

Tziel[™] (teplizumab-mzwv) (Intravenous)

Document Number: IC-0687

Last Review Date: 01/04/2024

Date of Origin: 01/03/2023

Dates Reviewed: 01/2023, 1/2024

I. Length of Authorization

Coverage will be provided for 14 doses and may NOT be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Tziel 2 mg/2 mL single-dose vial: 1 vial daily for 14 days

B. Max Units (per dose and over time) [HCPCS Unit]:

- 400 billable units (2,000 mcg) daily for 14 days

III. Initial Approval Criteria ^{1-3,5}

Coverage is provided in the following conditions:

- Patient is at least 8 years of age; **AND**
- Patient has not received prior therapy with teplizumab; **AND**
- Patient is up to date with all vaccinations, in accordance with current vaccination guidelines, prior to initiating therapy; **AND**
- Patient does not have an active infection, including clinically important localized infections; **AND**
- Patient has been evaluated and screened for the absence of acute infection with Epstein-Barr virus (EBV) or cytomegalovirus (CMV); **AND**
- Patient does not have any of the following laboratory indices:
 - 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; **AND**
- Patient will not receive live or live-attenuated vaccines within 8 weeks OR inactivated or mRNA vaccines within 2 weeks, prior to or during treatment; **AND**

- Therapy will not be used for Type 2 Diabetes Mellitus; **AND**
- Used as single agent therapy; **AND**

Diabetes Mellitus (Type 1) †

- Patient will receive treatment to delay the onset of Stage 3 type 1 diabetes: **AND**
- Patient has a confirmed diagnosis of Stage 2 Type 1 Diabetes as documented by the following:
 - Patient has two or more of the following pancreatic islet cell 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**
 - 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 without overt hyperglycemia may be appropriate*) defined as one of the following:
 - Fasting glucose 110-125 mg/dL
 - 2-hour postprandial plasma glucose 140-199 mg/dL
 - An intervening postprandial glucose level at 30, 60, or 90 minutes of ≥ 200 mg/dL

† FDA Approved Indication(s); ‡ Compendium Recommended Indication(s); Ⓞ Orphan Drug

IV. Renewal Criteria

Coverage cannot be renewed.

V. Dosage/Administration

Indication	Dose
T1DM	Administer Tziel by intravenous infusion (over a minimum of 30 minutes), using a body surface area-based dosing, once daily for 14 consecutive days as follows: <ul style="list-style-type: none"> • 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 Do not administer two doses on the same day. Refer to the prescribing information regarding missed doses.
– Premedicate prior to infusion for the first 5 days of dosing with: (1) a nonsteroidal anti-inflammatory drug (NSAID) or acetaminophen, (2) an antihistamine, and/or (3) an antiemetic. Administer additional doses of premedication if needed.	

VI. Billing Code/Availability Information

HCPCS code:

- J9381 – Injection, teplizumab-mzww, 5 mcg; 1 billable unit = 5 mcg

NDC:

- Tziel 2 mg/2 mL solution for injection as a single-dose vial: 73650-0316-xx

VII. References

1. Tziel [package insert]. Red Bank, NJ; Provention Bio, Inc.; November 2023. Accessed December 2023.
2. Leung SS, Borg DJ, McCarthy DA, et al. Soluble RAGE Prevents Type 1 Diabetes Expanding Functional Regulatory T Cells. *Diabetes*. 2022 Sep 1;71(9):1994-2008. doi: 10.2337/db22-0177.
3. Herold KC, Bundy BN, Long SA, Type 1 Diabetes TrialNet Study Group, et al. An Anti-CD3 Antibody, Teplizumab, in Relatives at Risk for Type 1 Diabetes. *N Engl J Med*. 2019 Aug 15;381(7):603-613. doi: 10.1056/NEJMoa1902226. Epub 2019 Jun 9. Erratum in: *N Engl J Med*. 2020 Feb 6;382(6):586.
4. 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 Oct;38(10):1964-74. doi: 10.2337/dc15-1419.
5. American Diabetes Association Professional Practice Committee; 3. Prevention or Delay of Diabetes and Associated Comorbidities: Standards of Care in Diabetes—2024. *Diabetes Care* 1 January 2024; 47 (Suppl._1): S43–S51. <https://doi.org/10.2337/dc24-S003>

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
E10.8	Type 1 diabetes mellitus with unspecified complications
E10.9	Type 1 diabetes mellitus without complications

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: <https://www.cms.gov/medicare-coverage-database/search.aspx>. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCA/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions

Jurisdiction	Applicable State/US Territory	Contractor
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC