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

DOSING AND ADMINISTRATION GUIDE FOR TZIELD® (teplizumab-mzwv)

TZIELD is supplied as a clear and colorless solution in a single-dose vial.[1]

Administer **TZIELD** by intravenous (IV) infusion (over a minimum of 30 minutes), using a body surface area (BSA)-based dosing, once daily for 14 consecutive days.[1]

INDICATION

TZIELD® (teplizumab-mzwv) 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.

Please see additional Important Safety Information throughout.
Please see full Prescribing Information, including Patient Selection Criteria, and Medication Guide.

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

INTRODUCTION

This guide includes information on dosing, preparation, and administration of TZIELD, and other important topics to discuss with your patients and their caregivers.

TABLE OF CONTENTS

Please see additional Important Safety Information throughout.
Please see full Prescribing Information, including Patient Selection Criteria, and Medication Guide.

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

PROPOSED MECHANISM OF ACTION OF TZIELD

TZIELD specifically binds to CD3 antigens present on the surface of T lymphocytes.[1]

TZIELD binds to CD3 molecules on the surface of both CD4+ and CD8+ T cells during treatment, with internalization of the TZIELD/CD3 complex from the surface of T cells

The mechanism may involve partial agonistic signaling and deactivation of pancreatic beta (β) 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; CD4+ = cluster of differentiation 4 positive; CD8+ = cluster of differentiation 8 positive.

IMPORTANT SAFETY INFORMATION (cont.)

WARNINGS AND PRECAUTIONS (cont.)

- **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.

Please see additional Important Safety Information throughout.
Please see full Prescribing Information, including Patient Selection Criteria, and Medication Guide.

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

RECOMMENDED DOSING FOR TZIELD[1]

TZIELD is administered by IV infusion (over a minimum of 30 minutes) once daily for 14 consecutive days.

The recommended TZIELD dosage for adults and pediatric patients aged 8 years and older uses body surface area (BSA)-based dosing and is administered according to the following regimen:

- **Day 1:** 65 mcg/m^2
- **Day 2:** 125 mcg/m^2
- **Day 3:** 250 mcg/m^2
- **Day 4:** 500 mcg/m^2
- **Days 5-14:** 1030 mcg/m^2

TZIELD is a clear and colorless solution supplied in a 2 mg/2 mL, single-dose vial.

DOSING REGIMEN

Day 1	Day 2	Day 3	Day 4	Days 5-14
65 mcg/m^2	125 mcg/m^2	250 mcg/m^2	500 mcg/m^2	1030 mcg/m^2

CALCULATION

How to calculate BSA using the Mosteller formula[2]:

BSA Equation:

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

Example: Male, 8 years old = 120 cm, 26 kg

$$\text{BSA } (m^2) = \sqrt{\frac{(120)(26)}{3600}} = 0.931 \text{ m}^2$$

When calculating BSA, round to the 100th using standard rounding rules. (example: 0.93 m^2).

Based on BSA dosing requirements, 2 vials may be needed for some individuals (BSA > 1.94m^2) for days 5-14.

RECOMMENDATIONS REGARDING MISSED DOSES

If a planned TZIELD infusion is missed, resume dosing by administering all remaining doses on consecutive days to complete the 14-day treatment course. Do not administer 2 doses on the same day.

Please see additional Important Safety Information throughout.
Please see full Prescribing Information, including Patient Selection Criteria, and Medication Guide.

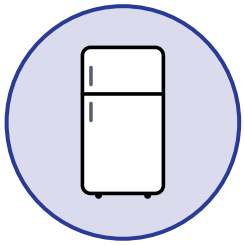
Tzield®
(teplizumab-mzwv)
Injection | 2 mg/2mL

HOW TZIELD IS SUPPLIED[1]

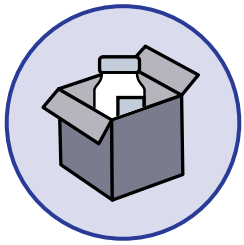
TZIELD is supplied as a sterile, preservative-free, clear, and colorless solution in a 2 mg/2 mL, single-dose vial.

2 mg/2 mL, single-dose vial

STORING AND HANDLING TZIELD[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 shake or freeze the vial

If not used immediately, store the infusion solution at room temperature [15°C to 30°C (59°F to 86°F)] and complete infusion within 4 hours of the start of preparation

Discard the infusion solution if not administered within 4 hours of preparation

Please see additional Important Safety Information throughout.
Please see full Prescribing Information, including Patient Selection Criteria, and Medication Guide.

