NOW APPROVED EXPANDED PEDIATRIC INDICATION
in children as young as 1 year of age with Stage 2 T1D

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

Updating Order Sets With TZIELD

For appropriate patients with Stage 2 type 1 diabetes (T1D)

INDICATION

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.

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. The majority of serious cases occurred in patients who continued TZIELD treatment despite persistent, severe lymphopenia.**
- **Test patients for active EBV and CMV infection prior to starting treatment. TZIELD is not recommended in patients with laboratory or clinical evidence of active 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.**

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

Background, instructions, and limitations

These instructions were created to provide you with information which you can use to update EHR order sets with TZIELD information and orders, and will not work for other conditions, treatments, or therapeutic areas.

The processes outlined in this piece are variable, and not all steps will 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. The practice is solely responsible for implementing, testing, monitoring, and ongoing operation of any EHR tools. This information is always discretionary to the health system.

A health system may choose to optimize existing order sets with TZIELD.

The following instructions outline the optimization process of order sets with TZIELD. Treatment selection is always a decision made by the healthcare provider, and order sets may be overridden to reflect this. An EHR newsletter or other communication medium may be considered to notify end users of the availability and contents of the updated order sets.

Notes

- The customers (ie, physician, medical group, IDN) shall be solely responsible for implementation, testing, and monitoring of the instructions to ensure proper orientation in each customer's EHR system
- Capabilities, functionality, and set-up (customization) for each individual EHR system vary. Sanofi shall not be responsible for revising the implementation instructions it provides to any Customer if Customer modifies or changes its software, or the configuration of its EHR system, after such time as the implementation instructions have been initially provided by Sanofi
- While Sanofi tests its implementation instructions on multiple EHR systems, the instructions are not guaranteed to work for all available EHR systems, and Sanofi shall have no liability thereto
- While EHRs may assist providers in identifying appropriate patients for consideration of assessment, treatment, and referral, the decision and action should ultimately be decided by a provider in consultation with the patient, after a review of the patient's records to determine eligibility, and Sanofi shall have no liability thereto
- The instructions have not been designed to, and are not tools and/or solutions for, meeting Advancing Care Information and/or any other quality/accreditation requirement
-

EHR = electronic health record; IDN = integrated delivery network.

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EHR protocol: suggested content

Updating order sets requires minimal time but must be implemented at the system level. The update of the order set may require first completing the individual components of the order set and then compiling the order set components in the final order set.

Diagnoses

Type 1 Diabetes[2]	Autoimmune Disease Diagnosis[2,3]
• Type 1 diabetes mellitus, presymptomatic, unspecified (E10.A0) • Type 1 diabetes mellitus, presymptomatic, Stage 1 (E10.A1) • Type 1 diabetes mellitus, presymptomatic, Stage 2 (E10.A2) • Endocrine disorder, unspecified (Endocrine disturbance NOS; Hormone disturbance NOS) (E34.9) • Impaired fasting glucose (Elevated fasting glucose) (R73.01) • Prediabetes (Latent diabetes) (R73.03)	• Autoimmune thyroiditis (Hashimoto's) (E06.3) • Graves' disease (E05.0, E05.00, E05.01) • Autoimmune gastritis (K29.40) • Autoimmune adrenalitis (E27.1) • Celiac disease (K90.0) • Hypothyroidism (E03.9 or E03.8) • Vitiligo (L80)

Histories[2,4]

- Family history of diabetes mellitus (Z83.3)
- Family history of other endocrine, nutritional, and metabolic diseases (Z83.49)
- Family history of autoimmune disease (Z83.2)

Notes/Progress Notes

- Type 1 diabetes mellitus, initial

Vital Signs

- Vital signs

TZIELD Patient Selection[1]

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 two positive pancreatic islet cell autoantibodies, and
- Dysglycemia without overt hyperglycemia using an oral glucose tolerance test (if an oral glucose tolerance test is not available, an alternative method for diagnosing dysglycemia without overt hyperglycemia may be appropriate)

Ensure the patient's diagnosis confirms an autoimmune origin and does not suggest type 2 diabetes or other forms of diabetes. These may include, but are not limited to, genetic forms of diabetes, maturity-onset diabetes of the young (MODY), latent autoimmune diabetes in adults (LADA), or diabetes secondary to medications or surgery.

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EHR protocol: suggested content (cont'd)

Medications[1]

Calculate the dosage using body surface area (BSA) and administer TZIELD once daily for 14 consecutive days as follows:

- **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 through 14:** 1030 mcg/m^2

Administer TZIELD by IV infusion 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

To calculate the BSA dosing, use the clinical BSA calculator in the EHR or use the following equation: square root of [(Height (cm) x Weight (kg))/3600].

