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

The PETITE-T1D study evaluated the safety of TZIELD in pediatric patients 1 year of age to <8 years of age.[1]

T1D=type 1 diabetes.

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

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

Early childhood T1D doesn't wait. **Neither should you.**

Clinical T1D is one of the most common chronic childhood conditions[2-4]:

- ✓ **~304,000** children and adolescents in the US live with T1D
- ✓ **1.2 million** children diagnosed worldwide
- ✓ **~4%** rising global incidence each year, especially in children under 5 years of age

T1D can occur at any age, but 2 noticeable childhood peaks occur between 4-7 and 10-14 years of age[5]

Early screening and monitoring of young children with T1D may help give more time to prepare for Stage 3 T1D[11,12]

Confirmation of a Stage 2 T1D diagnosis may offer a window to consider options for earlier intervention in children as young as 1 year of age[1]

A pediatric T1D diagnosis has unique challenges for patients and caregivers during critical developmental stages[6-10]

The speed of progression in young children from Stage 2 to Stage 3 T1D makes **the need to screen more urgent**[6,7]

The role of caregivers is elevated, requiring **24/7 monitoring and support**[8-10]

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. 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.

Select adult and pediatric patients 1 year of age and older with Stage 2 T1D for TZIELD treatment based on the confirmation of[1]:

- At least 2 islet AAbs
- Dysglycemia without overt hyperglycemia (eg, via OGTT*)

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.

*If an OGTT is not available, an alternative method for diagnosing dysglycemia without overt hyperglycemia may be appropriate.[1]
AAbs=autoantibodies; OGTT=oral glucose tolerance test.

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. 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.

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Hypothetical patient profile

Meet Jessie
6 years old

Relevant history
- Diagnosed with celiac disease following short stature workup
- Mother has Graves' disease

Reasons to screen
- Patients living with celiac disease have up to **3x increased risk** of developing T1D[13]
- Family history of autoimmune disease (eg, maternal Graves') is a supportive, non-specific risk signal[13]

Due to her increased risk for T1D, her pediatrician screened Jessie for T1D islet AAbs

- She was found to be positive for 2 AAbs
- Per the ADA Standards of Care, individuals with ≥2 islet AAbs should be referred to a specialist for staging and ongoing monitoring[14]

A Pediatric Endocrinologist reconfirmed the presence of 2 AAbs and tested her glucose levels. Jessie's HbA1c was found to be 6.2%, establishing a Stage 2 T1D diagnosis.

ADA=American Diabetes Association; HbA1c=hemoglobin A1c.

IMPORTANT SAFETY INFORMATION (CONT'D)
WARNINGS AND PRECAUTIONS (CONT'D)

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.

EXPANDED STAGE 2 PEDIATRIC INDICATION
TZIELD is now approved in patients with Stage 2 T1D as young as 1 year of age[1]

The PETITE-T1D study
evaluated the safety of TZIELD in pediatric patients 1 year of age to <8 years of age[1]

PETITE-T1D study design

The safety of TZIELD was evaluated in a non-randomized, single-arm, open-label, multicenter study in 23 pediatric patients age 1 year to less than 8 years with Stage 2 T1D. The median age was 4.9 years (1 patient was less than 2 years old; 52% were age 2 years to less than 5 years old).[1]

Use of TZIELD for this indication is supported by evidence from an adequate and well-controlled study (Study TN-10) in adult and pediatric patients 8 years of age and older (including 29 pediatric patients) with Stage 2 T1D and from additional pharmacokinetic and safety data in 23 pediatric patients aged 1 to <8 years of age with Stage 2 T1D (PETITE-T1D).[1]

The safety and effectiveness of TZIELD have not been established in pediatric patients younger than 1 year of age.[1]

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.

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TN-10 safety profile

Serious adverse reactions reported throughout the TN-10 study with greater frequency in TZIELD-treated patients vs placebo-treated patients[1]

Adverse reaction	TZIELD (n=44)	Placebo (n=32)
Cytokine release syndrome	2%	0%
Serious infections*	9%	0%
Lymphopenia	73%	6%
Hypersensitivity reactions and serum sickness	2%	0%

Common adverse reactions† (≥5%) in adult and pediatric patients 8 years of age and older with Stage 2 T1D[1‡]

Adverse reaction	TZIELD (n=44)	Placebo (n=32)
Lymphopenia	73%	6%
Rash§	36%	0%
Leukopenia	21%	0%
Headache	11%	6%
Neutropenia	7%	3%
Increased alanine aminotransferase	5%	3%
Nausea	5%	3%
Diarrhea	5%	0%
Nasopharyngitis	5%	0%

Cytokine release syndrome (CRS)

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.[1]

These manifestations typically occurred during the first 5 days of TZIELD treatment.[1] To mitigate CRS, premedicate with antipyretics, antihistamines and/or antiemetics prior to TZIELD treatment.[1]

Lymphopenia

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 two weeks after treatment completion and without dose interruption.[1]

- Lymphopenia occurred in the absence of T-cell depletion[1]

*Serious infections included cellulitis, gastroenteritis, pneumonia, and wound infection any time during or after the first dose of study treatment.[1]
†That occurred during treatment and through 28 days after the last study drug administration.[1]
‡Adverse reactions that occurred in 2 or more TZIELD-treated patients.[1]
§Composite of rash-related terms including rash erythematous, rash macular, rash papular, rash maculo-papular, rash pruritic.[1]
ALT=alanine aminotransferase; AST=aspartate aminotransferase.

