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

Infusion Preparation Guidebook

A step-by-step guide to help you prepare and administer TZIELD with confidence

INDICATION

TZIELD is indicated to delay the onset of Stage 3 type 1 diabetes (T1D) in adult and pediatric patients 1 year of age and older with Stage 2 T1D.

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.

Preparing TZIELD for infusion[1]

There are 2 methods for intravenous (IV) administration:

Infusion bag for IV administration

Syringe for IV infusion via syringe pump

- **There are 2 different methods for preparation of the infusion: infusion bag (Method 1) or syringe (Method 2, for syringe pump infusion). Use appropriate steps below depending on the selected method**
- **Review all instructions to ensure the correct method-specific pathway is followed**

Administration supplies

Before you start preparing TZIELD for infusion, ensure that you have all the essential supplies.

Ensure you have the appropriate amount of each of the following[1]:

- ☐ Vial(s) of TZIELD
- ☐ Sterile glass vial **or** sterile polyvinylchloride (PVC) with di-(2-ethylhexyl)phthalate (DEHP) infusion bag **or** sterile syringe (polypropylene [PP], polycarbonate [PC], or glass)
- ☐ Sterile diluent (0.9% sodium chloride for injection)
- ☐ Appropriately sized syringe

Additional supplies required if using the infusion bag for IV administration[1]:

- ☐ PVC with DEHP infusion bag containing 25 mL of 0.9% sodium chloride injection
- ☐ PVC with DEHP infusion set
- ☐ Ethylene vinyl acetate (EVA) bags for doses ≥240 mcg

Additional supplies required if using a syringe for IV infusion via syringe pump[1]:

- ☐ Syringe for IV infusion compatible with available syringe pump
- ☐ Syringe pump (should support rates as low as 1 mL/hour)
- ☐ IV infusion/extension sets

Read this entire section carefully before preparing TZIELD.[1]

- **Must dilute TZIELD prior to use.** This requires the preparation of 100 mcg/mL dilution followed by the preparation of an infusion solution
- Start the infusion after preparation is complete
- If the TZIELD infusion solution is not used immediately, store as instructed per corresponding infusion preparation method

BSA=body surface area; IV=intravenous.

Preparing your patient's dose[1]

	Day 1	Day 2	Day 3	Day 4	Day 5-14
Stage 2 T1D	65 mg/m²	125 mcg/m²	250 mcg/m²	500 mcg/m²	1030 mcg/m²

- ☐ Calculate patient's BSA using the Mosteller formula before treatment.

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

- ☐ Using the patient's BSA, calculate the dose based on treatment day.

$$\text{Dose (mcg)} = \text{Daily dosage level } \left(\frac{\text{mcg}}{m^2}\right) \times \text{BSA } (m^2)$$

- ☐ Calculate the volume of 100 mcg/mL TZIELD solution to be further diluted.

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

TZIELD 100 mcg/mL Dilution Preparation[1]:

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 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

If the calculated dose is **greater than 2000 mcg,** then prepare:

- 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

Prepare 18 mL of 0.9% sodium chloride injection in one of the following[1]:

- **Sterile glass vial**
- **Sterile syringe (PP, PC, or glass)**
- **Sterile PVC with DEHP infusion bag**

- ☐ 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 sterile syringes (PP, PC or glass), 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 TZIELD.
- ☐ 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.

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS

Viral Reactivation: Serious, life-threatening cases of viral reactivation, including EBV and CMV 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.

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

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TZIELD Infusion Solution Preparation[1]:

- Calculate the volume of TZIELD 100 mcg/mL dilution needed for the infusion.
  Volume of 100 mcg/mL dilution (mL) = Dose (mcg) / 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 2,000 mcg or less) or from both prepared 100 mcg/mL dilutions (for a calculated dose more than 2,000 mcg).
- [ ] 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 the infusion solution if the infusion is unable to be completed within 6 hours of preparation.

Method 2: Syringe for IV infusion via syringe pump[1]

- [ ] 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.

If the dose is 900 mcg or less

$$\text{Volume}_{\text{0.9\% sodium chloride injection}}(\text{mL}) = \text{Volume}_{\text{infusion}}(\text{mL}) - \text{Volume}_{\text{100 mcg/mL dilution}}(\text{mL})$$

If the calculated dose is greater than 900 mcg, the maximum infusion volume is capped at 60 mL.

If the dose is greater than 900 mcg: the maximum infusion volume is capped at 60 mL

$$\text{Volume}_{\text{0.9\% sodium chloride injection}}(\text{mL}) = 60\ \text{mL} - \text{Volume}_{\text{100 mcg/mL dilution}}(\text{mL})$$

FOR ALL DOSES

- [ ] Measure the appropriate volume of 0.9% sodium chloride injection from above 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 2,000 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
  Infusion administration rate may be slowed for patient's tolerability.
- [ ] **Do not manually push the syringe.**
- [ ] 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.

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

Viral Reactivation (Cont'd): 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 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.

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

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Compatible materials for TZIELD administration[1]

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

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 polyethylene sulfone (PES) filter
- Do not use light-protected (colored) infusion sets

PP=polypropylene; PC=polycarbonate; PVC with DEHP=polyvinylchloride with di-(2-ethylhexyl)phthalate; PE=polyethylene.

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

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; **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.

Storage and handling[1]

TZIELD injection is a clear and colorless solution (2 mg/2 mL (1 mg/mL)) supplied in a single-dose vial as follows:

Carton contents	NDC
1 single dose vial	NDC 73650-316-01

- Refrigerate TZIELD vials at 2 °C to 8 °C (36 °F to 46 °F) in the original carton to protect from light. Store upright. Do not freeze or shake the vials
- Once diluted, it is recommended that the product should be used immediately

Stage 2

Scan here to access the dosing calculator

Please contact your local TZIELD COMPASS Clinical Educator if you have any questions about dosing and administration

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.

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

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Scan to learn more[1]

TZIELD dosing for appropriate patients with Stage 2 T1D

INDICATION

TZIELD (teplizumab-mzwv) is indicated to delay the onset of Stage 3 type 1 diabetes (T1D) in adult and pediatric patients 1 year of age and older with Stage 2 T1D.

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.

For more information or questions about dosing and administration of TZIELD:

CALL TZIELD COMPASS at 1-844-778-2246 M-F 8AM-8PM ET

FAX 908-425-4840 **EMAIL** compass@sanofi.com **VISIT** TZIELDHCP.com

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

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.

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 the TZIELD treatment course, during treatment, or up to 6 weeks after completion of the treatment course.
- Live-attenuated vaccinations are not recommended within the 8 weeks prior to starting TZIELD treatment, during treatment, or up to 52 weeks after completion of the treatment course.

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.

Reference: 1. TZIELD Prescribing Information.

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

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