Tzield®
(teplizumab-mzwv)
Injection | 2 mg/2mL

Type 1 diabetes screening handbook

A comprehensive guide to early identification of T1D

INDICATION

TZIELD is a CD3-directed monoclonal antibody 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.

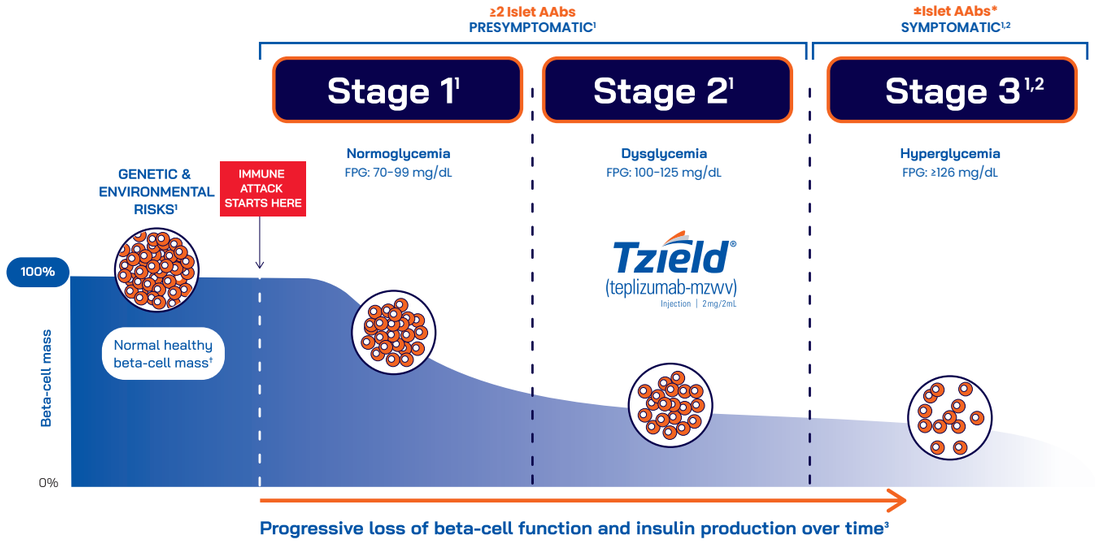
IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

- **Cytokine Release Syndrome (CRS):** CRS occurred in TZIELD-treated patients during the treatment period and through 28 days after the last drug administration. Prior to TZIELD treatment, premedicate with antipyretics, antihistamines and/or antiemetics, and treat similarly if symptoms occur during treatment. If severe CRS develops, consider pausing dosing for 1 day to 2 days and administering the remaining doses to complete the full 14-day course on consecutive days; or discontinue treatment. Monitor liver enzymes during treatment. Discontinue TZIELD treatment in patients who develop elevated alanine aminotransferase or aspartate aminotransferase more than 5 times the upper limit of normal (ULN) or bilirubin more than 3 times ULN.

Autoimmune T1D progression is not a matter of if, but when[1]

T1D occurs in 3 distinct and detectable stages determined by the presence of islet AAbs and glycemic status[1]



When positive for ≥2 islet AAbs, the lifetime risk for progression to Stage 3 T1D approaches 100%[1]

*AAbs may become absent at this stage.[2]
†For illustrative purposes only.
AAbs=autoantibodies; FPG=fasting plasma glucose; T1D=type 1 diabetes.

Presence of ≥2 AAbs in addition to glycemic status determines a patient's Stage of autoimmune T1D[1]

Key characteristics of each stage include:

	Stage 1[1,2,4]	Stage 2[1,2,4]	Stage 3[1,2,4]
Autoimmunity	≥2 autoantibodies	≥2 autoantibodies	± autoantibodies*
Symptoms	No symptoms	No symptoms	Symptomatic†
Glycemic Status	Normoglycemia	Dysglycemia	Hyperglycemia
• Fasting Plasma Glucose	70–99 mg/dL	100–125 mg/dL	≥126 mg/dL
• HbA1c	<5.7%	5.7%–6.4% or ≥10% increase in HbA1c	≥6.5%
• Oral Glucose Tolerance Test	<140 mg/dL	140–199 mg/dL	≥200 mg/dL

TZIELD is a CD3-directed monoclonal antibody 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.[5]

*AAbs may become absent at this stage.[2]
†Classic hyperglycemic symptoms include polyuria, polydipsia, and unexplained weight loss.[2]
HbA1c=hemoglobin A1c.

