BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

EVIDENCE-BASED CRITERIA	**ORIGINAL EFFECTIVE DATE: 07/15/2024**
SECTION: SPECIALTY MEDICAL DRUGS	**LAST REVIEW DATE:**
	CURRENT EFFECTIVE DATE: 07/15/2024
	LAST CRITERIA REVISION DATE:
NEXT ANNUAL REVIEW DATE: 2ND QTR 2025	**ARCHIVE DATE:**

TZIELD™ (teplizumab-mzwv) IV

Non-Discrimination Statement is located at the end of this document.

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Evidence-Based Criteria must be read in its entirety to determine coverage eligibility, if any.

This Evidence-Based Criteria 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 BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Evidence-Based Criteria are subject to change as new information becomes available.

For purposes of this Evidence-Based Criteria, the terms "experimental" and "investigational" are considered to be interchangeable.

EVIDENCE-BASED CRITERIA
SECTION: SPECIALTY MEDICAL DRUGS

ORIGINAL EFFECTIVE DATE: 07/15/2024
LAST REVIEW DATE:
CURRENT EFFECTIVE DATE: 07/15/2024
LAST CRITERIA REVISION DATE:
ARCHIVE DATE:

NEXT ANNUAL REVIEW DATE: 2ND QTR 2025

TZIELD™ (teplizumab-mzwv) IV

Criteria:

Refer to FDA website for current indications and dosage.

- **Criteria for initial therapy:** Tzield (teplizumab-mzwv) is considered ***medically necessary*** to delay onset of stage 3 type 1 diabetes and will be approved when **ALL** the following criteria are met:

  1. Prescriber is physician specializing in the patient's diagnosis or is in consultation with an Endocrinologist

  2. Individual is 8 years of age or older

  3. Individual has a confirmed diagnosis of stage 2 type 1 diabetes with **BOTH** of the following:

     - **TWO** or more of the following pancreatic islet autoantibodies

       a. Glutamic acid decarboxylase 65 (GAD) autoantibodies
       b. Insulin autoantibody (IAA)
       c. Insulinoma-associated antigen 2 autoantibody (IA-2A)
       d. Zinc transporter 8 autoantibody (ZnT8A)
       e. Islet cell autoantibody (ICA)

     - Oral Glucose Tolerance Test (OGTT) in previous 3 months documenting dysglycemia without overt hyperglycemia as confirmed by meeting **ONE** of the following:

       a. Fasting plasma glucose level ≥ 110 to < 126 mg/dL
       b. 2-hour post prandial plasma glucose level ≥ 140 to <200 mg/dL
       c. Intervening postprandial glucose level at 30, 60 or 90 minutes ≥ 200 mg/dL

  4. There is no history of prior Tzield use

  5. Individual has and meets **ALL** the following baseline tests completed before initiation of treatment with continued monitoring as clinically appropriate:

     - Lymphocyte count ≥ 1,000 lymphocytes/µL
     - Hemoglobin ≥ 10 g/dL
     - Platelet count ≥ 150,000 platelets/µL
     - Absolute neutrophil count ≥ 1,500 neutrophils/µL
     - Alanine aminotransferase (ALT) ≤ 2 times the upper limit of normal (ULN)
     - Aspartate aminotransferase (AST) ≤ 2 times the ULN
     - Bilirubin ≤ 1.5 times the ULN

  6. Individual does **NOT** have **ANY** of the following:

     - Type 2 diabetes

TZIELD™ (teplizumab-mzwv) IV

- Active serious or chronic infection, including but not limited to Epstein-Barr virus, cytomegalovirus, Hepatitis B, Hepatitis C, or HIV
- Live-attenuated vaccine administered in the 8 weeks prior to Tzield administration
- Inactivated or mRNA vaccines administered in the 2 weeks prior to Tzield administration
- Pregnancy

Initial approval duration: One 14-day course per lifetime

- Tzield (teplizumab-mzwv) for all other indications not previously listed is considered ***experimental or investigational*** and will not be covered when any **ONE** or more of the following criteria are met:

1. Lack of final approval from the appropriate governmental regulatory bodies (e.g., Food and Drug Administration); or
2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes; or
3. Insufficient evidence to support improvement of the net health outcome; or
4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives; or
5. Insufficient evidence to support improvement outside the investigational setting.

These indications include, *but are not limited to:*

- Use in individuals with Stage 1 type 1 diabetes
- Use in individuals with Stage 3 type 1 diabetes (diagnosis of type 1 diabetes)
- Repeat treatment courses of Tzield
- Treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, or duration.

Description:

Tzield (teplizumab-mzwv) is an anti-CD3 monoclonal antibody indicated to delay the onset of symptomatic disease of stage 3 type 1 diabetes mellitus in adults and pediatric patients 8 years of age or older with stage 2 type 1 diabetes.

Tzield binds to CD3 antigen on CD4+ and CD8+ T cells. This leads to changes in the ratio of circulating T cells which may lead to partial agonistic signaling and deactivation of pancreatic beta cell autoreactive T lymphocytes to delay onset of symptomatic type 1 diabetes mellitus.

Tzield monitoring should include liver enzymes to assess risk and occurrence of cytokine release syndrome (CRS). White blood cell counts should also be monitored during treatment for development of lymphopenia.

