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

Formulary Kit

For appropriate patients with Stage 2 and recently diagnosed Stage 3 type 1 diabetes (T1D) (within the last 8 weeks)

Intended for use with population health decision makers, including formulary committees, pharmacy and therapeutics committees, medical advisory boards, medical directors, and other individuals or entities who have responsibility for the selection of drugs, pursuant to FD&C Act Section 502(a).

INDICATIONS

TZIELD (teplizumab-mzwv) is indicated to:

- Delay the onset of Stage 3 type 1 diabetes (T1D) in adults and pediatric patients 1 year of age and older with Stage 2 T1D.
- Delay the decline in endogenous insulin production in adult and pediatric patients aged 8 to 17 years recently diagnosed with Stage 3 T1D. This indication is approved under accelerated approval based on evidence of reduced C-peptide decline. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

Limitations of Use:

- There is limited evidence of safety and effectiveness in patients aged 45 years and older with Stage 2 T1D.
- TZIELD is not effective as a disease modifying therapy in non-autoimmune dysglycemic conditions.

IMPORTANT SAFETY INFORMATION

WARNING: Viral Reactivation

- **Serious, life-threatening cases of viral reactivation, including Epstein-Barr virus (EBV) and cytomegalovirus (CMV) reactivation have been reported with TZIELD. Patients who are immunocompromised are at increased risk. Serious cases have also been reported in adults with higher body surface area or comorbid conditions, such as adrenal insufficiency or cardiovascular disease. The majority of serious cases occurred in patients who continued TZIELD treatment despite persistent, severe lymphopenia. Severe lymphopenia may be prolonged in adults.**
- **Test patients for active EBV and CMV infection prior to starting treatment. TZIELD is contraindicated in patients who are immunocompromised or have active viral infection (such as EBV or CMV infection). Adhere to lymphocyte count monitoring requirements and discontinuation recommendations. Monitor patients for signs and symptoms of viral reactivation following TZIELD treatment and for at least 2 months following the last infusion. If viral reactivation is suspected, discontinue TZIELD.**

CONTRAINDICATIONS

TZIELD is contraindicated in patients who are immunocompromised or have active viral infection (such as EBV or CMV infection).

Please see additional Important Safety Information throughout and full Prescribing Information, including Boxed WARNING and patient selection criteria.

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Product Profile[1]

Indications

TZIELD is indicated to:

- Delay the onset of Stage 3 type 1 diabetes (T1D) in adults and pediatric patients 1 year of age and older with Stage 2 T1D
- Delay the decline in endogenous insulin production in pediatric patients aged 8 to 17 years recently diagnosed with Stage 3 T1D. This indication is approved under accelerated approval based on evidence of reduced C-peptide decline. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s)

Limitations of Use:

- There is limited evidence of safety and effectiveness in patients aged 45 years and older with Stage 2 T1D
- TZIELD is not effective as a disease modifying therapy in non-autoimmune dysglycemic conditions

Contraindications:

TZIELD is contraindicated in patients who are immunocompromised or have active viral infection (such as EBV or CMV infection).

Description/Mechanism of Action

- TZIELD is a CD3-directed monoclonal antibody (humanized IgG1 kappa) that binds to CD3 (a cell surface antigen present on T lymphocytes) and delays the onset of Stage 3 T1D in adult and pediatric patients aged 1 year and older with Stage 2 T1D and delays the decline in endogenous insulin production in patients 8 to 17 years recently diagnosed with Stage 3 T1D (within the last 8 weeks)
- The mechanism may involve partial agonistic signaling and deactivation of pancreatic beta cell autoreactive T lymphocytes. TZIELD leads to an increase in the proportion of regulatory T cells and of exhausted CD8+ T cells in peripheral blood

CD3 = cluster of differentiation 3; CD8 = cluster of differentiation 8.

IMPORTANT SAFETY INFORMATION (cont'd)

CONTRAINDICATIONS

TZIELD is contraindicated in patients who are immunocompromised or have active viral infection (such as EBV or CMV infection).

WARNINGS AND PRECAUTIONS

Viral Reactivation: Serious, life-threatening cases of viral reactivation, including EBV and CMV infections have been reported with TZIELD. During and within 2 months of TZIELD treatment, if primary infection or reactivation of EBV or CMV occurs, it may present with increased severity, including EBV-associated lymphoproliferative disease and organ failure.

Patients who are immunocompromised, including patients with Down syndrome, may be at increased risk. The majority of serious viral reactivation cases occurred in patients who continued TZIELD despite persistent, severe lymphopenia. The duration of severe lymphopenia following TZIELD treatment may be prolonged in adults. Serious cases have also been reported in adults with higher body surface area or comorbid conditions, such as adrenal insufficiency or cardiovascular disease. (cont)

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Product Profile[1] (cont'd)

Patient Selection

Patients with Stage 2 T1D

- Select adult and pediatric patients 1 year of age and older with Stage 2 T1D for TZIELD treatment to delay the onset of Stage 3 T1D based on the confirmation of:
  - At least 2 positive pancreatic islet cell autoantibodies, and
  - Dysglycemia without overt hyperglycemia using an OGTT:
    - If an OGTT is not available, an alternative method for diagnosing dysglycemia without overt hyperglycemia may be appropriate

In adults aged 18 years or older, recommend following the definition of dysglycemia used in clinical trials to diagnose dysglycemia prior to use of TZIELD due to the lack of specificity of other measures.*

- Ensure the patient's diagnosis confirms an autoimmune origin and does not suggest insulin resistance due to obesity, T2D, or dysglycemia due to other forms of diabetes. These may include, but are not limited to, genetic forms of diabetes, MODY, LADA, or diabetes secondary to medications or surgery

Patients with Stage 3 T1D

- Select pediatric patients aged 8 to 17 years recently diagnosed (within the last 8 weeks) with Stage 3 T1D for TZIELD treatment to delay the decline in endogenous insulin production based on confirmation of:
  - At least 1 positive pancreatic islet cell autoantibody
  - Peak C-peptide ≥0.2 pmol/mL on an MMTT (if an MMTT is not available, an alternative method for measuring peak C-peptide ≥0.2 pmol/mL may be appropriate)

LADA = latent autoimmune diabetes in adults; MMTT = mixed-meal tolerance test; MODY = maturity-onset diabetes of the young; OGTT = oral glucose tolerance test; T2D = type 2 diabetes.

