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TZIELD (teplizumab):

Guide for HCPs

This guide is for healthcare professionals (HCPs) involved in the management of patients treated with teplizumab.

This guide contains important safety information healthcare professionals need to be aware of when treating patients with TZIELD (teplizumab).

Before any prescription / administration of teplizumab to patients please refer to the Summary of Product Characteristics (SmPC) for complete information.

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Objectives of this guide

TZIELD (Teplizumab) is 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.

This guide includes important information on administration of TZIELD that you should know before initiating TZIELD treatment.

It is designed to support HCPs informing patient / legal representative / caregiver and in managing the possible serious adverse reactions associated with the use of TZIELD :

- **Cytokine Release Syndrome (CRS)**
- **Lymphopenia**
- **Serious infections**
- **Hypersensitivity reactions**

For patients who are minors or without the capacity to make an informed decision, provide the information to their parents / legal representative / caregiver and make sure they clearly understand it.

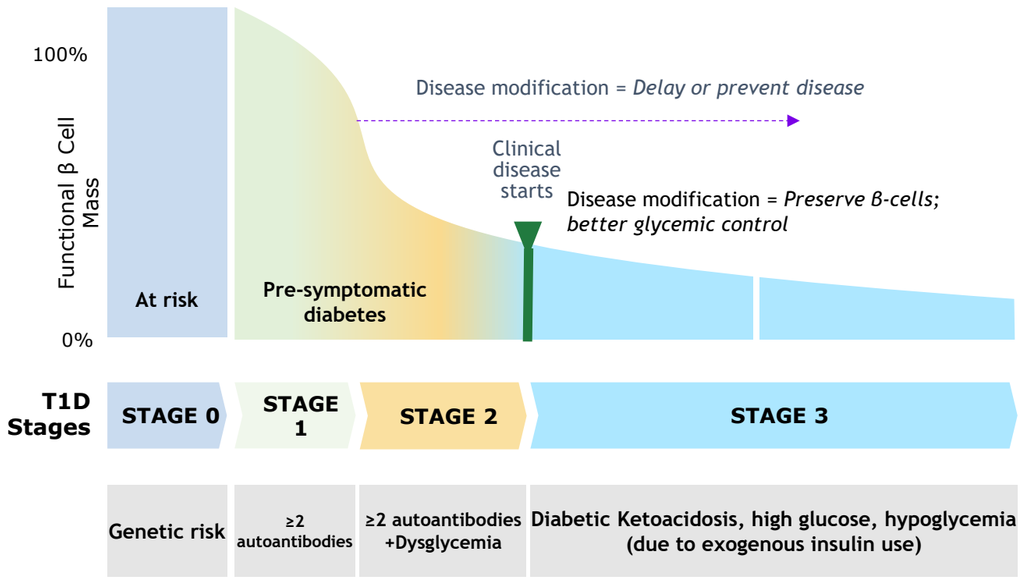
Before and during TZIELD treatment

	Overview
Patient eligibility	• **TZIELD is contraindicated in patients who have had hypersensitivity reactions, to teplizumab or any of its excipients.** • TZIELD is not recommended in pregnant and lactating women • Confirm Stage 2 T1D • Obtain a complete blood count and liver enzyme tests and bilirubin • Check for active serious or chronic infection and do not to treat during active EBV or CMV infection. If serious infection develops, treat appropriately, and discontinue TZIELD. • TZIELD may reduce vaccine effectiveness. Administer all age-appropriate vaccinations prior to starting TZIELD.
Premedication	**Premedicate** prior to TZIELD infusion for the first 5 days of dosing with: 1. antipyretics [nonsteroidal anti-inflammatory drug (NSAID) or paracetamol] 2. antihistamines, and/or 3. antiemetics Administer additional doses of premedication beyond day 5 if needed.
During treatment	Throughout the treatment course, monitor: • Liver enzymes for ALT, AST, and bilirubin • For signs and symptoms of infection or hypersensitivity reactions • 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 pages for management considerations.

See the Prescribing Information and next pages for further details.

Staging of autoimmune T1D

T1D Is a Progressive Autoimmune Condition Involving Loss of Beta Cell Function Over 3 Stages[1]:



Stage 1 represents individuals who have developed two or more type 1 diabetes–associated islet autoantibodies but are normoglycemic.

Stage 2, like stage 1, includes individuals with two or more islet autoantibodies but whose disease has now progressed to the development of glucose intolerance, or dysglycemia, from loss of functional beta-cell mass. The 5-year risk of symptomatic disease at this stage is approximately 75%, and the lifetime risk approaches 100%[1].

Stage 3 represents manifestations of the typical clinical symptoms and signs of diabetes, which may include polyuria, polydipsia, weight loss, fatigue, diabetic ketoacidosis (DKA), and others[1].

