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

**The first and only treatment approved to delay the onset of Stage 3 type 1 diabetes (T1D) in adult and pediatric patients aged 8 years and older with Stage 2 T1D.**[1]

See section 2.1 in the Prescribing Information for patient selection criteria.

# WHAT TO EXPECT DURING THE TZIELD INFUSION

### INDICATION

TZIELD 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.
- **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 Important Safety Information throughout and read the full Prescribing Information and Medication Guide.**

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

## TZIELD IS THE FIRST AND ONLY APPROVED, DISEASE-MODIFYING TREATMENT TO DELAY THE ONSET OF STAGE 3 T1D IN ADULT AND PEDIATRIC PATIENTS AGED 8 YEARS AND OLDER WITH STAGE 2 T1D[1]

### Autoimmune therapy for Stage 2 T1D[1]

TZIELD is a CD3-directed monoclonal antibody that binds to CD3 antigens presented on the surface of T cells and delays the onset of Stage 3 T1D.

### Mechanism of action[1]

The mechanism may involve partial agonistic signaling and deactivation of pancreatic beta cell autoreactive T cells.

## TZIELD DOSAGE FORM AND STRENGTH[1]:

### Dosage form and strength

TZIELD injection: 2 mg per 2 mL (1 mg/mL) clear and colorless solution in a single-dose vial.

### Dosing schedule for TZIELD

TZIELD is administered by intravenous infusion (over a minimum of 30 minutes), using a body surface area–based dosing, once daily for 14 consecutive days as follows[1]:

- 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$^2$

## 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. 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.

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## TZIELD SAFETY PROFILE (TN-10)

### Common adverse reactions* in the TN-10 trial[1†]

| Adverse Reactions | Placebo (N=32) | TZIELD (N=44) |
|---|---|---|
| Lymphopenia | 6% | 73% |
| Rash‡ | 0% | 36% |
| Leukopenia | 0% | 21% |
| Headache | 6% | 11% |
| Neutropenia | 3% | 5% |
| Alanine aminotransferase increase | 3% | 5% |
| Nausea | 3% | 5% |
| Diarrhea | 0% | 5% |
| Nasopharyngitis | 0% | 5% |

Adverse reactions observed in TZIELD-treated pediatric patients (8 years and older) were consistent with those reported in TZIELD-treated adults.[1]

*Adverse reactions that occurred in 2 or more TZIELD-treated patients.[1]
†That occurred during treatment and through 28 days of the last TZIELD administration.[1]
‡Composite of rash-related terms including rash erythematous, rash macular, rash papular, rash maculo-papular, rash pruritic.[1]

**The safety profile of TZIELD was also evaluated in a pooled analysis of >750 patients across 5 controlled, clinical studies.[1]**

In the pooled analysis, adverse reactions were evaluated in 773 TZIELD-treated patients, and 245 patients received placebo or standard of care (1 study in patients with Stage 2 T1D [Study TN-10], 3 placebo-controlled studies in an unapproved population, and 1 open-label standard-of-care controlled study of TZIELD in an unapproved population).[1]

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# PREPARING PATIENTS FOR THEIR TZIELD INFUSION

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## CONFIRM STAGE 2 PATIENT SELECTION[1]

TZIELD is only indicated in adult and pediatric patients 8 years of age and older who have a diagnosis of Stage 2 T1D. Confirm Stage 2 T1D by the following criteria:

- At least 2 positive pancreatic islet cell autoantibodies[1]:
  - 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 using an oral glucose tolerance test (OGTT) (if an OGTT is not available, an alternative method for diagnosing dysglycemia without overt hyperglycemia may be appropriate)[1]
- Clinical history of the patient does not suggest type 2 diabetes[1]

## PATIENT CONSIDERATIONS PRIOR TO INFUSION[1]

Starting TZIELD is **not recommended** in patients with:

- Lymphocyte count less than 1000 lymphocyte/mcL
- Hemoglobin less than 10 g/dL
- Platelet count less than 150,000 platelets/mcL
- Absolute neutrophil count less than 1500 neutrophils/mcL
- Elevated alanine aminotransferase (ALT) or aspartate aminotransferase (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 or cytomegalovirus
- Active serious infection other than localized skin infections

### Pregnancy

Although there are no data on teplizumab-mzwv, monoclonal antibodies can be actively transported across the placenta, and TZIELD may cause immunosuppression in the utero-exposed infant.[1]

To minimize exposure to a fetus, **avoid use of TZIELD during pregnancy and at least 30 days prior to planned pregnancy.**[1] Report pregnancies to the Provention Bio, Inc.'s Adverse Event reporting line at 1-800-633-1610.

