Policy and Procedure	
PHARMACY PRIOR AUTHORIZATION POLICY AND CRITERIA ORPTCEND079.0425	**ENDOCRINE AND METABOLIC DRUGS** **TZIELD®** (teplizumab-mzwv vial)
Effective Date: 6/1/2025	**Review/Revised Date**: 03/24, 02/25 (JEF)
Original Effective Date: 04/23	**P&T Committee Meeting Date**: 02/23, 04/24, 04/25
Approved by: Oregon Region Pharmacy and Therapeutics Committee	

SCOPE:
Providence Health Plan, Providence Health Assurance, Providence Plan Partners, and Ayin Health Solutions as applicable (referred to individually as "Company" and collectively as "Companies").

APPLIES TO:
Commercial
Medicare Part B
Medicaid

POLICY CRITERIA:

COVERED USES:
All Food and Drug Administration (FDA)-Approved Indications

REQUIRED MEDICAL INFORMATION:
Initial authorization requires all the following be met:

1. Diagnosis of stage 2 type 1 diabetes (meaning that the patient is at risk of developing symptomatic type 1 diabetes) as evidenced by both the following (a and b):
    a. Documentation of the presence of two or more of the following autoantibodies:
        i. Glutamic acid decarboxylase 65 (GAD) autoantibody
        ii. Insulin autoantibody (IAA)
        iii. Insulinoma-associated antigen 2 autoantibody (IA-2A)
        iv. Zinc transporter 8 autoantibody (ZnT8A)
        v. Islet cell autoantibody (ICA)
    b. Abnormal glucose confirmed within the last two months as determined by one of the following:
        i. A 2-hour post prandial blood glucose of 140-199 mg/dL during an oral glucose tolerance test.
        ii. Fasting plasma glucose 100–125 mg/dL. Note: If an oral glucose tolerance test is not available, an alternative method for diagnosing

dysglycemia without overt hyperglycemia may be considered such as fasting plasma glucose.

iii. HbA1c 5.7-6.4% or equal to or greater than 10% increase in HbA1c.

2. Dosing is within FDA-labeled guidelines

EXCLUSION CRITERIA:

- Stage 3 (symptomatic) type 1 diabetes
- Previous treatment with teplizumab (Tzield)

AGE RESTRICTIONS:
May be approved for patients aged eight years and older

PRESCRIBER RESTRICTIONS:
Must be prescribed by, or in consultation with, an endocrinologist

COVERAGE DURATION:
Authorization will be approved for one 14-day treatment course per lifetime

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Requests for indications that were approved by the FDA within the previous six (6) months may not have been reviewed by the health plan for safety and effectiveness and inclusion on this policy document. These requests will be reviewed using the New Drug and or Indication Awaiting P&T Review; Prior Authorization Request ORPTCOPS047.

Requests for a non-FDA approved (off-label) indication requires the proposed indication be listed in either the American Hospital Formulary System (AHFS), Drugdex, or the National Comprehensive Cancer Network (NCCN) and is considered subject to evaluation of the prescriber's medical rationale, formulary alternatives, the available published evidence-based research and whether the proposed use is determined to be experimental/investigational.

Coverage for Medicaid is limited to a condition that has been designated a covered line item number by the Oregon Health Services Commission listed on the Prioritized List of Health Care Services.

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case.

INTRODUCTION:
Teplizumab (Tzield®), is a CD3-directed monoclonal antibody to delay the onset of stage 3 type 1 diabetes in adults and pediatric patients aged eight years and older with stage 2 type 1 diabetes (T1D). Teplizumab is given as a single treatment course of a once daily intravenous infusion given for 14 consecutive days. Administration does not require hospital administration and can be given in an outpatient setting.

FDA APPROVED INDICATIONS:
To delay the onset of stage 3 T1D in adults and pediatric patients aged eight years and older with stage 2 T1D.

POSITION STATEMENT:
Type 1 diabetes (T1D) is due to cell-mediated autoimmune β-cell destruction and requires insulin replacement for survival. Both genetic and environmental factors appear to contribute to the risk of development. It most commonly occurs in children and young adults but can occur at any age. T1D accounts for 5-10% of all cases of diabetes[8]. A family history of T1D is present in about 10-15% of newly diagnosed T1D patients. The risk in general population is about 0.4-1% whereas it is about 5% in individuals with a first-degree relative. Other factors including genetic susceptibility and multiple first-degree relatives with T1D can further increase risk.[6]

Three distinct stages of T1D have been identified. In stage 1 there is autoimmunity, identified by two or more islet autoantibodies, and normoglycemia. In stage 2 there is autoimmunity and dysglycemia such as impaired fasting glucose and/or impaired glucose tolerance. In stage 3 there is autoimmunity and overt hyperglycemia. Individuals in stage 3 are symptomatic requiring insulin replacement and have diabetes by standard diagnosis criteria.[6,8]

The following table from the American Diabetes Association *Standards of Care in Diabetes – 2023*[8] outlines the three distinct stages of type 1 diabetes.