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

PREPARING PATIENTS FOR THEIR TZIELD INFUSION[1]

Advise your patients and their caregivers to read the FDA-approved Medication Guide and inform them of the following prior to infusion:

PATIENT COUNSELING FOR TZIELD:

Cytokine Release Syndrome (CRS)
Inform patients about the signs and symptoms of CRS, such as fever, nausea, feeling tired (fatigue), headache, muscle and joint pain, and increased liver enzymes in the patient's blood.

Serious Infections
Inform patients that TZIELD may lower the ability of the immune system to fight infections and that they should tell their healthcare provider if they develop any symptoms of infection. Inform patients that you may temporarily or completely stop their treatment with TZIELD if they have a serious infection.

Lymphopenia
Inform patients that although most TZIELD-treated patients had mild lymphopenia; a few had severe lymphopenia that required stopping TZIELD. Lymphopenia is a decrease in white blood cells that can affect the body's ability to fight infections. A decrease in white blood cell counts can happen after the first dose. White blood cell counts will start to go back to normal after the fifth dose of TZIELD.

Hypersensitivity Reactions
Advise patients on the symptoms of hypersensitivity reactions (difficulty breathing, swelling of the face, rash, or hives) and instruct them to stop taking TZIELD and seek medical attention promptly if such symptoms occur.

Vaccinations
TZIELD may affect how well a vaccine works. Advise patients to receive all age-appropriate vaccinations prior to starting TZIELD and avoid concurrent use of live, inactivated, and mRNA vaccines with TZIELD. Inactivated or mRNA vaccines are not recommended 6 weeks after treatment. Live-attenuated vaccines are not recommended up to 52 weeks after treatment.

Pregnancy
Advise patients that TZIELD may harm their unborn baby and to inform their healthcare provider of a known or suspected pregnancy. Advise patients that they should not receive TZIELD during pregnancy and at least 30 days before a planned pregnancy.

Advise patients who are exposed to TZIELD during pregnancy to contact Provention Bio, Inc.'s Adverse Event reporting line at 1-800-633-1610.

Lactation
Advise a lactating woman that she may interrupt breastfeeding and pump and discard breast milk during treatment and for 20 days after TZIELD administration in order to minimize drug exposure to a breastfed infant. It is not known if TZIELD passes into the breast milk or if it can harm the baby.

FDA = US Food and Drug Administration; mRNA = messenger ribonucleic acid.

Please see additional Important Safety Information throughout.
Please see full Prescribing Information, including Patient Selection Criteria, and Medication Guide.

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

PREPARING PATIENTS FOR THEIR TZIELD INFUSION[1] (cont.)

CONSIDERATIONS BEFORE PATIENTS START TZIELD:

Laboratory 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 the upper limit of normal (ULN) or bilirubin greater than 1.5 times ULN
  - Laboratory or clinical evidence of acute infection with Epstein-Barr virus (EBV) or cytomegalovirus (CMV)
  - Active serious infection or chronic active infection other than localized skin infections

Vaccinations

Administer all age-appropriate vaccinations prior to starting TZIELD:

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

Premedication

Premedicate prior to TZIELD infusion for the first 5 days of dosing with medications including: (1) a nonsteroidal anti-inflammatory drug (NSAID) or acetaminophen, (2) an antihistamine, and/or (3) an antiemetic. Administer additional doses of premedication if needed.

ALT = alanine aminotransferase; AST = aspartate aminotransferase.

ADMINISTRATION SUPPLIES FOR TZIELD MAY INCLUDE:

- A vial of TZIELD*
- A sterile glass vial or PVC infusion bag
- 0.9% Sodium Chloride Injection for use as a sterile diluent
- Syringes of various sizes
- 25 mL 0.9% Sodium Chloride Injection PVC infusion bag
- IV catheter
- Routine infusion supplies (eg, needles, gauze, tape, alcohol wipes, tourniquet, etc)

*A patient may need more than 1 vial (for BSA ≥1.94 m^2).

Please see additional Important Safety Information throughout.
Please see full Prescribing Information, including Patient Selection Criteria, and Medication Guide.

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

INFUSION PREPARATION FOR TZIELD[1]

1. Inspect TZIELD visually before use (the supplied solution is clear and colorless). Do not use TZIELD if particulate matter or coloration is seen.

2. Prepare TZIELD using aseptic technique. Each vial is intended for single dose only. Prepare a sterile glass vial with 18 mL of 0.9% Sodium Chloride Injection **or** polyvinylchloride (PVC) infusion bag with 18 mL of 0.9% Sodium Chloride Injection.

3. Remove 2 mL of TZIELD from the vial and slowly add to the 18 mL of 0.9% Sodium Chloride Injection. Mix gently by slowly inverting the vial or rocking the infusion bag. The resulting 20 mL diluted solution contains 100 mcg/mL of TZIELD.