**Please see Important Safety Information throughout and read the full Prescribing Information and Medication Guide.**

# PREPARING PATIENTS FOR THEIR TZIELD INFUSION (cont'd)

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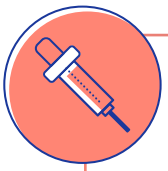
## VACCINATIONS PRIOR TO INFUSION[1]

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



**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

**See additional vaccination information below.**

## 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 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.

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# TZIELD INFUSION OVERVIEW

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## Once daily, consecutive 14-day course[1]

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

## ≥30-minute administration[1]

Administer TZIELD by IV infusion for a minimum of 30 minutes, using a body surface area–based dosing.

## DOSING SCHEDULE[1]

| DAY | DAY 1 | DAY 2 | DAY 3 | DAY 4 | DAYS 5-14 |
|---|---|---|---|---|---|
| Dose | 65 mcg/m$^2$ | 125 mcg/m$^2$ | 250 mcg/m$^2$ | 500 mcg/m$^2$ | 1030 mcg/m$^2$ |

**Premedication**

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

**Monitoring during treatment**

- Prior to initiating TZIELD, obtain a complete blood count and liver enzyme tests
- Throughout the treatment course, monitor:
  - Liver enzymes for ALT, AST, and bilirubin
  - For signs and symptoms of serious infection or hypersensitivity reaction
  - White blood cell counts for prolonged lymphopenia (<500 cells per mcL lasting 1 week or longer)
- If **CRS**, **serious infections**, **lymphopenia**, and/or **hypersensitivity reactions** were to occur, see the Prescribing Information and next page for management considerations

**Please see Important Safety Information throughout and read the full Prescribing Information and Medication Guide.**

## INFUSION-RELATED ADVERSE REACTIONS

| Infusion-related ARs | Management considerations |
|---|---|
| **Cytokine release syndrome (CRS)**[1] | |
| CRS has been observed in TZIELD-treated patients. Symptoms included fever, nausea, fatigue, headache, myalgia, arthralgia, increased ALT, increased AST, and increased total bilirubin; and, typically occurred during the first 5 days of treatment. | • Treat symptoms of CRS with antipyretics, antihistamines, and/or antiemetics. 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 discontinuing treatment<br>• **Discontinue** treatment in patients who develop elevated ALT or AST 5 times ULN or bilirubin 3 times ULN |
| **Serious infections**[1] | |
| Bacterial and viral infections have occurred in TZIELD-treated patients, including gastroenteritis, cellulitis, pneumonia, abscess, and sepsis. | • Monitor patients for signs and symptoms of infection. If serious infection develops, treat appropriately, and **discontinue** TZIELD<br>• Use of TZIELD is not recommended in patients with active serious infections other than localized skin infections |
| **Lymphopenia**[1] | |
| TZIELD-related effects included lymphopenia. For most patients, 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. | • If prolonged severe lymphopenia develops (<500 cells per mcL lasting one week or longer), **discontinue** TZIELD<br>• 0.5% of TZIELD-treated patients permanently discontinued due to lymphopenia |
| **Hypersensitivity reactions**[1] | |
| Acute hypersensitivity reactions, including serum sickness, angioedema, urticaria, rash, vomiting and bronchospasm, occurred in TZIELD-treated patients. | • If severe hypersensitivity reactions occur, **discontinue** use of TZIELD and treat promptly |

**Please see Important Safety Information throughout and read the full Prescribing Information and Medication Guide.**

Tzield® COMPASS

# A PERSONALIZED PATIENT ASSISTANCE AND SUPPORT PROGRAM WITH HELPFUL RESOURCES.

Our team will provide information about financial assistance options, reimbursement, educational tools and resources, and additional support from the day of enrollment.

**TZIELD COMPASS is a patient support program that helps patients gain access to TZIELD and provides patients with education and resources related to TZIELD. TZIELD COMPASS is not a healthcare service or an insurance provider and does not provide care coordination. TZIELD COMPASS and the COMPASS Navigator will not provide medical or treatment advice. TZIELD COMPASS services are available only to those who have been prescribed TZIELD and are intended for US residents only.**

**For more information about TZIELD COMPASS, call 1-844-778-2246, Monday through Friday, 8 AM-8 PM ET.**

**Click or scan the QR code to get your patients started with TZIELD**

## IMPORTANT SAFETY INFORMATION (cont'd)

### 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.

**Before prescribing TZIELD, please read the Prescribing Information, including patient selection criteria, and Medication Guide.**

**REFERENCE: 1.** TZIELD Prescribing Information. Provention Bio, Inc.

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