Certain groups may be at increased risk for autoimmune T1D[6-8]

Experts recommend screening for the following groups:

Relatives of patients with T1D[6]

First-degree family members have a **~15x greater risk** of T1D versus the general public

Those with personal/family history of certain autoimmune diseases, including[7]

- Hashimoto's disease
- Graves' disease
- Celiac disease

Those with abnormal glucose levels[2,8]

Over **40% of adults >30 years of age with T1D are initially diagnosed with T2D** and the risk of error increases with age

Proactive screening helps determine whether abnormal glucose levels are related to an autoimmune attack (type 1) or insulin resistance (type 2)

T2D=type 2 diabetes.

The American Diabetes Association (ADA) recommends screening for 4 islet AAbs[2,5*]

- Glutamic acid decarboxylase 65 AAb **(GADA)**
- Insulinoma-associated antigen 2 AAb **(IA-2A)**
- Insulin AAb **(IAA)**
- Zinc transporter-8 AAb **(ZnT8A)**

Screening identifies those at risk of T1D and gives them the potential to[3,9,10]:

- Reduce the risk of DKA at T1D diagnosis
- Prepare for disease management
- Consider management and treatment options

TZIELD is a CD3-directed monoclonal antibody 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.[5]

*Islet cell AAb (ICA) is also available for testing, but is not recommended as it is an imprecise biological assay.[7]
AAb=autoantibody; DKA=diabetic ketoacidosis.

AAb screening guidance from the Barbara Davis Center for Diabetes[11]

Guidance on initial screening[11]

Children	Adults
Screen during recommended well-child visits to improve feasibility, starting as early as age 1. **Screen at:** ✓ 1-2 years of age ✓ 4-6 years of age ✓ 11-13 years of age	Screen during recommended yearly visits to help improve feasibility.

If negative for AAbs[11]

Children	Adults
• Rescreen patients with increased risk in 1 year • For all other patients, rescreen around 6 years and 9-11 years	• Rescreen patients with increased risk in 1 year

If positive for 1 AAb[12]

Children	Adults
• Conduct confirmatory tests and consider collaborating with specialists • **If <3 years:** rescreen every 6 months for 3 years, then annually for 3 more years – If no additional AAbs, stop AAb screening • **If ≥3 years:** rescreen annually for 3 years – If no additional AAbs, stop AAb screening	• Conduct confirmatory tests • **For patients with increased risk:** to monitor for risk of progression, screen annually • **For all other patients:** repeat screen every 3 years

If positive for ≥2 AAbs, collaborate and/or refer to a specialist based on stage[12]

Monitoring guidance to track disease progression[12]

Patients positive for 1 AAb*†

Children	Adults
• **After first positive screen:** RBG and HbA1c with AAb screening for 2 years	• **Consider annual monitoring** if the patient has a first-degree relative with T1D or elevated T1D genetic risk, dysglycemia, or history of stress hyperglycemia • **If no risk factors,** perform metabolic monitoring every 3 years

Patients with Stage 1 T1D*†

Children	Adults
• **Repeat HbA1c with RBG or 10-14 day CGM:** – **If <3 years of age:** every 3 months – **If 3-9 years of age:** every 6 months – **If >9 years of age:** annually • **To diagnose progression to Stage 2 or Stage 3:** use OGTT or a 2-hour blood glucose test	• **Provide SMBG meters/strips to check glucose with illness or symptoms** • **Repeat HbA1c annually** – Adjust frequency according to individual risk – If HbA1c changes by ≥10%, perform OGTT to stage – If normoglycemic for 5 years, reduce monitoring to every 2 years

Patients with Stage 2 T1D*†

Children	Adults
• **Provide SMBG meters/strips** • **Monitor metabolic status every 3 months**	• **Monitor metabolic status every 6 months using HbA1c and one of the following:** blinded CGM, higher frequency SMBG, or 2-hour plasma glucose following OGTT – If HbA1c changes by ≥10%, perform OGTT to stage • **Consider C-peptide assessment to ensure proper classification**