4. Using an appropriately sized syringe (e.g., 5 mL), withdraw the volume of diluted TZIELD solution required for that day's calculated dose from the 100 mcg/mL solution.

5. Slowly add contents of the syringe containing the TZIELD dose to a 25 mL 0.9% Sodium Chloride Injection PVC infusion bag. Gently rock the infusion bag to ensure that the solution mixes sufficiently. Do not shake.

6. Discard unused portion of remaining diluted TZIELD solution in the sterile glass vial or PVC infusion bag.

7. Start the TZIELD infusion within 2 hours of preparation. If not used immediately, store the infusion solution at room temperature [15°C to 30°C (59°F to 86°F)] and complete infusion within 4 hours of the start of preparation. Discard the infusion solution if not administered within 4 hours of preparation.

8. When the TZIELD infusion solution has been completely administered, infuse an additional volume of 0.9% sodium chloride solution for injection (i.e., normal saline) equal to the volume contained in the infusion tubing at the same constant rate as TZIELD infusion to ensure that all the medication has been given.

EXAMPLE

Dose 1

$65\ mcg/m^2 \times 0.93\ m^2$ (BSA) = 60.45 mcg

60.45 mcg ÷ 100 mcg/mL (dilution concentration) = 0.6045 mL

→ Round to 1 decimal place using standard rounding

→ Add 0.6 mL of TZIELD 100 mcg/mL dilution to final container of 25 mL 0.9% sodium chloride solution

ADMINISTERING TZIELD[1]

Administer TZIELD as an IV infusion over a minimum period of 30 minutes each day once daily for 14 consecutive days.

Please see additional Important Safety Information throughout.
Please see full Prescribing Information, including Patient Selection Criteria, and Medication Guide.

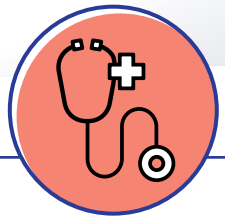
Tzield®
(teplizumab-mzwv)
Injection | 2 mg/2mL

MONITORING FOR ADVERSE REACTIONS WITH TZIELD[1]

Throughout the course of treatment, monitor for

- **Cytokine release syndrome**
  - Premedicate with antipyretics, antihistamines, and/or antiemetics prior to TZIELD treatment
  - Monitor liver enzymes during treatment. Discontinue TZIELD treatment in patients who develop elevated ALT or AST more than 5 times upper limit of normal or bilirubin more than 3 times upper limit of normal
  - Treat symptoms of CRS with antipyretics, antihistamines, and/or antiemetics. If severe CRS develops, consider temporarily pausing dosing for 1 to 2 days (and administer the remaining doses to complete the full 14-day course on consecutive days) or discontinuing treatment
- **Serious infections**
  - Monitor patients for signs and symptoms of infection during and after TZIELD treatment. If serious infection develops, treat appropriately, and discontinue TZIELD
- **Lymphopenia**
  - Monitor white blood cell counts during the treatment period. If prolonged severe lymphopenia (<500 cells per mcL lasting 1 week or longer) develops, discontinue TZIELD
- **Hypersensitivity reactions**
  - If severe hypersensitivity reactions occur, discontinue use of TZIELD and treat promptly

Please see additional Important Safety Information throughout.
Please see full Prescribing Information, including Patient Selection Criteria, and Medication Guide.



Individuals should be closely monitored for the development of signs and symptoms of adverse reactions during and after receiving TZIELD, including

- Cytokine release syndrome
- Serious infections
- Lymphopenia
- Hypersensitivity reactions

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

FREQUENTLY ASKED QUESTIONS

DOSING[1]

1. WHAT IS THE RECOMMENDED DOSE OF TZIELD?

TZIELD dosing is based on BSA and administered according to the following 14-day regimen:

- Day 1: 65 mcg/m^2
- Day 2: 125 mcg/m^2
- Day 3: 250 mcg/m^2
- Day 4: 500 mcg/m^2
- Days 5-14: 1030 mcg/m^2

2. WHAT HAPPENS IF A PATIENT MISSES A DOSE?

If a planned infusion of TZIELD is missed, resume dosing by administering all remaining doses on consecutive days to complete the 14-day treatment course. Do not administer 2 doses on the same day.[1]

3. IS THERE ANY NEED FOR DOSAGE ADJUSTMENTS, TEMPORARY PAUSING OR PERMANENT DISCONTINUATION?

Dosing is calculated based on BSA. There are no additional recommended dosing adjustments in the FDA-approved label. If severe CRS develops, consider temporarily pausing TZIELD. TZIELD should be discontinued in those that develop elevated ALT or AST more than 5 times the upper limit of normal or bilirubin more than 3 times ULN. If prolonged severe lymphopenia develops lasting one week or longer, discontinue TZIELD. If serious infection develops, discontinue TZIELD. If severe hypersensitivity reactions occur, discontinue use of TZIELD and treat promptly.