Tzield dosing recommendations:
Recommended to administer by intravenous infusion (over a minimum of 30 minutes),

using a body surface area-based dosing, once daily for 14 consecutive days as follows:
• 65 mcg/m2 body surface area (BSA) on Day 1;
• 125 mcg/m2 BSA on Day 2;
• 250 mcg/m2 BSA on Day 3;
• 500 mcg/m2 BSA on Day 4;
• 1,030 mcg/m2 BSA once daily on Days 5 through 14.

Type 1 diabetes (T1D) is a chronic, life-long condition in which there is autoimmune pancreatic beta cell destruction that leads to absolute insulin deficiency. There are multiple autoantibodies that serve as autoimmune markers: islet cell, GAD, zinc transport 8, insulin, and tyrosine phosphatases islet antigen 2 autoantibodies. The rate of beta cell destruction is variable, making the onset of T1D rapid in some and slow in others. If manifested as a child T1D is often characterized by diabetic ketoacidosis (DKA), polyuria, and polydipsia. As adults, it is more common to manifest with modest fasting hyperglycemia until infection or some bodily stress processes it to DKA. People with T1D are also prone to other autoimmune diseases such as vitiligo, Addison disease, celiac disease, and others.

According to the American Diabetes Association, classification of diabetes type is not always straightforward, as various genetic and environmental factors can impact the cause of hyperglycemia in both type 1 and type 2 diabetes. As the incidence of T1D increases, screening for presence of autoantibodies in relatives of those with T1D can effectively identify those who will develop T1D. Once identified, these at-risk individuals can be educated on the symptoms and prevention of DKA and are candidates for Tzield therapy to delay overt diabetes development.

Definitions:

Staging of type 1 diabetes

	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), IGT (impaired glucose tolerance), IFG (impaired fasting glucose), 2-h PG (2 hour plasma glucose)

EVIDENCE-BASED CRITERIA
SECTION: SPECIALTY MEDICAL DRUGS

ORIGINAL EFFECTIVE DATE: 07/15/2024
LAST REVIEW DATE:
CURRENT EFFECTIVE DATE: 07/15/2024
LAST CRITERIA REVISION DATE:
ARCHIVE DATE:

NEXT ANNUAL REVIEW DATE: 2ND QTR 2025

TZIELD™ (teplizumab-mzwv) IV

Criteria for the diagnosis of diabetes in nonpregnant individuals

Meets ONE of the following:	Additional Information
1. A1c ≥ 6.5%.	The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay
2. FPG ≥ 126mg/dl	Fasting is defined as no caloric intake for at least 8 hours
3. 2-hour PG ≥ 200mg/dl during OGTT	The test should be performed as described by the WHO, using glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water
4. In an individual with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥ 200 mg/dl	Random is any time of the day without regard to time since previous meal

DCCT, Diabetes Control and Complications Trial; FPG, fasting plasma glucose; OGTT, oral glucose tolerance test, NGSP, National Glycohemoglobin Standardization Program; WHO, World Health Organization;

Stage 2 type 1 diabetes:
A presymptomatic form of type 1 diabetes where oral glucose tolerance test indicates dysglycemia and can be confirmed by positive type 1 diabetes related autoantibodies.

History:	Date:	Activity:
Pharmacy and Therapeutics Committee	05/16/24	Approved Guideline (effective 07/15/24)
Clinical Pharmacist	05/03/24	Development

Coding:

HCPCS: J9381

TZIELD™ (teplizumab-mzwv) IV

Resources:

Literature reviewed 05/16/24. We do not include marketing materials, poster boards and non-published literature in our review.

1. American Diabetes Association. Standards of care in diabetes – 2023. *Diabetes Care*. 2023;46(Suppl1):S1-S274.

2. Tzield. Prescribing information. Provention Bio, Inc; December 2023. Accessed April 17, 2024.

EVIDENCE-BASED CRITERIA	**ORIGINAL EFFECTIVE DATE: 07/15/2024**
SECTION: SPECIALTY MEDICAL DRUGS	**LAST REVIEW DATE:**
	CURRENT EFFECTIVE DATE: 07/15/2024
	LAST CRITERIA REVISION DATE:
NEXT ANNUAL REVIEW DATE: 2ND QTR 2025	**ARCHIVE DATE:**

TZIELD™ (teplizumab-mzwv) IV

Non-Discrimination Statement:

Blue Cross Blue Shield of Arizona (BCBSAZ) complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability or sex. BCBSAZ provides appropriate free aids and services, such as qualified interpreters and written information in other formats, to people with disabilities to communicate effectively with us. BCBSAZ also provides free language services to people whose primary language is not English, such as qualified interpreters and information written in other languages. If you need these services, call (602) 864-4884 for Spanish and (877) 475-4799 for all other languages and other aids and services.

If you believe that BCBSAZ has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability or sex, you can file a grievance with: BCBSAZ's Civil Rights Coordinator, Attn: Civil Rights Coordinator, Blue Cross Blue Shield of Arizona, P.O. Box 13466, Phoenix, AZ 85002-3466, (602) 864-2288, TTY/TDD (602) 864-4823, crc@azblue.com. You can file a grievance in person or by mail or email. If you need help filing a grievance BCBSAZ's Civil Rights Coordinator is available to help you. You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at: U.S. Department of Health and Human Services, 200 Independence Avenue SW., Room 509F, HHH Building, Washington, DC 20201, 1–800–368–1019, 800–537–7697 (TDD). Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html