1. Insel RA, et al. Diabetes Care. 2015; 38(10): 1964-1974.

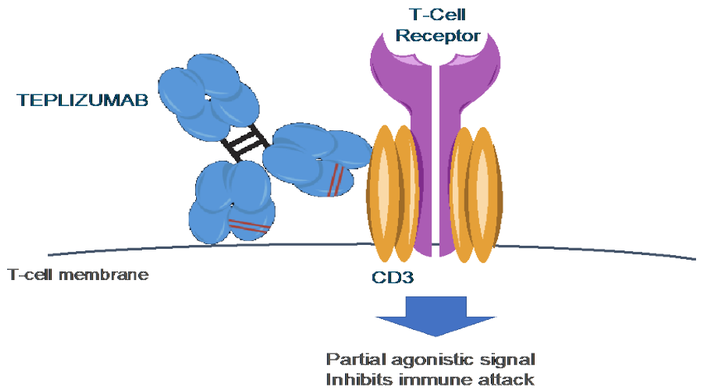
Mechanism of action of teplizumab

Autoimmune therapy for Stage 2 T1D

Teplizumab is a CD3-directed monoclonal antibody that binds to CD3 antigens present on the surface of T lymphocytes and delays the onset of Stage 3 T1D.

Mechanism of action

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



Eligibility of patient

1. CONFIRM STAGE 2 PATIENT

TZIELD is only for adult and pediatric patients 8 years of age and older who have a diagnosis of Stage 2 T1D.

Therefore **Stage 2 T1D should be confirmed by the following criteria:**

- At least 2 positive pancreatic islet cell autoantibodies
- Dysglycemia without overt hyperglycemia using an oral glucose tolerance test (OGTT) or an alternative method as appropriate
- Clinical history of the patient does not suggest type 2 diabetes

2. LABORATORY PARAMETERS PRIOR TO INFUSION INITIATION

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

- Lymphocyte count less than 1,000 lymphocytes/mcL
- Hemoglobin less than 10 g/dL
- Platelet count less than 150,000 platelets/mcL
- Absolute neutrophil count less than 1,500 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 (EBV) or cytomegalovirus (CMV) as it is important not to treat during active EBV or CMV infection
- Active serious infection or chronic active infection other than localized skin infections

3. VACCINATIONS PRIOR AND AFTER INFUSION

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 vaccines at least 8 weeks prior to treatment
- Administer inactivated (killed) or mRNA vaccines at least 2 weeks prior to treatment

Vaccination after the treatment

- Live-attenuated vaccines are not recommended up to 52 weeks after treatment
- Inactivated or mRNA vaccines are not recommended 6 weeks after treatment

Possible serious adverse reactions of TZIELD and how to mitigate them

Possible adverse reactions	How to mitigate these adverse reactions
Cytokine release syndrome (CRS)	
CRS has been observed in TZIELD-treated patients. The partial agonistic effect of teplizumab to T lymphocytes may lead to cytokine release. The CRS symptoms included: • fever • nausea • fatigue • headache • myalgia • arthralgia • increased ALT, increased AST and increased total bilirubin These symptoms typically occurred during the first 5 days of treatment.	• **Premedicate** prior to teplizumab infusion for the first 5 days of dosing with: 1. a nonsteroidal anti-inflammatory drug (NSAID) or paracetamol 2. an antihistamine, and/or 3. an antiemetic Administer additional doses of premedication beyond day 5 if needed. • **Monitor** liver enzymes ALT, AST and bilirubin during treatment • **Discontinue** treatment in patients who develop elevated ALT or AST 5 times ULN or bilirubin 3 times ULN • **Treat** symptoms of CRS with antipyretics, antihistamines, and/or antiemetics. • **If severe CRS develops, consider temporarily pausing dosing for 1 day - 2 days** (and administer the remaining doses to complete the full 14-day course on consecutive days) **or discontinuing treatment**. • Follow strictly instructions on the infusion preparation and the dosing regimen.
Inform patients on such signs and symptoms and if they occur, to urgently seek medical advice / contact their treating HCPs to receive adequate treatment.	

Possible adverse reactions	How to mitigate these adverse reactions
Lymphopenia	
Lymphopenia has been reported in most TZIELD-treated patients. For most patients treated with teplizumab who experience 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.	• **Monitor** white blood cell counts during the treatment period. • If prolonged severe lymphopenia (<500 cells per mcL lasting one week or longer) develops, **discontinue** TZIELD. • Follow strictly the instructions on the infusion preparation and the dosing regimen.
Inform patients that you will be monitoring white blood cell counts, and if this is too low for a prolonged period of time, TZIELD may have to be discontinued.	
Serious infections	
Bacterial and viral infections have occurred in TZIELD-treated patients, including: • gastroenteritis • cellulitis • pneumonia • abscess • sepsis	• Use of TZIELD is not recommended in patients with active serious infection or chronic active 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**
In case of infection symptoms **inform patients** to urgently seek medical advice / contact their treating HCPs: to receive an adequate treatment.	