Note: A Therapy Plan for TZIELD may be considered if this functionality is available and aligns with the order set conventions of the health system.

Recommendations Regarding Missed Dose(s)

- 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

Nursing Orders[1]

TZIELD Nursing/Pharmacy Orders

- Administer TZIELD once daily for 14 consecutive days
- Administer TZIELD by IV infusion 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

Recommendations Regarding Missed Dose(s)

- 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

Additional Preparation and Administration Instructions

Using the dose calculated according to BSA *[see Dosage and Administration (2.4)]*, **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
- 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

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

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EHR protocol: suggested content (cont'd)

Additional Preparation and Administration Instructions[1] (cont'd)

- **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
- 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 inverting the vial or rocking the infusion bag. 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 containing 18 mL of 0.9% Sodium Chloride Injection**

TZIELD Infusion Solution Preparation:

- Using an appropriately sized syringe, withdraw the volume of diluted TZIELD solution required for that day's calculated dose from the 100 mcg/mL dilution (**for a calculated dose 2000 mcg or less**) or from both prepared 100 mcg/mL dilutions (**for a calculated dose more than 2000 mcg**)
- Discard unused portion of remaining diluted TZIELD solution in the glass vial or infusion bag
- Slowly add contents of the syringe containing the TZIELD dose to 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
- Prime the PVC with DEHP IV infusion set with the TZIELD infusion solution. Do not waste any infusion solution during the priming process
- 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 the infusion at room temperature (15°C to 30°C [59°F to 86°F]). Discard the TZIELD infusion solution if the infusion is unable to be completed within 4 hours of preparation

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

IV Access for Infusions[4]

- TZIELD infusions can be administered via peripheral (peripheral IV, midline catheters) or central (peripherally inserted central catheter [PICC]) venous access
- The selection of IV access is influenced by family preference, the presence of trained personnel, and local hospital policies
- Some hospitals may not permit the maintenance of a peripheral IV outside the hospital facility, necessitating the need for a new peripheral IV daily or a PICC line

EHR protocol: suggested content (cont'd)

Treatment Conditions[1]

Laboratory and Infection Evaluation, and Vaccination

- Prior to initiating TZIELD:
  - Obtain a complete blood count and liver enzyme tests. Use of TZIELD is not recommended in patients with *[see Warnings and Precautions (5) and Adverse Reactions (6.1)]*:
    - Laboratory or clinical evidence of active EBV or CMV infection *[see Dosage and Administration (2.2)]*
    - 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 ULN or bilirubin greater than 1.5 times ULN
    - Active serious infection or chronic active infection other than localized skin infections *[see Warnings and Precautions (5.3)]*
  - Prior to initiating TZIELD, evaluate patients for active EBV and CMV infection and confirm undetectable viral load (eg, polymerase chain reaction [PCR] testing):
    - Use of TZIELD is not recommended in patients with laboratory or clinical evidence of active infection with EBV or CMV *[see Warnings and Precautions (5.1)]*
  - Administer all age-appropriate vaccinations *[see Warnings and Precautions (5.6)]*:
    - 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

Recommended Monitoring During 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 *[see Warnings and Precautions (5.1)]*
- Monitor liver enzymes and bilirubin during treatment. Discontinue TZIELD treatment in patients who develop elevated ALT or AST more than 5 times the ULN or bilirubin more than 3 times ULN *[see Warnings and Precautions (5.2)]*

Warnings and Precautions[1]

- Viral reactivation
- Cytokine release syndrome
- Serious infections
- Lymphopenia
- Hypersensitivity reactions
- Vaccinations

ALT = alanine aminotransferase; AST = aspartate aminotransferase; mRNA = messenger ribonucleic acid; ULN = upper limit of normal.

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EHR protocol: suggested content (cont'd)

Warnings and Precautions[1] (cont'd)

- **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. 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 *[see Warnings and Precautions 5.4]*.

  Prior to initiating treatment with TZIELD, evaluate patients for active EBV and CMV infection and confirm undetectable viral load (eg, PCR testing). TZIELD is not recommended in patients with laboratory or clinical evidence of active EBV or CMV infection *[see Dosage and Administration (2.2)]*.

  During treatment with TZIELD, regularly monitor lymphocyte counts *[see Dosage and Administration (2.6), Warnings and Precautions (5.4)]* 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 (eg, PCR) promptly. Consider appropriate expert consultation for diagnostic testing recommendations as some diagnostic tests may give inaccurate results in immunosuppressed patients. If viral reactivation is confirmed, permanently discontinue TZIELD *[see Dosage and Administration (2.6)]*. Consider appropriate expert consultation for the management of severe viral reactivation.