4. SHOULD I EXPECT ANY WASTAGE FOR TZIELD AND CAN IT BE USED FOR ANOTHER PATIENT?

Discard unused dilution solution and infusion solution. The unused solutions should not be used for another patient.

INFUSION PREPARATION AND ADMINISTRATION

5. IN WHICH SITES OF CARE CAN TZIELD BE ADMINISTERED?

Depending on insurance coverage and other factors, you and your patient can evaluate which of the following infusion site location options is appropriate. Options could include hospital outpatient departments, clinics, ambulatory infusion centers, or in the patient's home.

6. HOW FAR IN ADVANCE OF ADMINISTRATION CAN I PREPARE THE PRODUCT FOR INFUSION?

Prepare the infusion solution to be able to complete the infusion within 4 hours of preparation.[1]

7. CAN NON-PVC BAGS BE USED FOR INFUSION?

Only PVC should be used for TZIELD infusions.[1] For more information, contact TZIELD COMPASS by calling 1-844-778-2246 Monday through Friday, 8 AM-8 PM ET.

Please see additional Important Safety Information throughout.
Please see full Prescribing Information, including Patient Selection Criteria, and Medication Guide.

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

FREQUENTLY ASKED QUESTIONS (cont.)

SAFETY

8. IF A PATIENT IS EXPERIENCING CYTOKINE RELEASE SYNDROME, WHAT IS THE RECOMMENDED PROTOCOL?

Treat symptoms of CRS with antipyretics, antihistamines, and/or antiemetics. If severe CRS develops, consider temporarily pausing dosing for 1 to 2 days (and administer the remaining doses to complete the full 14-day course on consecutive days) or discontinuing treatment.[1]

9. IF YOU DELAY TREATMENT BY A DAY DUE TO SIDE EFFECTS, HOW QUICKLY CAN YOU RESUME? CAN I RESUME TREATMENT LATER IN THE DAY?

Please refer to the Prescribing Information for guidance related to adverse reactions, temporarily pausing dosing and resuming treatment or discontinuing treatment.[1]

10. WHO SHOULD I CONTACT IF A PATIENT EXPERIENCES AN ADVERSE REACTION?

To report suspected adverse reactions, contact Provention Bio at 1-800-633-1610 or the FDA at 1-800-FDA-1088 or **www.fda.gov/medwatch**.

ADDITIONAL SUPPORT

11. WHO CAN I CONTACT FOR QUESTIONS ABOUT PRODUCT ORDERING?

TZIELD is available through a limited distribution network. For more information, call TZIELD COMPASS at 1-844-778-2246 Monday through Friday, 8 AM-8 PM ET, fax at 908-425-4840, email Compass@sanofi.com, or visit **https://tzieldhcp.com/patient-support**.

12. WHO CAN I CONTACT FOR QUESTIONS ABOUT PRODUCT DOSING AND ADMINISTRATION?

To help prepare for treatment administration, a Clinical Nurse Educator can provide your infusion site team with education and training for TZIELD. In-person and/or virtual training will be provided once you have:

- Prescribed TZIELD for your patient, or
- Identified TZIELD as an appropriate treatment for your patient

For more information, call TZIELD COMPASS at 1-844-778-2246 Monday through Friday, 8 AM-8 PM ET, fax at 908-425-4840, email Compass@sanofi.com, or visit **https://tzieldhcp.com/patient-support**.

Please see additional Important Safety Information throughout.
Please see full Prescribing Information, including Patient Selection Criteria, and Medication Guide.

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.
- **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 see additional Important Safety Information throughout.
Please see full Prescribing Information, including Patient Selection Criteria, and Medication Guide.

FOR MORE INFORMATION OR QUESTIONS ABOUT DOSING AND ADMINISTRATION FOR TZIELD

CALL
TZIELD COMPASS at
1-844-778-2246 Monday through Friday,
8 AM-8 PM ET

EMAIL
Compass@sanofi.com

FAX
908-425-4840

VISIT
https://tzieldhcp.com/patient-support

References: 1. TZIELD. Prescribing Information. Provention Bio, Inc. **2.** Mosteller RD. Simplified calculation of body-surface area. *N Engl J Med*. 1987;317(17):1098. doi: 10.1056/NEJM198710223171717.

sanofi

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