

TZIELD (teplizumab)

Guide for patients

This guide is for patients treated with TZIELD (teplizumab) and / or their legal representatives / caregivers

This guide contains important safety information patients / legal representatives / caregiver should be aware of when treated with TZIELD.

Please read the Patient leaflet for more information.

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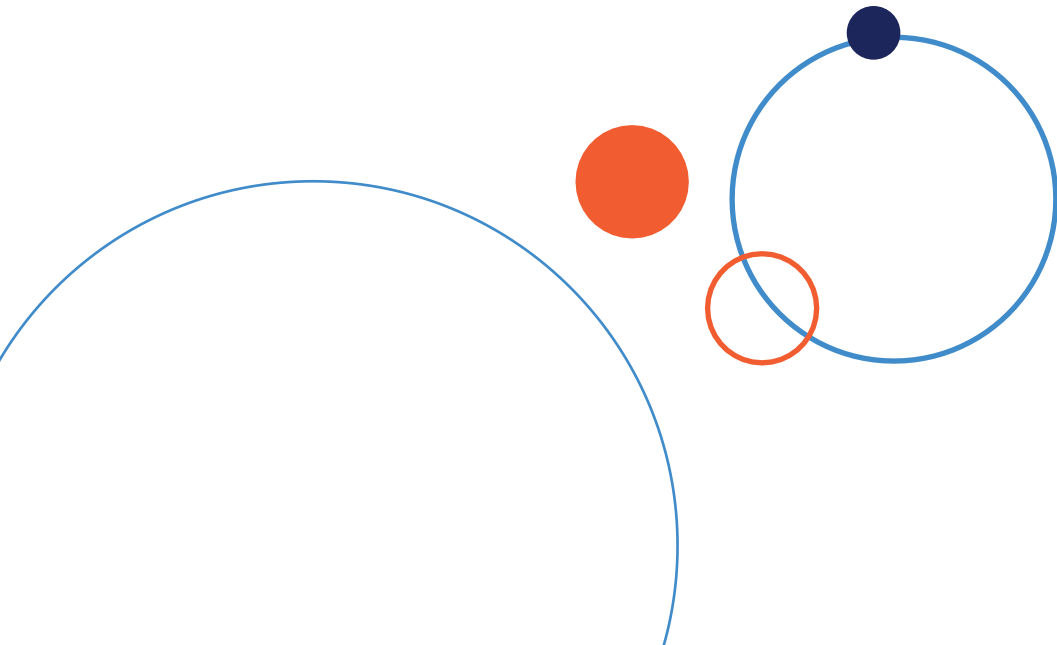
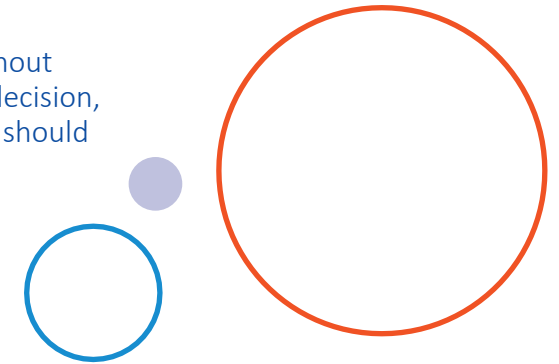
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Objectives of this guide

This guide includes important information about the treatment with TZIELD and some serious side effects that could occur when treated with TZIELD:

- Cytokine Release Syndrome (CRS)
- Decrease in white blood cells (Lymphopenia)
- Serious infections
- Hypersensitivity reactions

For patients who are minors or without the capacity to make an informed decision, the legal representative / caregiver should read this guide.