- **Cytokine Release Syndrome (CRS)**
  - CRS has been observed in TZIELD-treated patients. In clinical trials, CRS was reported in 5% of TZIELD-treated patients compared to 0.8% of control-treated patients during the treatment period and through 28 days after the last study drug administration. CRS manifestations 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 *[see Adverse Reactions (6.1)]*. To mitigate CRS:
    - Premedicate with antipyretics, antihistamines and/or antiemetics prior to TZIELD treatment *[see Dosage and Administration (2.3)]*
    - Monitor liver enzymes and bilirubin during treatment. Discontinue TZIELD treatment in patients who develop elevated ALT or AST more than 5 times the ULN or bilirubin more than 3 times ULN
    - Treat symptoms of CRS in TZIELD-treated patients with antipyretics, antihistamines and/or antiemetics. If severe CRS develops, consider:
      - Temporarily pausing TZIELD dosing for 1-2 days and if symptoms have resolved or significantly improved, subsequently administering the remaining doses on consecutive days to complete the full 14-day course, **or**
      - Discontinuing TZIELD treatment

- **Serious Infections**

  Bacterial and viral infections have occurred in TZIELD-treated patients. In clinical trials, TZIELD-treated patients had a higher rate of serious infections (3.5%) than control-treated patients (2%), including gastroenteritis, cellulitis, pneumonia, abscess, sepsis *[see Adverse Reactions (6.1)]*. 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 treatment. If serious infection develops, treat appropriately, and discontinue TZIELD.

EHR protocol: suggested content (cont'd)

Warnings and Precautions[1] (cont'd)

- **Lymphopenia**
  - In clinical trials, 78% of TZIELD-treated patients developed lymphopenia compared to 11% of control-treated patients. For most TZIELD-treated patients who experienced lymphopenia, lymphocyte levels began to recover after the fifth day of treatment and returned to pretreatment values within 2 weeks after treatment completion and without dose interruption. Severe lymphopenia (<500 cells per mcL) lasting 1 week or longer occurred in 0.9% of TZIELD-treated patients, and 0.5% of TZIELD-treated patients permanently discontinued TZIELD because of lymphopenia *[see Adverse Reactions (6.1)]*
  - Obtain a CBC prior to starting TZIELD and monitor white blood cell counts during TZIELD treatment. If prolonged severe lymphopenia (<500 cells per mcL lasting 1 week or longer) develops, permanently discontinue TZIELD
- **Hypersensitivity Reactions**

  Acute hypersensitivity reactions including serum sickness, angioedema, urticaria, rash, vomiting and bronchospasm occurred in TZIELD-treated patients *[see Adverse Reactions (6.1)]*. If severe hypersensitivity reactions occur, discontinue use of TZIELD and treat promptly.
- **Vaccinations**

  The safety of immunization with live-attenuated vaccines in TZIELD-treated patients has not been studied. Additionally, TZIELD may interfere with the immune response to vaccination and decrease vaccine efficacy.
  - Administer all age-appropriate vaccinations prior to starting TZIELD *[see Dosage and Administration (2.2)]*
  - Inactivated or mRNA vaccinations are not recommended within the 2 weeks prior to TZIELD treatment, during treatment, or up to 6 weeks after completion of treatment
  - Live-attenuated vaccinations are not recommended within the 8 weeks prior to starting TZIELD treatment, during treatment, or up to 52 weeks after treatment

Premedications[1]

Prior to each of the first 5 days of TZIELD infusion *[see Warnings and Precautions (5.2)]*:

- Premedicate with a nonsteroidal anti-inflammatory drug (NSAID) or acetaminophen
- Premedicate with an antihistamine, and
- Consider premedication with an antiemetic

If needed, administer additional premedication doses.

Hydration[4]

- IV fluids (0.9% NS 20 mL/kg IV bolus)

Laboratory (Labs)

- Complete blood count with differential[4]
- A1C test[4]
- Glucose, point-of-care testing[4]
- EBV and CMV Infections[4]
- Hepatitis B/C[4]
- HIV Serology[4]

CBC = complete blood count; HIV = human immunodeficiency virus; NS = normal saline.

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EHR protocol: suggested content (cont'd)

Laboratory (Labs)(cont'd)

- Tuberculosis (TB) testing (QuantiFERON Gold™)[4]
- Liver enzyme test[1]
- Complete metabolic panel (CMP)[1]
- Autoantibody testing for TZIELD patient selection[1]
  - Glutamic acid decarboxylase 65 (GAD) autoantibody
  - Insulinoma-associated antigen 2 autoantibody (IA-2A)
  - Insulin autoantibody (IAA)
  - Zinc transporter 8 autoantibody (ZnT8A)
  - Islet cell autoantibody (ICA)
- Liver function testing[1]
- INR (if needed for PICC placement)[1,5]
- COVID viral load (PCR)[1,5]

Immunizations

TZIELD Immunizations[1]

The safety of immunization with live-attenuated vaccines in TZIELD-treated patients has not been studied. Additionally, TZIELD may interfere with the immune response to vaccination and decrease vaccine efficacy.