*Please refer to the full consensus monitoring guidance led by Breakthrough T1D (formerly JDRF) for recommendations on psychological assessment and support for screened patients.
†The full consensus monitoring guidance recommends metabolic monitoring in clinic via the following methods: HbA1c, OGTT, and random BG, plus SMBG at home.
Breakthrough T1D was formerly known as the Juvenile Diabetes Research Foundation (JDRF).
BG=blood glucose; OGTT=oral glucose tolerance test; RBG=random blood glucose; SMBG=self-monitoring blood glucose.

Screening options in your community for those at risk of autoimmune T1D

	TEST	WHERE	ELIGIBILITY	ADA Recommended[2] GADA	IAA	IA-2A	ZnT8A	ICA
Commercial Labs[2,3]	Blood draw	• At commercial lab (eg, Labcorp, Quest Diagnostics) or HCP's office • Results shared with patient and provider	• Any individual with a valid script from a licensed HCP • Cost based on insurance coverage • Most insurance plans cover some or all of the patient cost	✓	✓	✓	✓	✓
Type 1 Diabetes Screening Central	Blood draw or finger stick	• In lab or kit sent to patient from Screening Central telemed practitioner, if appropriate • Via telehealth appointment	• Costs are variable based on service	✓	✓	✓	✓	Varies depending on method of screening
Online Ordering[13,14]	Dried blood spot	• Testing kits can be sent by vendors, such as Enable Biosciences clinical@enablebiosciences.com • Results shared with both patient and provider	• Any individual regardless of family history of T1D • May be processed and covered by insurance • Most insurance plans cover some or all the patient cost	✓	✓	✓		
Autoimmunity Screening for Kids (ASK)[15-17] AskHealth.org	Blood draw or finger stick	• At Barbara Davis Center for Diabetes in Aurora or other Colorado locations • At-home screening kits available for families • Results shared with patient with option for provider	• Any individual (age 1 or older) with or without a family history of T1D • No out-of-pocket costs	✓	✓	✓	✓	
TrialNet[3]*† TrialNet.org/participate	Blood draw or finger stick	• At TrialNet location, event, or health fair • Patient may also administer a kit at home or bring it to Labcorp or Quest Diagnostics • Only patient is notified with results	• Only for those individuals with a family history of T1D with certain age restrictions‡ or those who already tested positive through another program • No out-of-pocket costs	✓	✓	AAb testing available after ≥1 AAbs are found†		

This may not be an exhaustive list of available screening options. The appropriateness of any AAb screening test and the validity of the test results are up to the requesting physician to determine.

*TrialNet will initially test for 2 autoantibodies. If 1 or more autoantibodies are found with the first test, additional testing may be done to screen for other autoantibodies as indicated by the ≥ symbols.[18]
†In screening, a simple blood test is done to screen for the presence of diabetes-related biochemical autoantibodies (GADA and mIAA). Additional autoantibodies ICA, IA-2A, and ZnT8A will also be measured in individuals positive for mIAA. ICA, IA-2A, and ZnT8A will be measured in individuals positive for GADA.[18]
‡TrialNet has an age limit of 2-45 years for first-degree relatives and 2-20 years for second-degree relatives.[19]
mIAA=micro-insulin autoantibodies.

Sample codes for testing*

This is a list of autoimmune T1D codes available as of October 2024; appropriate codes can vary by patient, setting of care, and payer

Determination, verification, and use of correct coding are the sole responsibility of the provider submitting the claim for the item or service. Sanofi does not make any representation or guarantees concerning reimbursement or coverage for any service or item.