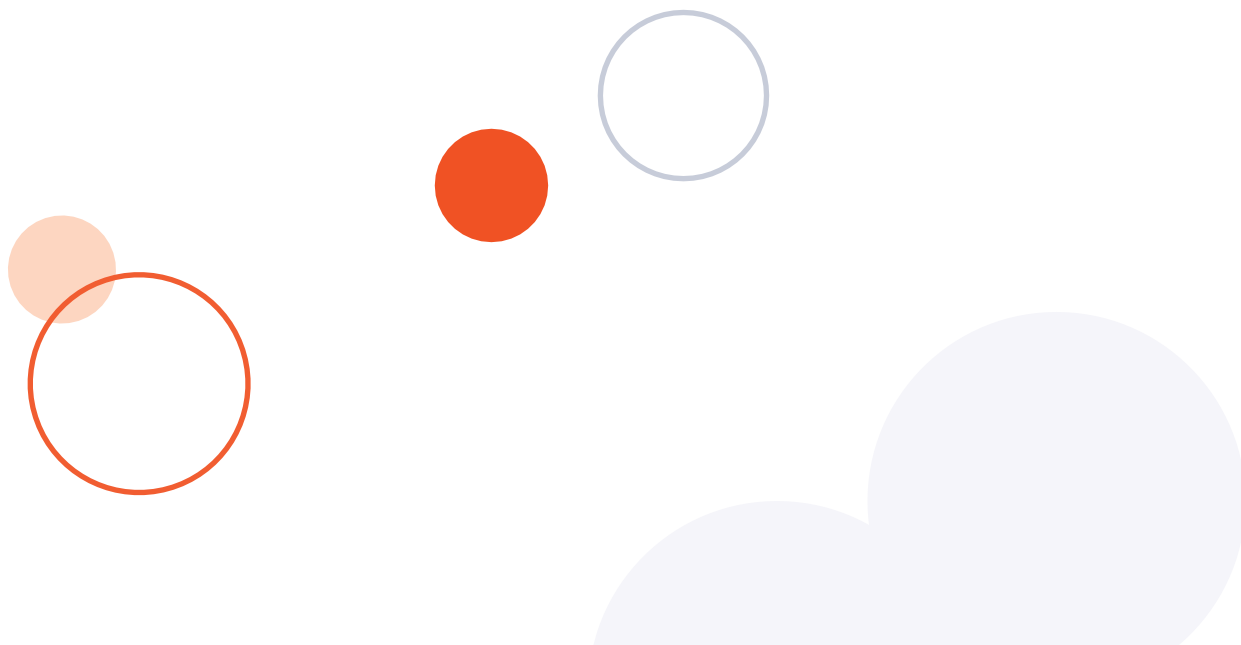
What is autoimmune type 1 diabetes (T1D)

Type 1 diabetes is an autoimmune disease in which the immune system attacks the beta cells in the pancreas that make insulin. The disease progresses in stages:

- **Stage 1:** No clinical symptoms are present, but autoantibodies can be detected in the blood, and blood sugar levels remain normal.
- **Stage 2:** Blood sugar levels begin to rise (dysglycemia), and autoantibodies are still detectable, but insulin therapy is not yet required.
- **Stage 3:** A significant portion of the beta cells have been destroyed by the autoimmune attack. At this point, clinical symptoms may appear, such as increased thirst, frequent urination, unexplained weight loss, blurred vision, and generalized fatigue. Insulin treatment is required at this stage to control blood sugar levels and prevent complications.

How TZIELD works

TZIELD is a treatment for adults and children aged 8 years or more that have stage 2 T1D. It delays the stage 3 of type 1 diabetes.



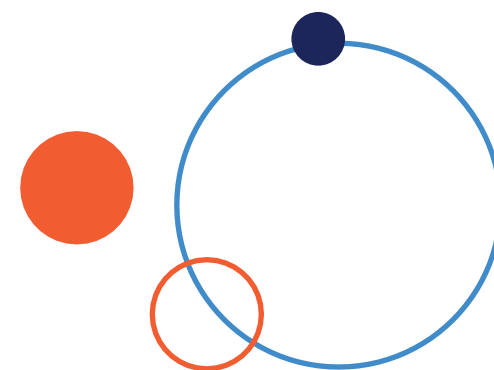
Can I receive a treatment with TZIELD?

Your doctor will perform lab tests to confirm that you suffer from stage 2 type 1 diabetes and have no contraindications to receive TZIELD treatment.

1. Confirmation of my stage 2 T1D

You are treated with TZIELD because:

- you have been tested positive for 2 or more type 1 diabetes-related autoantibodies
- you have abnormal blood sugar levels and
- you do not have Type 2 diabetes



2. Prior to starting my treatment with TZIELD

Before starting and during the treatment with TZIELD your doctor will do blood tests to check:

- your liver function
- your complete blood counts

and check:

- laboratory or clinical evidence of acute infection of Epstein-Barr virus, EBV (mononucleosis) or cytomegalovirus (CMV)
- if you currently have an active serious or chronic infection

What should I do:

Tell your doctor about all your medical conditions, including if you:

- have experienced a severe allergic reaction, including anaphylaxis, to teplizumab or any of its excipients
- have a serious or chronic infection or if you develop signs / symptoms of an infection
- have recently received or are scheduled to receive any vaccine
- are pregnant or plan to become pregnant as TZIELD should not be received during pregnancy and at least 30 days before a planned pregnancy
- are breastfeeding or plan to breast feed as it is not known if TZIELD passes into your breast milk