Possible adverse reactions	How to mitigate these adverse reactions
Hypersensitivity reactions	
Acute hypersensitivity reactions, including: • serum sickness • angioedema • urticaria • rash • vomiting • bronchospasm occurred in TZIELD-treated patients.	• TZIELD is **contraindicated** in patients who have had hypersensitivity reactions, to teplizumab or any of its excipients. • If severe hypersensitivity reactions occur, **discontinue** use of TZIELD and **treat promptly.**
If such symptoms occur **inform patients** to seek medical attention promptly / contact their treating HCPs: to receive an adequate treatment.	

Recommended dosing for TZIELD

TZIELD is administered by IV infusion (over a minimum of 30 minutes) once daily for 14 consecutive days.

Once daily, consecutive 14-day course

If a planned 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.

≥30-minute administration

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

The recommended TZIELD dosage for adults and pediatric patients aged 8 years and older uses body surface area (BSA)-based dosing and is administered according to the following regimen:

DOSING REGIMEN

Day 1	Day 2	Day 3	Day 4	Day 5-14
65 mcg/m^2	125 mcg/m^2	250 mcg/m^2	500 mcg/m^2	1030 mcg/m^2

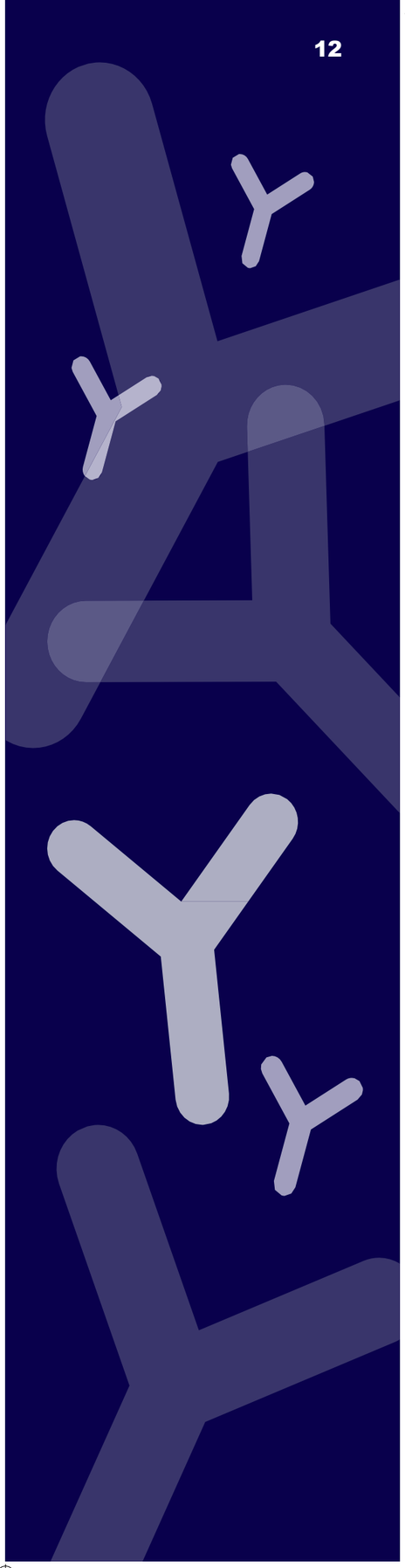
Based on BSA dosing requirements, 2 vials may be needed for some individuals (BSA > 1.94m^2) for days 5-14[2].

2. Mosteller RD. Simplified calculation of body-surface area. N Engl J Med. 1987;317(17):1098. doi: 10.1056/NEJM198710223171717.

How to use TZIELD: Infusion preparation

- Prepare TZIELD using aseptic technique.
- Based on BSA dosing requirements (e.g., >1.94 m^2), 2 vials may be needed for days 5 through 14.
- Start the TZIELD infusion within 2 hours of preparation. If not used immediately, store the infusion solution at room temperature [15°C to 30°C] and complete infusion within 4 hours of the start of preparation.

Please refer to the Prescribing Information for full guidance on the infusion preparation.



For more information about teplizumab, please contact Sanofi at : 09-8633081

In case of any suspected adverse reaction please report via the national reporting system using an online form: https://sideeffects.health.gov.il/
and to Sanofi at: 09-8633081.

This guide, format and content have been approved by the Ministry of Health in November 2025.

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Notes