CPT® codes for T1D-related pancreatic islet AAb immunoassays[20,21]

Description	Code
Glutamic acid decarboxylase 65 AAb (GADA)†	86341
Insulinoma-associated antigen 2 AAb (IA-2A)†	
Zinc transporter-8 AAb (ZnT8A)†	
Islet cell autoantibody (ICA)	
Insulin autoantibody (IAA)†	86337

CPT® codes for measuring dysglycemia[22]

Description	Code
Glucose tolerance test (GTT), 3 specimens (includes glucose)	82951
Glucose; quantitative, blood (except reagent strip)	82947
Glucose post glucose dose (includes glucose)	82950
Hemoglobin glycosylated (A1c)	83036

ICD-10 codes for T1D-related pancreatic islet AAb testing[23,24]

Description	Code
Type 1 diabetes mellitus	E10.1-E10.9
Type 1 diabetes mellitus, presymptomatic, unspecified	E10.A0
Type 1 diabetes mellitus, presymptomatic, Stage 1	E10.A1
Type 1 diabetes mellitus, presymptomatic, Stage 2	E10.A2
Endocrine disorder, unspecified	E34.9
Encounter for screening for diabetes mellitus	Z13.1
Family history of diabetes mellitus	Z83.3
Family history of other endocrine, nutritional, and metabolic diseases	Z83.49

CPT is the registered trademark of the American Medical Association. Other third-party marks are the property of their respective owners.
*A specific test code may be required in addition to the CPT code. Please confirm which codes are required for your preferred laboratory.
†ADA-recommended pancreatic islet AAbs.
CPT=Current Procedural Terminology; ICD-10=International Classification of Diseases, 10th Revision.

Commercial lab order codes

Quest Diagnostics[25]

Description	Code
Diabetes Type 1 Autoantibody Panel (includes GADA, IA-2A, IAA, and ZnT8A)*	13621
ICA Screen with Reflex to Titer	36741

Labcorp[21]

Description	Code
Diabetes Autoimmune Profile (includes GADA, IA-2A, IAA, and ZnT8A)*	504050
Antipancreatic Islet Cells	160721

The average national out-of-pocket cost for T1D AAb screening is ~$12†

Cost for AAb screening varies by health plan, benefit design, and test.
Please check with the patient's health plan to confirm coverage and out-of-pocket costs.

*ADA-recommended pancreatic islet AAbs.
†n=[15,000]. Analysis has been conducted using LAAD Medical and Remittance data from [January 2024 to December 2024]. Includes commercial claims with one of the following current procedural technology (CPT) codes: 86341 and/or 86337. Note: The analysis does not differentiate between the number of autoantibodies tested within each claim.[26]

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Injection | 2 mg/2mL

TZIELD gives you another reason to proactively screen.[5] Scan to learn more

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

- **Serious Infections:** Use of TZIELD is not recommended in patients with active serious infection or chronic infection other than localized skin infections. Monitor patients for signs and symptoms of infection during and after TZIELD administration. If serious infection develops, treat appropriately, and discontinue TZIELD.
- **Lymphopenia:** Lymphopenia occurred in most TZIELD-treated patients. For most patients, lymphocyte levels began to recover after the fifth day of treatment and returned to pretreatment values within two weeks after treatment completion and without dose interruption. Monitor white blood cell counts during the treatment period. If prolonged severe lymphopenia develops (<500 cells per mcL lasting 1 week or longer), discontinue TZIELD.
- **Hypersensitivity Reactions:** Acute hypersensitivity reactions including serum sickness, angioedema, urticaria, rash, vomiting and bronchospasm occurred in TZIELD-treated patients. If severe hypersensitivity reactions occur, discontinue TZIELD and treat promptly.
- **Vaccinations:** The safety of immunization with live-attenuated (live) vaccines with TZIELD-treated patients has not been studied. TZIELD may interfere with immune response to vaccination and decrease vaccine efficacy. Administer all age-appropriate vaccinations prior to starting TZIELD.
  - Administer live vaccines at least 8 weeks prior to treatment. Live vaccines are not recommended during treatment, or up to 52 weeks after treatment.
  - Administer inactivated (killed) vaccines or mRNA vaccines at least 2 weeks prior to treatment. Inactivated vaccines are not recommended during treatment or 6 weeks after completion of treatment.

ADVERSE REACTIONS

Most common adverse reactions (>10%) were lymphopenia, rash, leukopenia, and headache.

USE IN SPECIFIC POPULATIONS

- **Pregnancy**: May cause fetal harm.
- **Lactation**: A lactating woman may consider pumping and discarding breast milk during and for 20 days after TZIELD administration.

[Please read the accompanying Prescribing Information, including patient selection criteria, and Medication Guide above.]

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