PETITE-T1D safety profile

Overall, the safety profile of TZIELD observed in pediatric patients <8 years of age with Stage 2 T1D was consistent with the safety profile observed in patients ≥8 years of age with Stage 2 T1D[1]

The most common adverse reactions that occurred in patients <8 years of age were vomiting (52%) and diarrhea (30%).[1]

Procedure-related venous thrombosis

Venous thrombus and thrombophlebitis have been reported in patients receiving TZIELD intravenously administered via peripherally inserted central catheter (PICC). In the pool of 5 clinical trials of patients, deep vein thrombus was reported in 0.4% of TZIELD-treated patients compared to 0 placebo-treated patients. One TZIELD-treated patient (4.3%) in the PETITE-T1D study experienced a deep vein thrombosis.[1]

The safety of TZIELD has been established in pediatric patients 1 year of age and older with Stage 2 T1D[1]

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.[1]

Intervene younger than ever before

TZIELD is now approved to delay the onset of Stage 3 T1D, starting as young as 1 year of age[1]

TEST

Screening and monitoring for progression can identify T1D early[11,12]

TRIAL

Overall, the safety profile of TZIELD observed in patients less than 8 years of age with Stage 2 T1D was consistent with that observed in patients 8 years of age and older with Stage 2 T1D[1]

TREAT

Consider TZIELD in eligible patients with Stage 2 T1D as young as 1 year of age[1]

Scan to learn more about TZIELD

IMPORTANT SAFETY INFORMATION (CONT'D)

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

References: 1. TZIELD Prescribing Information. Provention Bio, Inc. **2.** Kandemir N, Vuralli D, Ozon A, et al. Epidemiology of type 1 diabetes mellitus in children and adolescents: a 50-year, single-center experience. *J Diabetes.* 2024;16(5):e13562. **3.** Buchmann M, Tuncer O, Auzanneau M, et al. Incidence, prevalence, and care of type 1 diabetes in children and adolescents in Germany: time trends and regional socioeconomic situation. *J Health Monit.* 2023;8(2):57-78. **4.** National diabetes statistics report. Centers for Disease Control and Prevention. Accessed February 25, 2026. https://www.cdc.gov/diabetes/php/data-research/index.html **5.** Type 1 diabetes—symptoms and causes. Mayo Clinic. March 27, 2024. Accessed February 25, 2026. https://www.mayoclinic.org/diseases-conditions/type-1-diabetes/symptoms-causes/syc-20353011 **6.** Jensen ET, Stafford JM, Saydah S, et al. Increase in prevalence of diabetic ketoacidosis at diagnosis among youth with type 1 diabetes: the SEARCH for diabetes in youth study. *Diabetes Care.* 2021;44(7):1573-1578. **7.** Rugg-Gunn CE, Dixon E, Jorgensen AL, et al. Factors associated with diabetic ketoacidosis at onset of type 1 diabetes among pediatric patients: a systematic review. *JAMA Pediatr.* 2022;176(12):1248-1259. **8.** Azimi T, Johnson J, Campbell SM, Montesanti S. Caregiver burden among parents of children with type 1 diabetes: a qualitative scoping review. *Heliyon.* 2024;10(6):e27539. **9.** Harrington KR, Boyle CT, Miller KM, et al. Management and family burdens endorsed by parents of youth <7 years old with type 1 diabetes. *J Diabetes Sci Technol.* 2017;11(5):980-987. **10.** Commissariat PV, Harrington KR, Whitehouse AL, et al. "I'm essentially his pancreas": parent perceptions of diabetes burden and opportunities to reduce burden in the care of children <8 years old with type 1 diabetes. *Pediatr Diabetes.* 2020;21(2):377-383. **11.** Scheiner G, Weiner S, Kruger D, Pettus J. Screening for type 1 diabetes: role of the diabetes care and education specialist. *ADCES Pract.* 2022;10(5):20-25. **12.** Insel RA, Dunne JL, Atkinson MA, et al. Staging presymptomatic type 1 diabetes: a scientific statement of JDRF, the Endocrine Society, and the American Diabetes Association. *Diabetes Care.* 2015;38(10):1964-1974. **13.** Edelman SV, Agardh D, Cui N, et al. Risk of new-onset type 1 diabetes in individuals with celiac disease and thyroid disease—an observational study. *Diabetes Obes Metab.* 2025;27(8):4229-4238. **14.** American Diabetes Association Professional Practice Committee for Diabetes. Standards of care in diabetes—2026. *Diabetes Care.* 2026;49(suppl 1):S1-S371.

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