3. Vaccination

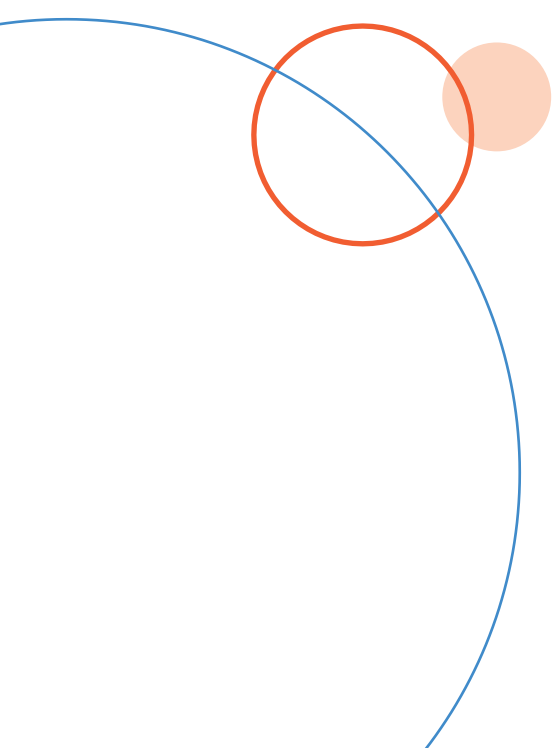
TZIELD may affect how well a vaccine works. Depending on the type of vaccine, your doctor will tell you when you can safely receive any vaccine prior to and after the treatment with TZIELD. For some vaccines it may be required to wait for up to 1 year after the treatment with TZIELD to receive it.

What should I do:

Tell your doctor if you:

- have recently received or are scheduled to receive a vaccine
- are receiving / received treatment with TZIELD before receiving any vaccine as TZIELD may affect how well a vaccine works.
- Tell your doctor that you are being treated with TZIELD before receiving vaccine. Routine vaccinations should be completed before starting treatment with TZIELD. Live attenuated, inactivated, or mRNA vaccines should be avoided while taking TZIELD.

How is the treatment with TZIELD organized?



Your doctor will explain to you how you will receive the treatment.

Prior to receiving your TZIELD infusion

On the first 5 days of treatment your doctor will give you some medications to avoid having some side effects, this is called premedication.

These medications include:

1. ibuprofen or naproxen or other anti-fever medicines such as paracetamol
2. an antihistamine
3. if needed, an anti-nausea medicine

These medicines may help reduce symptoms of Cytokine Release Syndrome (CRS) such as fever, headache, muscle and joint pain, or nausea. Your doctor may decide to continue with this treatment for longer, if needed.

Your TZIELD treatment

You will receive TZIELD in a vein (intravenous) once a day, every day for 14 days. Each TZIELD infusion will last a minimum of 30 minutes. For safety reasons, the dose of TZIELD will be gradually increased over the first days of infusion. If you miss an infusion, your doctor will continue your treatment on the next day to complete the 14-day course.

You will not receive 2 infusions on the same day.

During and after your treatment with TZIELD

Your doctor will do blood tests and check for any side effects, and treat you as needed.

Your doctor may also temporarily or completely stop your treatment with TZIELD, if you develop liver problems, have a serious infection, or if your blood counts stay too low.

What are the possible serious side effects when using TZIELD?

The below side effects may be serious, although not all patients get them.

Cytokine release syndrome (CRS)

Cytokine Release Syndrome has been observed in patients treated with TZIELD. The signs and symptoms of CRS may include:

- fever
- feeling tired
- muscle and joint pain
- nausea
- headache
- increased liver function test values in your blood.

These signs and symptoms may start during the first 5 days of TZIELD treatment.

What should I do, what will my doctor do?

- **Prior to infusion, your doctor will treat you with anti-fever, antihistamine, and/or anti-nausea medicines for the first five days of treatment to prevent / reduce these potential side effects.** Additional doses could be administered beyond the first five days if needed.
- **Tell your doctor or seek medical advice right away** if you develop any signs and symptoms of CRS during your treatment with TZIELD.
- **During your treatment with TZIELD your doctor will do blood tests to check your liver enzymes.**
- **Your doctor may temporarily or completely stop your treatment with TZIELD, if you develop severe stage of CRS.**

What are the possible serious side effects when using TZIELD?

Decrease in white blood cells (Lymphopenia)

TZIELD may cause a decrease in a type of white blood cell called lymphocytes. A decrease in white blood cells is a serious, but very common side effect that can affect your body's ability to fight infections.

A decrease in white blood cell counts can happen after your first dose. Your white blood cell counts are expected to begin returning to normal values after your fifth dose of TZIELD, and will return to pre-treatment values within two weeks after completing the treatment.

Some people may develop longer and more severe decreases in lymphocytes.

What should I do, what will my doctor do?

- **During the treatment with TZIELD your doctor will do blood tests to check your white blood cells values.**
- **Your doctor may temporarily or completely stop your treatment with TZIELD, if your blood counts stay too low.**

Serious infections

TZIELD may lower the ability of your immune system to fight infection. Bacterial and viral infections have been reported in patients treated with TZIELD.

What should I do, what will my doctor do?

- **Tell your doctor** if you have a serious infection or an infection that does not go away or that keeps coming back (chronic infection).
- If signs or symptoms of a serious infection develop during your treatment with TZIELD, **tell your doctor or seek medical advice right away.**
- Your doctor will **treat it appropriately and stop your treatment with TZIELD.**



The format and content of this Patient guide was approved by the Ministry of Health in November 2025.

Reporting suspected adverse reactions to the Ministry of Health by using an online form <https://sideeffects.health.gov.il> or report directly to Sanofi: 09-8633081