Neighborhood Health Plan OF RHODE ISLAND™
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Tzield™ (teplizumab-mzwv)
(Intravenous)

Effective Date: 8/01/2023
Dates Reviewed: 6/29/2023, 12/7/2023, 01/04/2024, 05/08/2024
Scope: Medicaid, Commercial, Medicare-Medicaid Plan (MMP)

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]:

- Tzield 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. Summary Of Evidence

Tzield is 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. The TN-10 clinical trial enrolled 76 patients 8-49 years of age with stage 2 T1D who were a direct relative of a patient with T1D, had ≥2 autoantibodies, and evidence of dysglycemia. The median time from randomization to Stage 3 T1D diagnosis was 50 months in the Tzield group and 25 months in the placebo group [hazard ratio 0.41 (95% CI: 0.22 to 0.78; p=0.0066)]. Over a median follow-up of 51 months, 20/44 (45%) in Tzield group and 23/32 (72%) in placebo group were diagnosed with stage 3 T1D.

IV. Initial Approval Criteria [1-3]

Coverage is provided in the following conditions:

- Patient is at least 8 years of age; **AND**
- The medication must be prescribed by or in consultation with an endocrinologist; **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**
- Documentation of clinical history of patient does not suggest therapy will be used for Type 2 Diabetes Mellitus; **AND**
- Used as single agent therapy**; AND**
- 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 within the past 6 months:
    - 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) within the past 2 months* defined as:
    - Fasting glucose 100-125 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 on two occasions
  - Member does not have symptoms associated with type 1 diabetes (e.g., increased urination, excessive thirst, weight loss); **AND**
- Documentation of member's current BSA (m^2) and member will not exceed a one-time 14-day treatment course consisting of the dosing schedule referenced in Section V: Dosage/ Administration; **AND**
- *MMP members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements

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

V. Renewal Criteria

Coverage cannot be renewed.

VI. Dosage/Administration

Indication	Dose
T1DM	Administer Tzield by intravenous infusion (over a minimum of 30 minutes), using a body surface area-based dosing, once daily for 14 consecutive days as follows:

	• 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.	

VII. Billing Code/Availability Information

HCPCS code:

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

NDC:

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

VIII. References

1. Tzield [package insert]. Red Bank, NJ; Provention Bio, Inc.; November 2023. Accessed November 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.

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)

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 Determination (NCD), Local Coverage Articles (LCAs) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered 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

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
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

Policy Rationale:

Tzield was reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Tzield according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For INTEGRITY (Medicare-Medicaid Plan) members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.