Table 2.1—Staging of type 1 diabetes (12,16)

	Stage 1	Stage 2	Stage 3
Characteristics	• Autoimmunity • Normoglycemia • Presymptomatic	• Autoimmunity • Dysglycemia • Presymptomatic	• Autoimmunity • Overt hyperglycemia • Symptomatic
Diagnostic criteria	• Multiple islet autoantibodies • No IGT or IFG	• Islet autoantibodies (usually multiple) • Dysglycemia: IFG and/or IGT • FPG 100–125 mg/dL (5.6–6.9 mmol/L) • 2-h PG 140–199 mg/dL (7.8–11.0 mmol/L) • A1C 5.7–6.4% (39–47 mmol/mol) or ≥10% increase in A1C	• Autoantibodies may become absent • Diabetes by standard criteria

FPG, fasting plasma glucose; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; 2-h PG, 2-h plasma glucose.

Prospective cohort studies give insight into the risk of developing symptomatic T1D (stage 3 T1D). These studies have included those with increased genetic risk identified through HLA screening in newborns, relatives of those with T1D and individuals in the general population, i.e., no confirmed family history. One study looking at risk of progression to symptomatic T1D in children with two or more islet autoantibodies (stage 1 T1D) found 44% developed symptomatic T1D within five years, 70% within ten years and 85% within fifteen years.[5,8] For individuals with two

or more islet autoantibodies and dysglycemia (stage 2 T1D) there is approximately 60% risk of developing symptomatic T1D within two years and a 75% risk in five years of developing symptomatic T1D. Lifetime risk of developing stage 3 T1D approaches 100% for those with stage 2 T1D.[6] Screening for autoantibodies can identify those at risk of progression to clinical diabetes (stage 3). The Standards of Care in Diabetes from the American Diabetes Association currently recommends screening to detect autoantibodies in the setting of a research study or as an option for individuals with a first-degree family member with T1D[8].

Efficacy data for teplizumab comes from one phase 2 trial (TN-10)[7]. In the TN-10 trial teplizumab delayed the onset of stage 3 type 1 diabetes (T1D) in high-risk patients by a median of two years compared to placebo. The primary endpoint was time from randomization to the clinical diagnosis of diabetes as assessed by oral glucose tolerance test. High risk patients were identified as those with stage 2 T1D (autoimmunity and dysglycemia). Autoimmunity was defined as two or more the following islet autoantibodies: glutamic acid decarboxylase 65 (GAD) autoantibody, insulin autoantibody (IAA), insulinoma-associated antigen 2 autoantibody (IA-2A), zinc transporter 8 autoantibody (ZnT8A) and/or islet cell autoantibody (ICA). Dysglycemia was defined as a fasting plasma glucose of 110 to 125 mg/dL or a 2-hour postprandial plasma glucose of 140–199 mg/dL or an intervening postprandial glucose level at 30, 60, or 90 minutes that was greater than 200 mg/dL. Participants less than 18 years needed to have one abnormal glucose test whereas those 18 years or older needed two abnormal glucose tests, both within 52 days before enrollment.

Most common adverse events were lymphopenia, rash, leukopenia and headache. Lymphopenia was transient and resolved by day 45 in all participants except for one individual.

Potential future uses for teplizumab may include an age range expansion down to two years of age, re-dosing prior to diagnosis of clinical T1D and/or treatment courses after diagnosis of type 1 diabetes. Currently additional treatment courses beyond one 14-day course has not been studied. Teplizumab is currently under investigation in the PROTECT trial (NCT03875729) to determine whether it slows β cell loss and preserves β cell function in those recently diagnosed with T1D in the previous six weeks. At this time there is insufficient evidence to establish safety and efficacy for use in recent onset clinical type 1 diabetes (stage 3).

REFERENCE/RESOURCES:

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5. Ziegler AG, Rewers M, Simell O, *et al*. Seroconversion to multiple islet autoantibodies and risk of progression to diabetes in children. *JAMA*. 2013 Jun 19;309(23):2473-9.
6. 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.
7. Herold KC, Bundy BN, Long SA, *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.
8. ElSayed NA, Aleppo G, Aroda VR, *et al*. Diabetes Technology: Standards of Care in Diabetes-2023. *Diabetes Care*. 2023 Jan 1;46(Supplement_1):S111-S127.
9. Mital S, Nguyen HV. Cost Effectiveness of Teplizumab for Prevention of Type 1 Diabetes Among Different Target Patient Groups. *Pharmacoeconomics*. 2020 Dec;38(12):1359-1372.