12: 850 mcg/m^2	9 mg/m^2/ treatment course; 2 treatment courses total .

VI. Product Availability

Single-dose vial: 2 mg/2 mL

VII. References

1. Tzield Prescribing Information. Red Bank, NJ: Provention Bio, Inc; June 2026. Available at: https://www.tzield.com. Accessed June 24, 2026.
2. Insel RA, Dunne JL, Atkinson MA, et al. Staging presymptomatic type 1 diabetes: A scientific statement of JDRF, the Endocrine Society, and the American Diabetes Association. Diabetes Care. 2015; 38(10): 1964-1974.
3. Couper JJ, Haller MJ, Greenbaum CJ, et al. ISPAD clinical practice consensus guidelines 2018: Stages of type 1 diabetes in children and adolescents. Pediatric Diabetes. 2018; 19(S27): 20-27.
4. Mehta S, Ryabets-Lienhard A, Patel N, et al. Pediatric Endocrine Society statement on considerations for use of teplizumab (Tzield™) in clinical practice. Horm Res Paediatr. Published online April 30, 2024. DOI: 10.1159/000538775
5. Philip M, Achenbach P, Addala A, et al. Consensus guidance for monitoring individuals with islet autoantibody-positive pre-stage 3 type 1 diabetes. Diabetes Care. 2024; 47(8): 1276-1298.
6. American Diabetes Association. Standards of medical care in diabetes—2026. Diabetes Care. January 2026; 49(suppl 1): S1-S371. Accessed June 24, 2026.

Prevention of T1DM

7. Herold KC et al. An anti-CD3 antibody, teplizumab, in relatives at risk for type 1 diabetes. New Engl J Med. 2019; 381(7): 603-613. doi: 10.1056/NEJMoa1902226. Epub 2019 Jun 9. Erratum in: N Engl J Med. 2020 Feb 6; 382(6): 586.
8. Provention Bio, Inc. Teplizumab for prevention of type 1 diabetes in relatives "at-risk". Available at: https://clinicaltrials.gov/ct2/show/NCT01030861. Accessed November 6, 2024.
9. Sims EK et al. Teplizumab improves and stabilizes beta cell function in antibody-positive high-risk individuals. Science Translational Medicine. 2021; 13(583): eabc8980.

Treatment of T1DM

10. Sherry N et al. Teplizumab for treatment of type 1 diabetes (Protégé study): 1-year results from a randomized, placebo-controlled trial. Lancet. 2011; 378(9790): 487-497.

11. Hagopian W et al. Teplizumab preserves C-peptide in recent-onset type 1 diabetes: two-year results from the randomized, placebo-controlled Protégé trial. Diabetes. 2013; 62(11): 3901-3908.
12. Herold KC et al. Teplizumab (anti-CD3 mAb) treatment preserves C-peptide responses in patients with new-onset type 1 diabetes in a randomized controlled trial: Metabolic and immunologic features at baseline identify a subgroup of responders. Diabetes. 2013; 62: 3766-3774.
13. Provention Bio, Inc. Recent-onset type 1 diabetes trial evaluating efficacy and safety of teplizumab (PROTECT). Available at: https://clinicaltrials.gov/ct2/show/NCT03875729. Accessed October 21, 2025.
14. Nourelden AZ et al. Safety and efficacy of teplizumab for treatment of type one diabetes mellitus: A systematic review and meta-analysis. Endocr Metab Immune Disord Drug Targets. 2021; 21(10): 1895-1904.
15. Ramos EL, Dayan CM, Chatenoud L, et al. Teplizumab and β-cell function in newly diagnosed type 1 diabetes. N Engl J Med. 2023; 289: 2151-2161.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

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

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2022 annual review: no significant changes as drug is not yet FDA-approved; references reviewed and updated.	03.30.22	08.22
Template changes applied to other diagnoses/indications.	10.03.22	
RT1: drug is now FDA approved – updated criteria per FDA labeling: modified language to refer to various stages of T1D, added that member should not have type 2 diabetes, and revised max dose; added that member should not have symptoms of diabetes; added requirement for documentation of current BSA for dose calculation purposes; references reviewed and updated.	11.21.22	02.23
Added HCPCS code [J9381] and deleted HCPCS code [C9399].	05.24.23	
1Q 2024 annual review: removed HCPCS code [J3590]; updated Appendix D; references reviewed and updated.	10.18.23	02.24
1Q 2025 annual review: added ZnT8A and IA-2A as additional diabetes-related autoantibody options per pivotal study design and specialist feedback; removed requirement for familial history of T1D as lack of familial history does not preclude the diagnosis; added information about PROTECT trial to Appendix D; references reviewed and updated.	11.19.24	02.25

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2026 annual review: no significant changes; references reviewed and updated	11.13.25	02.26
RT4: revised age requirement from ≥ 8 years to ≥ 1 year to reflect pediatric extension and added new boxed warning (viral reactivation) per updated prescribing information.	04.29.26	
RT4: drug is now FDA approved for recently diagnosed Stage 3 T1D – updated criteria per FDA labeling: added upper age limit of 17 years and revised definition of recently diagnosed from 6 to 8 weeks; added new contraindication to Appendix C; added ICHRA line of business; references reviewed and updated.	06.24.26	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible

for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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