*Dysglycemia without overt hyperglycemia on oral glucose tolerance testing (OGTT) was defined as fasting plasma glucose ≥110mg/dL, and <126 mg/dL or 2 hour plasma glucose ≥140mg/dL, and <200 mg/dL or 30, 60, or 90 minute value on OGTT ≥200 mg/dL. In patients 18 years of age and older: two consecutive OGTTs, each demonstrating dysglycemia without overt hyperglycemia (as defined above) were required.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Viral Reactivation (cont'd):

Prior to initiating treatment with TZIELD, evaluate patients for active EBV and CMV infection and confirm absence of active infection on assessment of viral load (e.g., PCR testing). During treatment with TZIELD, regularly monitor lymphocyte counts and monitor patients for signs and symptoms of viral reactivation during treatment and for at least 2 months following the last infusion. If viral reactivation is suspected, discontinue TZIELD and obtain viral load (e.g., PCR) promptly. If viral reactivation is confirmed, permanently discontinue TZIELD.

Cytokine Release Syndrome (CRS): CRS occurred in TZIELD-treated patients during the treatment period and through 28 days after the last drug administration. Manifestation of CRS in TZIELD-treated patients included fever, nausea (with or without vomiting), fatigue, headache, myalgia, arthralgia, increased ALT, increased AST, and increased total bilirubin. These manifestations typically occurred during the first 5 days of TZIELD treatment. 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 if symptoms have resolved or significantly improved, subsequently administering the remaining doses on consecutive days to complete the full 14-day treatment course in patients with Stage 2 T1D or each of the two 12-day courses in patients with Stage 3 T1D; **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.

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Stage 3 T1D Clinical Data[1]

The safety and efficacy of TZIELD in the treatment of recently diagnosed patients with Stage 3 T1D was investigated in the PROTECT study.

PROTECT study design	A randomized, double-blind, placebo-controlled, multinational, multicenter study
Treatment regimen	Patients were randomized to receive TZIELD or placebo once daily by intravenous infusion for a 12-day course followed by another 12-day course 6 months later (or at approximately 12 months for a subset of 28 patients)
Eligible patients	• 328 patients 8 to 17 years of age recently diagnosed with Stage 3 T1D (within 6 weeks of diagnosis) • This trial enrolled patients with residual beta cell function, as indicated by peak stimulated C-peptide >0.2 pmol/mL on a mixed-meal stimulation test • In the PROTECT study, 43% of patients were female; 86% White, 3% Black or African American, 2% Asian, and 2% reported multiracial background; 6% were Hispanic or Latino ethnicity. The median age was 12 years (42% were <12 years old)
Efficacy endpoint	**Primary endpoint:** Change from baseline in stimulated C-peptide at Week 78, as a marker of beta-cell function

PROTECT Study Efficacy Results

- A statistically significant difference in decline of C-peptide AUC from baseline at Week 78 was observed in TZIELD-treated patients compared to placebo

Change from baseline in C-peptide ln(AUC+1) (pmol/mL) at Week 78 in patients with Stage 3 T1D* (PROTECT study)

	TZIELD (N=217)	Placebo (N=111)
Baseline, mean (SD)	0.54 (0.20)	0.53 (0.17)
Change from baseline, LSMean (95% CI)	0.09 (-0.11, -0.07)	-0.22 (-0.25, -0.18)
Difference from placebo, LSMean (95% CI)	0.13 (0.08, 0.17)*	

*Two-sided $p<.001$.

Notes: Primary analysis; ITT population including all randomized participants. Baseline is defined as the most recent value collected prior to the first dose of study drug. The threshold value of 0.04 µg/L is used to populate below detectable C-peptide values. Missing data at Week 78 [29 (13%) in TZIELD arm; 23 (21%) in placebo arm] are multiply imputed using a pattern-mixture model under the missing not at random assumption. Estimates and the *p*-value are obtained from an ANCOVA model with response variable change from baseline in C-peptide log (AUC +1) at Week 78 that includes treatment, age group at randomization, baseline C-peptide ln(AUC+1), and categorized peak C-peptide as independent variables.

ANCOVA = analysis of covariance; CI = confidence interval; DKA = diabetic ketoacidosis; ITT= intent to treat; ln(AUC+1) = natural logarithm of the area under the curve; LSMean = least squares mean; SD = standard deviation.

PROTECT trial limitations[2]: The trial was complicated by COVID-19, including having to account for missed visits and disrupted data collection; however, dropout rates remained within expectations and impacted treatment and placebo groups equally. While the study population aligned with other T1D trials, most participants were White, which is not representative of patients who report new-onset disease in the general population. DKA rates were lower than typically observed in new-onset T1D cohorts. Complete blinding with this type of biologic agent is challenging, but the primary endpoint was objective and was probably unaffected by the possible unblinding of the trial data to the investigators.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Serious Infections: Bacterial and viral infections have occurred in TZIELD-treated patients. Adults may have a longer duration of severe lymphopenia following TZIELD treatment, which may increase the risk of 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.

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Stage 3 T1D Clinical Data[1] (cont'd)

PROTECT Study Safety Analysis

Adverse reactions occurring in ≥5% of participants in the TZIELD group, higher in TZIELD compared to placebo, in treatment course 1 through 28 days after the last dose.

Adverse Reactions	TZIELD (n=217)	Placebo (n=111)
Course 1		
Lymphopenia*	51%	3%
Rash*	51%	9%
Leukopenia*	34%	3%
Nausea	34%	12%
Headache	29%	16%
Vomiting	26%	5%
Neutropenia*	23%	5%
Abdominal pain *	18%	11%
Pyrexia	16%	3%
Alanine aminotransferase increased	11%	0%
Diarrhea	10%	6%
Cytokine release syndrome	7%	1%
Hypotension	7%	6%
Aspartate aminotransferase increased	7%	1%
Hemoglobin decreased*	5%	4%
Chills	5%	0%

No new adverse reactions were observed with the second course of TZIELD treatment. Incidence rates were similar to those reported during the first treatment course.

In PROTECT:

Serious Adverse Reactions[1]

Throughout the PROTECT study, greater incidences of these serious adverse reactions were reported in TZIELD-treated patients vs placebo-treated patients

- Cytokine release syndrome (9% vs 1%)
- Severe lymphopenia (1.4% vs 0%)

*Grouped term includes other related terms.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

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. Severe lymphopenia (<500 cells per mcL) lasting 1 week or longer has been reported in TZIELD-treated patients.

Severe lymphopenia following TZIELD treatment may be more prolonged in adults. Obtain a CBC prior to starting TZIELD and monitor lymphocyte counts during TZIELD treatment. If prolonged severe lymphopenia develops (<500 cells per mcL lasting 1 week or longer), permanently discontinue TZIELD.

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Stage 2 T1D Clinical Data[1]

TN-10 Study Design

The safety and efficacy of TZIELD in the treatment of adult and pediatric patients ages 8 years and older with Stage 2 T1D was investigated in Study TN-10.

TN-10 study design	A randomized, double-blind, event-driven, placebo-controlled study
Treatment regimen	Patients were randomized to receive TZIELD or placebo once daily by intravenous infusion for 14 days. Patients in the TZIELD group had a total drug exposure that was comparable to the total drug exposure achieved with the recommended total TZIELD dosage
Eligible patients	• 76 patients 8 to 49 years of age with Stage 2 T1D • Stage 2 T1D was defined as having both of the following: – Two or more of the following pancreatic islet 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) – Dysglycemia without overt hyperglycemia on OGTT defined as: • Fasting plasma glucose ≥ 110mg/dL, and <126 mg/dL or • 2-hour plasma glucose ≥140mg/dL, and <200 mg/dL or • 30, 60, or 90 minute value on OGTT ≥200 mg/dL • In patients 18 years of age and older: 2 consecutive OGTTs, each demonstrating dysglycemia without overt hyperglycemia (as defined above) were required • In this study, 45% were female; 97% White, 1% Asian, and 1% reported multiracial background; 3% were Hispanic or Latino ethnicity; and 95% were from the United States. The median age was 14 years: The age range was 8.5 to 49.5 years old (72% were <18 years old; 14% were ≥35 years old)
Primary endpoint	Median time from randomization to development of Stage 3 T1D diagnosis

TN-10 Study Efficacy Results

- In Study TN-10, Stage 3 T1D was diagnosed in 20 (45%) of the patients treated with TZIELD and in 23 (72%) of the placebo-treated patients
- A Cox proportional hazards model, stratified by age and oral glucose tolerance test status at randomization, demonstrated that the median time from randomization to Stage 3 T1D diagnosis was 50 months in the TZIELD group and 25 months in the placebo group, for a difference of 25 months
- With a median follow-up time of 51 months, therapy with TZIELD resulted in a statistically significant delay in the development of Stage 3 T1D, hazard ratio 0.41 (95% CI: 0.22 to 0.78; p=.0066)
- Study TN-10 was not designed to assess whether there were differences in the effectiveness between subgroups based on demographic characteristics or baseline disease characteristics

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

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.

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Stage 2 T1D Clinical Data[1] (cont'd)

TN-10 Adverse Events

The safety and efficacy of TZIELD in the treatment of adult and pediatric patients ages 8 years and older with Stage 2 T1D was investigated in Study TN-10.

Common adverse reactions in adult and pediatric patients 8 years and older in the TN-10 study*,†

Adverse reactions	Placebo (N=32)	TZIELD (N=44)
Lymphopenia‡	6%	73%
Rash‡	0%	36%
Leukopenia‡	0%	21%
Headache	6%	11%
Neutropenia‡	3%	5%
Increased alanine aminotransferase	3%	5%
Nausea	3%	5%
Diarrhea	0%	5%
Nasopharyngitis	0%	5%

The approval of TZIELD was supported by a pooled safety analysis spanning 5 clinical studies, including 773 patients (44 patients with Stage 2 T1D and 729 patients with Stage 3 T1D)[1,§]

Serious Adverse Reactions[1]

- Viral Reactivation
- Cytokine release syndrome
- Serious infections‖
- Lymphopenia
- Hypersensitivity reactions

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

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.

- Inactivated or mRNA vaccinations are not recommended within the 2 weeks prior to any TZIELD treatment course, during treatment, or up to 6 weeks after completion of any treatment course.
- Live-attenuated vaccinations are not recommended within the 8 weeks prior to starting TZIELD treatment, during treatment, between treatment courses, or up to 52 weeks after completion of final treatment course.

*That occurred during treatment and through 28 days after the last study drug administration.
†Adverse reaction that occurred in 2 or more patients treated with TZIELD.
‡Grouped term includes other related terms.
§In these studies, 436 patients received either a 14-day or 12-day dosing regimen of TZIELD with total drug exposure comparable to the recommended dosage (Study TN-10), 168 patients received a 14-day course of TZIELD with lower total drug exposure to TZIELD, and 169 patients received a 6-day course of TZIELD with lower total drug exposure to TZIELD.
‖Serious infections included cellulitis, gastroenteritis, pneumonia, and wound infection any time during or after the first dose of study treatment.

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PETITE-T1D Study Design

The safety of TZIELD was evaluated in a non-randomized, single-arm, open-label, multicenter study in 23 pediatric patients age 1 to less than 8 years with Stage 2 T1D.

Patient characteristic		TZIELD (n=23)
Patients completing 14-day course, %		87
Age at Day 1, years	Median	4.9
	Min, max	1.7, 6.8
Age distribution, %	<2	4.3
	2 to <5	52
	5 to <8	44
Race, %	White	96
	Asian	4
	Hispanic/Latino	13
First-degree relatives with T1D, %		87
Positive for ≥3 islet AAbs, %		87
AAb distribution, %	IAA	87
	ICA	85
	GAD	83
	ZnT8	74
	IA-2A	68
HbA1c at baseline	Median	5.5

PETITE-T1D Adverse Events

- Overall, the safety profile of TZIELD observed in pediatric patients less than 8 years of age with Stage 2 T1D was consistent with that observed in patients aged 8 years and older with Stage 2 T1D
- The most common adverse reactions that occurred in patients less than 8 years of age were
  - Diarrhea (30%)
  - Vomiting (52%)
- Procedure-related venous thrombosis: One TZIELD-treated patient (4.3%) in the PETITE-T1D study experienced a deep vein thrombosis

AAb = autoantibody; HbA1c = glycated hemoglobin.

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Dosing and Administration for TZIELD

TZIELD is administered by IV infusion using BSA-based dosing[1]

Stage 3 T1D recommended dosage and administration

- Initiate treatment as soon as possible following Stage 3 T1D diagnosis but no later than 8 weeks from diagnosis
- Administer TZIELD by IV infusion over a minimum of 30 minutes once daily for 12 consecutive days for each of 2 treatment courses using the BSA-based dosing schedule

	COURSE 1				COURSE 2		
Day	1	2	3-12	Administer the second 12-day treatment course 6 months after the first treatment course. If the second course is delayed, administer the second treatment course within 6 to 12 months after the first treatment course.	1	2	3-12
Dose mcg/m²	106	425	850		106	425	850

Stage 2 T1D recommended dosage and administration

- Administer TZIELD once daily for 14 consecutive days using BSA-based dosing by IV infusion over a minimum of:
  - 30 minutes in adult and pediatric patients ≥8 years
  - 2 hours in pediatric patients aged 1 to <8 years

Day	1	2	3	4	5-14
Dose mcg/m²	65	125	250	**500**	**1030**

How to calculate BSA using the Mosteller formula[3]:

BSA Equation:

$$\text{BSA } (m^2) = \sqrt{\frac{[\text{height (cm)} \times \text{weight (kg)}]}{3600}}$$

Using the patient's BSA, calculate the dose based on treatment day:

Dose (mcg) = Daily dosage (mcg/m²) x BSA (m²)

Administration supplies for TZIELD may include

- One or 2 (depending on calculated dose) of the following:
  - Sterile glass vial(s) with 18 mL of 0.9% Sodium Chloride Injection, **OR**
- ≤50 mL PVC with DEHP infusion bag(s) with 18 mL of 0.9% Sodium Chloride Injection
- Sterile syringe(s) (polypropylene (PP), polycarbonate (PC) or glass)
  - Appropriately sized syringe
- IV catheter
- Routine infusion supplies (eg, needles, gauze, tape, alcohol wipes, tourniquet, etc)

For additional information on dosing and administration of TZIELD, scan the QR code above or click here.

BSA = body surface area; DEHP = di-(2-ethylhexyl) phthalate; IV = intravenous; PVC = polyvinyl chloride.

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Preparing TZIELD for IV Infusion[1]

Preparation Instructions

Using the dose calculated according to BSA, dilute TZIELD prior to preparing the infusion according to the instructions below:

TZIELD Dilution Preparation:

- Prior to dilution, inspect TZIELD visually before use (the supplied solution is clear and colorless). Do not use TZIELD if particulate matter or coloration is seen
- Prepare TZIELD using aseptic technique. Each vial is intended for one-time use only, discard any unused portion
- If the calculated dose is:
  - 2000 mcg or less, then prepare:
    - **One** sterile syringe (PP, PC, or glass) **or**
    - **One** sterile glass vial with 18 mL of 0.9% Sodium Chloride Injection **or**
    - **One** ≤50 mL PVC with DEHP infusion bag with 18 mL of 0.9% Sodium Chloride Injection
  - Greater than 2000 mcg, then prepare:
    - **Two** sterile syringes (PP, PC, or glass) **or**
    - **Two** sterile glass vials with 18 mL of 0.9% Sodium Chloride Injection **or**
    - **Two** ≤50 mL PVC with DEHP infusion bags with 18 mL of 0.9% Sodium Chloride Injection
- Remove the cap from the TZIELD vial — this is the preparation start time
- Remove 2 mL of TZIELD from the single-dose vial and slowly add to the glass vial or PVC with DEHP infusion bag containing 18 mL of 0.9% Sodium Chloride Injection
- Mix gently by slowly swirling the vial or rocking the infusion bag or syringe. The resulting 20 mL diluted TZIELD solution contains 100 mcg/mL of teplizumab-mzwv
- If preparing a dose greater than 2000 mcg, repeat the above process with second TZIELD vial and the glass vial, or PVC with DEHP infusion bag or syringe (PP, PC, or glass) containing 18 mL of 0.9% Sodium Chloride Injection

TZIELD Infusion Solution Preparation:

- Calculate the volume of TZIELD 100 mcg/mL dilution needed for the infusion

$$\text{Volume of 100 mcg/mL dilution (mL)} = \frac{\text{Dose (mcg)}}{\text{100 mcg/mL}}$$

There are 2 different methods for preparation of the infusion: infusion bag (Method 1) or syringe (Method 2, for syringe pump infusion). Use the appropriate steps below depending on the selected method.

METHOD 1: Infusion bag for intravenous administration

- Using an appropriately sized syringe, withdraw the volume of TZIELD 100 mcg/mL dilution required for that day's calculated dose (for a calculated dose 2000 mcg or less) or from both prepared 100 mcg/mL dilutions (for a calculated dose more than 2000 mcg)

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Preparing TZIELD for IV Infusion[1] (cont'd)

Preparation Instructions (cont'd)

TZIELD Infusion Solution Preparation: (cont'd)

METHOD 1: Infusion bag for intravenous administration (cont'd)

- Discard unused portion of remaining TZIELD dilution in the syringe, sterile glass vial or PVC with DEHP infusion bag
- Slowly add contents of the syringe containing the TZIELD dose to a PVC with DEHP infusion bag containing 25 mL of 0.9% Sodium Chloride Injection **(for a calculated dose more than 2000 mcg, add the cumulative volume for the calculated dose to a single infusion bag)**. Gently rock the infusion bag to ensure that the solution mixes sufficiently. Do not shake

Infusion bag administration:

- Prime the IV infusion set with the TZIELD infusion solution. Do not waste any infusion solution during the priming process.
- Infusion administration has a minimum duration of:
  - 30 minutes in adult and pediatric patients aged 8 years and older
  - 2 hours in pediatric patients aged 1 to less than 8 years
- Rate may be slowed for patient's tolerability
- After infusion, flush the IV set with a volume of 0.9% Sodium Chloride Injection greater than or equal to the priming volume, to ensure full dose is administered. Same infusion rate should be used for flushing
- If the TZIELD infusion solution is not used immediately, store at room temperature between 15°C to 25°C (59°F to 77°F). Discard if the infusion is unable to be completed within 6 hours of preparation

METHOD 2: Syringe for intravenous infusion via syringe pump

- Requires an appropriately sized sterile syringe (up to 60 mL) [i.e., infusion syringe] which is compatible with available syringe pump. The syringe pump should support rates as low as 1 mL/hour
- The final concentration range is 15 mcg/mL to 60 mcg/mL with a maximum infusion volume of 60 mL
- To fit technical constraints of syringe pump, a lower volume may be used as long as the concentration is between 15 mcg/mL and 60 mcg/mL

If the calculated dose is:

- 900 mcg or less:
  - Calculate the maximum volume that can be administered for the calculated dose (based on treatment day, dose and patient BSA) using a minimum infusion concentration of 15 mcg/mL

$$\text{Volume}_{\text{Infusion}}(\text{mL}) = \frac{\text{Dose (mcg)}}{\text{Minimum infusion concentration 15 mcg/mL}}$$

  - Calculate the volume of 0.9% Sodium Chloride Injection to be added to the infusion syringe:

$$\text{Volume}_{\text{0.9\% Sodium Chloride Injection}}(\text{mL}) = \text{Volume}_{\text{Infusion}}(\text{mL}) - \text{Volume}_{\text{100 mcg/mL dilution}}(\text{mL})$$

- Greater than 900 mcg: the maximum infusion volume is capped at 60 mL.

$$\text{Volume}_{\text{0.9\% Sodium Chloride Injection}}(\text{mL}) = 60\ \text{mL} - \text{Volume}_{\text{100 mcg/mL dilution}}(\text{mL})$$

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Preparing TZIELD for IV Infusion[1] (cont'd)

Preparation Instructions (cont'd)

TZIELD Infusion Solution Preparation: (cont'd)

For all doses:

- Measure the appropriate volume of 0.9% Sodium Chloride Injection from previous calculation into the infusion syringe
- Using an appropriately sized syringe, withdraw the volume of TZIELD 100 mcg/mL dilution required for that day's calculated dose (for a calculated dose 2000 mcg or less) and add it to the infusion syringe. For a calculated dose more than 2000 mcg, add the cumulative volume from both prepared 100 mcg/mL dilutions to a single infusion syringe
- Gently rock the infusion syringe to ensure that the solution mixes sufficiently. Do not shake

Syringe administration:

- Prime the IV extension set with the TZIELD infusion solution. Do not waste any infusion solution during the priming process
- Attach infusion syringe to a syringe pump
- The infusion must be administered over a minimum of:
  - 30 minutes in adult and pediatric patients aged 8 years and older
  - 2 hours in pediatric patients aged 1 to less than 8 years
- **Do not manually push the syringe**
- Infusion administration rate may be slowed for patient's tolerability
- After infusion, flush the IV extension set with a volume of 0.9% Sodium Chloride Injection greater than or equal to the priming volume at the same infusion rate to ensure full dose is administered
- If the TZIELD infusion solution is not used immediately, store refrigerated at 2°C to 8°C (36°F to 46°F) for up to 12 hours, followed by a maximum of 6 hours at room temperature between 15°C to 25°C (59°F to 77°F) which includes infusion time. Discard if the infusion is unable to be completed within 15 hours of preparation

Compatible Materials for Administration

Compatibility has been demonstrated with the materials listed below. Other materials should not be used.

Compatible Materials for TZIELD Administration

Step	Equipment	Product Contact Material
Initial dilution	Containers	PP, PC, glass, PVC with DEHP IV bag
	Syringes	PP, PC, glass
Infusion with IV bags	IV bags	PVC with DEHP for all doses EVA bags for doses ≥ 240 mcg
	Infusion sets	PVC with DEHP
Infusion with syringe pump	Infusion dilution container	Syringe: PP, PC
	Syringes	PP, PC
	Infusion/extension sets	PE, PVC with or without DEHP

Use of in-line filter is not recommended. If necessary, use a PES filter.
Do not use light protected (colored) infusion sets.

EVA = ethylene-vinyl acetate; PES = polyethylene sulfone.

Please see additional Important Safety Information throughout and full Prescribing Information, including Boxed WARNING and patient selection criteria.

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

Preparing Patients for Infusion With TZIELD[1]

Considerations Before Patients Start TZIELD

Laboratory and infection evaluation prior to initiation

- Prior to initiating TZIELD, obtain a complete blood count and liver enzyme tests
- Use of TZIELD is not recommended in patients with:
  - Lymphocyte count less than 1000 lymphocytes/mcL
  - Hemoglobin less than 10 g/dL
  - Platelet count less than 150,000 platelets/mcL
  - Absolute neutrophil count less than 1500 neutrophils/mcL
  - Elevated ALT or AST greater than 2 times ULN or bilirubin greater than 1.5 times ULN
  - Active serious infection or chronic active infection other than localized skin infections
- Prior to initiating treatment, evaluate patients for active EBV and CMV infection, including assessment of viral load (eg, PCR testing). Consider expert consultation for appropriate laboratory and clinical evaluation to assess for active EBV or CMV infection. Use of TZIELD is contraindicated in patients who are immunocompromised or have active viral infection (such as EBV or CMV infection)

Vaccinations

Administer all age-appropriate vaccinations prior to starting TZIELD:

- Administer live-attenuated (live) vaccines at least 8 weeks prior to TZIELD treatment
- Administer inactivated (killed) vaccines or mRNA vaccines at least 2 weeks prior to treatment

Considerations for Premedication and Monitoring During and After Treatment With TZIELD

Premedication

Prior to each of the first 5 days of TZIELD infusion

- Premedicate with an NSAID or acetaminophen
- Premedicate with an antihistamine, and
- Consider premedication with an antiemetic

If needed, administer additional premedication doses.

Recommended monitoring during and after treatment with TZIELD

- Monitor lymphocyte count regularly (every 2-3 days) during TZIELD infusion, and monitor for lymphocyte recovery following completion of TZIELD
- If prolonged severe lymphopenia (<500 cells per mcL lasting 1 week or longer) develops, permanently discontinue TZIELD
- Monitor patients for signs and symptoms of viral reactivation during TZIELD treatment and for at least 2 months following the last infusion. If viral reactivation is suspected, discontinue TZIELD
- Monitor liver enzymes and bilirubin during treatment. Discontinue TZIELD treatment in patients who develop elevated ALT or AST more than 5 times ULN or bilirubin more than 3 times ULN

ALT = alanine aminotransferase; AST = aspartate aminotransferase; mRNA = messenger ribonucleic acid; NSAID = nonsteroidal anti-inflammatory drug; PCR = polymerase chain reaction; ULN = upper limit of normal.

Please see additional Important Safety Information throughout and full Prescribing Information, including Boxed WARNING and patient selection criteria.

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

Accessing TZIELD

Site of Care

For Stage 2 T1D, TZIELD is administered by intravenous infusion once daily for 14 consecutive days over a minimum of[1]:

- 30 minutes in adult and pediatric patients aged 8 years and older
- 2 hours in pediatric patients aged 1 to less than 8 years

For Stage 3 T1D, TZIELD is administered by intravenous infusion over a minimum of 30 minutes, once daily for 12 consecutive days for each treatment course, for a total of two treatment courses, 6 months apart. TZIELD may be infused in a variety of outpatient settings, depending on patient and provider preference, site of care resources, and payer coverage. For most payers, the site(s) of care will affect the coding and billing requirements.

Infusion scenarios may include

Daily outpatient infusions on each of the treatment days in a doctor's office, a hospital, an infusion center, or other healthcare facility

At-home infusion on each of the treatment days

A hybrid model that begins with outpatient infusions and transitions to at-home infusions for the remainder of the treatment

How to Order TZIELD

- TZIELD is available for purchase from Cardinal Health Specialty Pharmacy Distribution for buy-and-bill treatment centers and through a limited network of specialty pharmacies
- TZIELD is available in single-dose vials through Cardinal Health Specialty Distribution. If a patient will be treated at more than one site of care and you need to discuss other options, contact TZIELD COMPASS directly at 1-844-778-2246 (Monday through Friday, 8 AM–8 PM ET)

Specialty distributor		
Cardinal Health	**P:** 855-740-1867	GMB-SPD-MFGSERVICESSP@cardinalhealth.com
Cardinal Health Puerto Rico	**P:** 787-625-4200 **F:** 787-625-4398	cuserv@cardinalhealth.com

To establish a new account with Cardinal Health Specialty Distribution, call 866-677-4844.

Specialty pharmacies		
Amber™ Specialty Pharmacy	**P:** 888-370-1724	**F:** 877-274-4329
Chartwell Specialty Pharmacy	**P:** 800-366-6020	**F:** 412-920-1869
Orsini® Specialty Pharmacy	**P:** 800-670-5321	**F:** 877-655-4364

Sanofi does not influence or advocate the use of any one product source.
We make no representation or guarantee of service or coverage of any item.

Please see additional Important Safety Information throughout and full Prescribing Information, including Boxed WARNING and patient selection criteria.

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

How Supplied/Storage and Handling

How Supplied[1]

TZIELD injection is supplied as a sterile, preservative-free, clear and colorless solution in a 2 mg/2 mL (1 mg/mL), single-dose vial for intravenous use. Each mL contains 1 mg teplizumab-mzwv, dibasic sodium phosphate (0.26 mg), monobasic sodium phosphate (0.98 mg), polysorbate 80 (0.05 mg), sodium chloride (8.78 mg), and water for injection. The pH is 6.1.

Storage and handling[1]

- **Keep refrigerated** at 36°F to 46°F (2°C to 8°C)
- **Keep TZIELD vial in the original packaging** to protect from light
- **Store upright**
- **DO NOT freeze or shake** the vial
- **Once diluted, it is recommended that the product should be used immediately**
- **Storage of Tzield Infusion Solution:**
  Infusion bag:
  - If the TZIELD infusion solution is not used immediately, store at room temperature between 15°C to 25°C (59°F to 77°F). Discard if the infusion is unable to be completed within 6 hours of preparation.

  Syringe:
  - If the TZIELD infusion solution is not used immediately, store refrigerated at 2°C to 8°C (36°F to 46°F) for up to 12 hours, followed by a maximum of 6 hours at room temperature between 15°C to 25°C (59°F to 77°F) which includes infusion time. Discard if the infusion is unable to be completed within 15 hours of preparation.

NDC Numbers for TZIELD[1]

NDC Number*	Description	WAC†
73650-316-01	1 TZIELD (teplizumab-mzwv) (2 mg/2 mL (1 mg/mL)), single-dose vial	$15,218.05

*Some payers may require an 11-digit NDC code. In such cases, add a 0 in front of the second set of numbers, eg, 73650-316-01 would become 73650-**0316**-01.
†The list price does not reflect discounts, rebates, chargebacks, and other terms or distribution arrangement that may reduce actual sales price. Price as of July 1, 2026. Price subject to change.

NDC = National Drug Code.

Please see additional Important Safety Information throughout and full Prescribing Information, including Boxed WARNING and patient selection criteria.

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

Sample Coding for TZIELD

The following codes may be useful when coding and billing for TZIELD infusion. **Please note that these codes do not include office visits for diagnosis and prescribing of medication.** These codes are provided as examples only and are not all-inclusive; appropriate codes can vary by patient, setting of care, and payer. This guide is not meant to provide medical or legal advice or recommendations regarding the use of specific codes for billing purposes. The provider submitting the claim is solely responsible for determining the medical necessity, appropriate coding, and accuracy of claims. Sanofi does not make any representation or guarantee concerning reimbursement or coverage for any service or item.

Stage 2 T1D ICD-10-CM diagnosis codes[4]

A diagnosis of T1D in Stage 2 patients is required to substantiate the medical necessity of TZIELD. The following codes may be relevant when documenting a patient's **Stage 2** diagnosis.

Condition	Code
Type 1 diabetes mellitus with unspecified complications	E10.8
Type 1 diabetes mellitus without complications	E10.9
Type 1 diabetes mellitus, presymptomatic, unspecified	E10.A0
Type 1 diabetes mellitus, presymptomatic, Stage 2 Confirmed islet autoimmunity with dysglycemia	E10.A2

Stage 3 T1D ICD-10-CM diagnosis codes[4]

A diagnosis of type 1 diabetes in Stage 3 patients is required to substantiate the medical necessity of TZIELD. The following codes may be relevant when documenting a patient's **Stage 3** diagnosis.

Condition	Code
Type 1 diabetes mellitus	E10
Type 1 diabetes mellitus with ketoacidosis	E10.1
Type 1 diabetes mellitus with ketoacidosis without coma	E10.10
Type 1 diabetes mellitus with ketoacidosis with coma	E10.11
Type 1 diabetes mellitus other specified complications	E10.6
Type 1 diabetes mellitus with hyperglycemia	E10.65
Type 1 diabetes mellitus with unspecified complications	E10.8
Type 1 diabetes mellitus without complications	E10.9

ICD-10-CM = International Classification of Diseases, 10th Revision, Clinical Modification; NOS = not otherwise specified.

Please see additional Important Safety Information throughout and full Prescribing Information, including Boxed WARNING and patient selection criteria.

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

Sample Coding for TZIELD (cont'd)

Stage 2 T1D & Stage 3 T1D HCPCS code for TZIELD[5]

TZIELD is billed under an HCPCS J-code.

Description	Code
Injection, teplizumab-mzwv, 5 mcg	J9381

When billing for TZIELD with HCPCS code J9381, 1 unit represents 5 mcg of TZIELD. TZIELD should be billed based on units, not the number of micrograms.

Utilization of the J-code is required when billing for TZIELD. Please ensure the billing system at your organization has been updated accordingly to support accurate coding and billing processes.

Stage 2 T1D & Stage 3 T1D Administration procedure CPT® codes[6]

Description	Code
IV infusion, for therapy, prophylaxis, or diagnosis; initial, up to 1 hour	96365
+ each additional hour (list separately in addition to code for primary procedure; report 96366 for infusion intervals of greater than 30 minutes beyond 1-hour increments)	+96366
Chemotherapy administration, intravenous technique; up to 1 hour, single or initial substance/drug	96413*
+ each additional hour (use 96415 in conjunction with 96413; report 96415 for infusion intervals of greater than 30 minutes beyond 1-hour increments)	+96415
Home infusion/specialty drug administration, per visit (up to 2 hours)	99601

*TZIELD is an anti-CD3, humanized, monoclonal antibody.[1] TZIELD is not chemotherapy, however, some payers may utilize these codes in the reimbursement process. For payers who do not recognize TZIELD as approved for chemotherapy administration code 96413, other administration codes, such as 96365, may be used depending on individual payer policy.

CPT = Current Procedural Terminology; HCPCS = Healthcare Common Procedure Coding System.

Please see additional Important Safety Information throughout and full Prescribing Information, including Boxed WARNING and patient selection criteria.

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

Sample Coding for TZIELD (cont'd)

Stage 2 T1D & **Stage 3 T1D** Home infusion HCPCS codes[5]

Description	Code
Home infusion therapy, chemotherapy infusion; administrative services, professional pharmacy services, care coordination, and all necessary supplies and equipment (drugs and nursing visits coded separately), per diem (do not use this code with S9330 or S9331)	S9329*
Home infusion therapy, infusion therapy, not otherwise classified; administrative services, professional pharmacy services, care coordination, and all necessary supplies and equipment (drugs and nursing visits coded separately), per diem	S9379

For additional information on coding and billing for TZIELD, scan the QR code at left or click here.

*TZIELD is an anti-CD3, humanized, monoclonal antibody.[1] TZIELD is not chemotherapy, however, some payers may utilize these codes in the reimbursement process. For payers who do not recognize TZIELD as approved for chemotherapy administration code 96413, other administration codes, such as 96365, may be used depending on individual payer policy.

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

Sample Codes for Testing

Stage 2 T1D & Stage 3 T1D ICD-10-CM codes for T1D-related pancreatic islet autoantibody testing[4]

Description	Code
Type 1 diabetes mellitus	E10.1-E10.9
Type 1 diabetes mellitus, presymptomatic, unspecified	E10.A0
Endocrine disorder, unspecified	E34.9
Encounter for general adult medical examination without abnormal findings Encounter for adult health check-up NOS	Z00.00
Encounter for screening for diabetes mellitus	Z13.1
Family history of diabetes mellitus Conditions classifiable to E08-E13	Z83.3
Family history of other endocrine, nutritional, and metabolic diseases	Z83.49

Stage 2 T1D & Stage 3 T1D CPT codes for T1D-related pancreatic islet autoantibody immunoassays[6,7]

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

IMPORTANT SAFETY INFORMATION (cont'd)

ADVERSE REACTIONS

Most common adverse reactions were lymphopenia, vomiting, rash, leukopenia, diarrhea, neutropenia, increased liver transaminase and headache.

Please see additional Important Safety Information throughout and full Prescribing Information, including Boxed WARNING and patient selection criteria.

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

Sample Codes for Testing (cont'd)

Stage 3 T1D CPT code for C-peptide testing

Prior to initiating TZIELD, confirm that the patient recently diagnosed with **Stage 3 T1D** (within the last 8 weeks) has C-peptide levels ≥0.2 pmol/mL[1] using an MMTT or alternative method if appropriate and MMTT is not available.

Description	Code
C-peptide test[6]	84681*,†

CPT codes for glycemic testing[6]

Stage 2 T1D

In adults aged 18 years or older, recommend following the definition of dysglycemia used in clinical trials to diagnose dysglycemia prior to use of TZIELD due to the lack of specificity of other measures. In the TN-10 trial, in patients 18 years of age and older: two consecutive OGTTs, each demonstrating dysglycemia without overt hyperglycemia were required.[1]

Stage 3 T1D

Confirm overt hyperglycemia using an A1C, FPG, or 2-hour plasma glucose test.[1,8] In the absence of unequivocal hyperglycemia results from a single test, diagnosis requires abnormal results from 2 different tests which may be obtained at the same time (eg, A1C and FPG), or the same test at 2 different time points.[8]

Description	Code
Glucose tolerance test (GTT), 3 specimens (includes glucose)[8]	82951*
Glucose; quantitative, blood (except reagent strip)[8]	82947‡
Glucose post glucose dose (includes glucose)[8]	82950§
Hemoglobin glycosylated (A1C)[8]	83036

*Measured at 30-, 60-, and 90-minute time points.[8]
†If drawing a mixed-meal tolerance test, codes 82951 and 82952 may be appropriate.
‡Also known as fasting plasma glucose.[8]
§Measured at 2 hours post glucose.[8]

IMPORTANT SAFETY INFORMATION (cont'd)

USE IN SPECIFIC POPULATIONS

- **Pregnancy:** May cause fetal harm. To minimize exposure to a fetus, avoid use of TZIELD during pregnancy and at least 30 days prior to planned pregnancy. Report pregnancies to us at our Adverse Event reporting line at 1-800-633-1610 or visit https://ae.reporting.sanofi
- **Lactation:** A lactating woman may consider pumping and discarding breast milk during and for 20 days after TZIELD administration.

Please see additional Important Safety Information throughout and full Prescribing Information, including Boxed WARNING and patient selection criteria.

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

Integrating TZIELD Into Electronic Health Record Order Sets

For health systems that choose to update their electronic health record (EHR) to include TZIELD information and orders, this section outlines the information that may be considered for inclusion in order sets with TZIELD. This information is specific to TZIELD and will not work for other conditions, treatments, or therapeutic areas.

Treatment selection is always a decision made by the healthcare provider, and order sets may be overridden to reflect this. The processes outlined in this piece are variable, as not all steps apply to every customer. Any steps or settings that are not part of a customer's standard process should be excluded or modified accordingly. Any questions should be directed to the EHR vendor.

Updating order sets requires minimal time but must be implemented at the system level. It may be necessary to complete the individual components of the order set first to compiling them in the final order set

Suggested content to include in order sets

- Accurate diagnosis codes for TZIELD and other autoimmune disorders[4,9]
- Patient vital signs[10]
- Family history of T1D[10]
- Dosage and administration information for TZIELD[1]
- Treatment conditions, including laboratory evaluation and vaccination prior to initiation[1]
- Warnings and precautions, including patient selection[1]
- Adverse reactions management[10]
- Premedications[1]
- Immunizations[1,10]

Nursing order sets may also include:

- Dosing and administration guidance[1]
- Recommendations regarding missed doses[1]
- Preparation and administration instructions[1]
- IV access information[10]

For additional information on how to integrate TZIELD into EHR and workflows, scan the QR code at left or click here.

Please see additional Important Safety Information throughout and full Prescribing Information, including Boxed WARNING and patient selection criteria.

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

Educational and Personalized Support

Tzield® COMPASS

TZIELD COMPASS supports patients with a collaborative, comprehensive team

Field Reimbursement Managers (FRMs) offer providers education on:

- TZIELD payer policies, coverage, and reimbursement
- Best practices for prior authorization (PA) submissions and appeals
- Product procurement options
- Considerations for navigating sites of care and scheduling infusions

Clinical Educators (CEs) offer providers education and training on:

- TZIELD infusion process and dosing
- Infusion coordination and scheduling
- Nursing order sets

COMPASS Navigators provide one-on-one support to patients, including:

- Help navigating TZIELD product access, including the PA process and scheduling of infusions
- Education on insurance benefits, potential out-of-pocket costs, and potential financial assistance options
- Information on financial assistance options like the TZIELD Copay Program* and Patient Assistance Program (PAP)

Helping patients navigate treatment cost and coverage

Copay Support

Eligible commercially insured patients may pay as little as

$0 for TZIELD

*Not valid for prescriptions covered by or submitted for reimbursement under Medicare, Medicaid, VA, DoD, TRICARE, or similar federal or state programs including any state pharmaceutical programs. Not valid where prohibited by law. Sanofi reserves the right to modify or terminate the Copay Program at any time without notice. Any savings provided by the Copay Program may vary depending on patients' out-of-pocket costs. Upon registration, patients receive all program details.

Eligibility requirements and terms and conditions apply. Click here for more information.

For more information on the TZIELD COMPASS program offerings, scan the QR code at left or click here.

Please see additional Important Safety Information throughout and full Prescribing Information, including Boxed WARNING and patient selection criteria.

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

Informational Resources

Clinical and operational information for TZIELD

Dosing and Administration

For additional information on the dosing, preparation, and administration of TZIELD, scan the QR code or click download below.

Download

Distribution Network

To learn more about the distribution network for TZIELD, please scan the QR code or click download below.

Download

EHR Integration

For additional information on how to integrate TZIELD into EHR and workflows, scan the QR code or click download below.

Download

Billing and Coding Guide for TZIELD

For additional information on the coding and billing of TZIELD, scan the QR code or click download below.

Download

TZIELD COMPASS

For additional information on the TZIELD COMPASS Patient Support Program, scan the QR code or click download below.

Download

Please see additional Important Safety Information throughout and full Prescribing Information, including Boxed WARNING and patient selection criteria.

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

Important Safety Information

CONTRAINDICATIONS

TZIELD is contraindicated in patients who are immunocompromised or have active viral infection (such as EBV or CMV infection)

WARNINGS AND PRECAUTIONS

Viral Reactivation: Serious, life-threatening cases of viral reactivation, including EBV and CMV infections have been reported with TZIELD. During and within 2 months of TZIELD treatment, if primary infection or reactivation of EBV or CMV occurs, it may present with increased severity, including EBV-associated lymphoproliferative disease and organ failure.

Patients who are immunocompromised, including patients with Down syndrome, may be at increased risk. The majority of serious viral reactivation cases occurred in patients who continued TZIELD despite persistent, severe lymphopenia. The duration of severe lymphopenia following TZIELD treatment may be prolonged in adults. Serious cases have also been reported in adults with higher body surface area or comorbid conditions, such as adrenal insufficiency or cardiovascular disease.

Prior to initiating treatment with TZIELD, evaluate patients for active EBV and CMV infection and confirm undetectable viral load (e.g., PCR testing). TZIELD is not recommended in patients with laboratory or clinical evidence of active EBV or CMV infection. During treatment with TZIELD, regularly monitor lymphocyte counts and monitor patients for signs and symptoms of viral reactivation during treatment and for at least 2 months following the last infusion. If viral reactivation is suspected, discontinue TZIELD and obtain viral load (e.g., PCR) promptly. If viral reactivation is confirmed, permanently discontinue TZIELD.

Cytokine Release Syndrome (CRS): CRS occurred in TZIELD-treated patients during the treatment period and through 28 days after the last drug administration. Manifestation of CRS in TZIELD-treated patients included fever, nausea (with or without vomiting), fatigue, headache, myalgia, arthralgia, increased ALT, increased AST, and increased total bilirubin. These manifestations typically occurred during the first 5 days of TZIELD treatment. 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.

Serious Infections: Bacterial and viral infections have occurred in TZIELD-treated patients. Adults may have a longer duration of severe lymphopenia following TZIELD treatment, which may increase the risk of 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. Severe lymphopenia (<500 cells per mcL) lasting 1 week or longer has been reported in TZIELD-treated patients.

Severe lymphopenia following TZIELD treatment may be more prolonged in adults. Obtain a CBC prior to starting TZIELD and monitor white blood cell counts during TZIELD treatment. If prolonged severe lymphopenia develops (<500 cells per mcL lasting 1 week or longer), permanently 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.

Please see additional Important Safety Information throughout and full Prescribing Information, including Boxed WARNING and patient selection criteria.

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

Important Safety Information (cont'd)

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 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.
- Administer live vaccines at least 8 weeks prior to treatment. Live vaccines are not recommended during treatment, or up to 52 weeks after treatment.

ADVERSE REACTIONS

Most common adverse reactions were lymphopenia, vomiting, rash, leukopenia, diarrhea, neutropenia, increased liver transaminase and headache.

USE IN SPECIFIC POPULATIONS

- **Pregnancy:** May cause fetal harm. To minimize exposure to a fetus, avoid use of TZIELD during pregnancy and at least 30 days prior to planned pregnancy. Report pregnancies to us at our Adverse Event reporting line at 1-800-633-1610 or visit https://ae.reporting.sanofi
- **Lactation:** A lactating woman may consider pumping and discarding breast milk during and for 20 days after TZIELD administration.

Please see full Prescribing Information, including Boxed WARNING and patient selection criteria.

References: 1. TZIELD Prescribing Information. Provention Bio, Inc. **2.** Ramos EL, Dayan CM, Chatenoud L, et al. Teplizumab and β-cell function in newly diagnosed type 1 diabetes. *N Engl J Med*. 2023;389(23):2151-2161. **3.** Mosteller RD. Simplified calculation of body-surface area. *N Engl J Med*. 1987;317(17):1098. doi:10.1056/NEJM198710223171717. **4.** CMS. 2025 ICD-10-CM tabular list of diseases and injuries. Accessed June 11, 2026. https://www.cms.gov/medicare/coding-billing/icd-10-codes. **5.** CMS. HCPCS Quarterly Update: April 2025. Updated May 21, 2026. Accessed June 11, 2026. https://www.cms.gov/medicare/coding-billing/healthcare-common-procedure-system/quarterly-update. **6.** American Medical Association. CPT® 2025 Professional Edition. American Medical Association; 2024. **7.** Simmons KM, Steck AK. American Association for Clinical Chemistry. Islet autoantibody testing. Published July 1, 2017. Accessed June 11, 2026. https://www.myadlm.org/cln/articles/2017/july/islet-autoantibody-testing-predicting-and-diagnosing-type-1-diabetes. **8.** American Diabetes Association Professional Practice Committee. Diagnosis and classification of diabetes: standards of care in diabetes—2025. *Diabetes Care*. 2025;48(suppl 1):S27-S49. **9.** Popoviciu MS, Kaka N, Sethi Y, et al. Type 1 diabetes mellitus and autoimmune diseases: A critical review of the association and the application of personalized medicine. *J Pers Med*. 2023;13(3):422. **10.** Mehta S, Ryabets-Lienhard A, Patel N, et al. Pediatric Endocrine Society Statement on Considerations for Use of Teplizumab (Tzield™) in Clinical Practice. *Horm Res Paediatr*. Published online April 30, 2024. doi:10.1159/000538775.

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