- Administer all age-appropriate vaccinations prior to starting TZIELD *[see Dosage and Administration (2.2)]*
- Inactivated or mRNA vaccinations are not recommended within the 2 weeks prior to TZIELD treatment, during treatment, or up to 6 weeks after completion of treatment
- Live-attenuated vaccinations are not recommended within the 8 weeks prior to starting TZIELD treatment, during treatment, or up to 52 weeks after treatment

INR = international normalized ratio.

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EHR protocol: suggested content (cont'd)

Special Populations

Pregnancy and Lactation[1,4]

- Available case reports from clinical trials with TZIELD are insufficient to identify a drug-associated risk of major birth defects, miscarriage or other adverse maternal or fetal outcomes. Although there are no data on TZIELD in nonclinical studies, monoclonal antibodies can be actively transported across the placenta, and TZIELD may cause immunosuppression in the utero-exposed infant *(see Clinical Considerations)*
- 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
- A lactating woman may interrupt breastfeeding and pump and discard breast milk during treatment and for 20 days after TZIELD administration to minimize drug exposure to a breastfed child

Orders[4]

- Continuous glucose monitoring according to current practice guidelines

Patient Education and Support

- Type 1 Diabetes Patient Education
- TZIELD COMPASS Support

Follow Up

- Add as desired

References

- How to Screen for Type 1 Diabetes | TZIELD® (teplizumab-mzwv) for HCPs (tzieldhcp.com)
- TZIELD Prescribing Information: https://products.sanofi.us/tzield/tzield.pdf
- Pediatric Endocrine Society Statement on Considerations for Use of Teplizumab (Tzield™) in Clinical Practice: https://karger.com/hrp/article/doi/10.1159/000538775/906682/Pediatric-Endocrine-Society-Statement-on

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EHR protocol: suggested content (cont'd)

Additional Considerations for Use

Daily infusion checklist for patients diagnosed with Stage 2 T1D

TZIELD is administered once daily for 14 consecutive days, for a single treatment course.[1]

Consecutive Infusion Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14
CBC/differential[1,5]	✓				✓			✓						✓
AST/ALT/direct bilirubin[1,5]	✓				✓			✓						✓
Urine pregnancy test (in females of reproductive age)[1,5]	✓													
Premedicate with an NSAID or acetaminophen[1,5]	✓	✓	✓	✓	✓	(✓)	(✓)	(✓)	(✓)	(✓)	(✓)	(✓)	(✓)	(✓)
Premedicate with an antihistamine[1,5]	✓	✓	✓	✓	✓	(✓)	(✓)	(✓)	(✓)	(✓)	(✓)	(✓)	(✓)	(✓)
Premedicate with an antiemetic[1]	(✓)	(✓)	(✓)	(✓)	(✓)	(✓)	(✓)	(✓)	(✓)	(✓)	(✓)	(✓)	(✓)	(✓)
For patients aged 8 years and older, administer infusion over a minimum of 30 minutes[1]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
For patients aged 1 to <8 years, administer infusion over a minimum of 2 hours[1]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Infusion dose (mcg/kg/m^2)[1]	65	125	250	500	1030	1030	1030	1030	1030	1030	1030	1030	1030	1030
Monitor post-infusion[1]	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

Frequency recommendations based on normal or expected results, with more frequent treatment or monitoring as indicated for abnormal findings or the presence of clinical symptoms. (✓) denotes consider but not required.

Adapted from Teplizumab-mzwv: Perspective on Clinical Practice & Use at a Single Institution, by J.L. Felton, A. Tuttle and E.K. Sims, SMART-MD Journal of Precision Medicine, Volume 2, Issue 2, 2025, with permission from SMART-MD Publishing LLC.

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

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INDICATION

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.

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. The majority of serious cases occurred in patients who continued TZIELD treatment despite persistent, severe lymphopenia.**
- **Test patients for active EBV and CMV infection prior to starting treatment. TZIELD is not recommended in patients with laboratory or clinical evidence of active 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.**

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. 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. 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. CRS manifestations 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: 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. 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.

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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.

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

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References: 1. TZIELD. Prescribing Information. Provention Bio, Inc. **2.** Centers for Medicare and Medicaid Services. Accessed March 3, 2026. https://www.cms.gov/files/zip/2026-code-tables-tabular-and-index.zip **3.** Popoviciu MS, et al. *J Pers Med*. 2023;13(3):422. **4.** Mehta S, et al. *Horm Res Paediatr*. 2024:1-12. **5.** Felton JL, et al. *SMART-MD J Precis Med*. 2025;2(2):e149-e157.

sanofi

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