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

Tzield® COMPASS

PATIENT START FORM: INSTRUCTIONS

TZIELD® (teplizumab-mzwv) Injection 2 mg/2 mL

To submit the START Form, click here, fax to 908-425-4840, or email COMPASS@sanofi.com. For questions or to learn more about TZIELD COMPASS, call 1-844-778-2246 Monday through Friday, 8 AM–8 PM ET.

INDICATIONS

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.
- 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.

Now that you have decided to prescribe TZIELD for your patient, please review the helpful guide below before you complete the Patient START Form. Note that all fields must be completed in order to receive support through TZIELD COMPASS.

INSTRUCTIONS FOR HEALTHCARE PROVIDERS

To prevent delays in support, be sure to confirm the following before submitting the START Form:

PATIENT AND PRESCRIBER INFORMATION

- ☐ **All fields have been completed and clinical labs are attached**
- ☐ **Patient or Parent/Legal Guardian has signed Patient Consent. If not, COMPASS will reach out to obtain eConsent**

REQUIRED CLINICAL LABS TO CONFIRM CLINICAL ELIGIBILITY

- ☐ **Patient has tested positive for at least 2 or more islet cell autoantibodies (Stage 2 T1D) OR at least 1 or more islet cell autoantibodies (Stage 3 T1D) of the following pancreatic islet cell autoantibodies within the specified period of time*:**
  - Glutamic acid decarboxylase 65 (GAD) autoantibody
  - Insulin autoantibody (IAA)
  - Insulinoma-associated antigen 2 autoantibody (IA-2A)
  - Zinc transporter 8 autoantibody (ZnT8A)
  - Islet cell autoantibody (ICA)
- ☐ ***I understand the clinical and laboratory monitoring requirements during and after TZIELD infusion, including criteria for treatment interruption or discontinuation, and I have reviewed the Boxed WARNING and evaluated the benefit-risk profile for this patient, taking the associated safety considerations into account**
- ☐ ***I will perform necessary laboratory testing prior to infusion, including assessment of blood counts, liver enzymes, and Epstein–Barr virus (EBV) and cytomegalovirus (CMV) viral load (eg, polymerase chain reaction [PCR]), and understand that TZIELD should not be administered to patients with active infection, are immunocompromised, or with laboratory values outside the ranges specified in the Prescribing Information**
- ☐ **Stage 2 T1D: Patient's clinical history demonstrates dysglycemia without overt hyperglycemia per an OGTT*,†**
- ☐ **Stage 3 T1D: Patient's clinical labs demonstrate hyperglycemia per A1C, FPG, 2-hour OGTT, or random plasma glucose with symptoms***
- ☐ **Stage 3 T1D: Peak C-peptide ≥0.2 pmol/mL on a mixed meal tolerance test ‡**
- ☐ **Stage 3 T1D: Date of diagnosis _____**
- ☐ ***I confirm the patient's diagnosis confirms an autoimmune origin and does not suggest insulin resistance due to obesity, type 2 diabetes (T2D) or dysglycemia due to 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**

*Timelines for lab requirements may vary by individual plan. †If an oral glucose tolerance test is not available, an alternative method for diagnosing dysglycemia without overt hyperglycemia may be appropriate. For patients 18 years and older, recommend following the definition of dysglycemia used in clinical trials as described in the Prescribing Information. In the TN-10 trial, adults were required to have 2 consecutive OGTTs. ‡If a mixed meal tolerance test is not available, an alternative method for measuring peak C-peptide ≥0.2 pmol/mL may be appropriate.

FPG = fasting plasma glucose; OGTT = oral glucose tolerance test.

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.**

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

PATIENT ENGAGEMENT

Be sure to discuss the following with your patient and/or their parent/legal guardian prior to completing the START Form:

- What the patient can expect during their treatment, including options as to where the patient can receive their infusion. TZIELD COMPASS can provide support during these conversations
- Patient consent is required for enrollment. If the patient or parent/legal guardian does not sign while in the office, a COMPASS Navigator will reach out to obtain eConsent

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.

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.

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 lymphocyte 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.

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.

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

IMPORTANT SAFETY INFORMATION (cont'd)

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

TZIELD COMPASS is a patient support program that helps eligible patients gain access to TZIELD and provides them with education and resources related to TZIELD.

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