Tzield® ▽
(teplizumab)

TZIELD® ▽
(teplizumab)

Infusion Guidebook

Preparing for a confident infusion journey for both you and your patients

TZIELD is indicated to delay the onset of Stage 3 Type 1 diabetes (T1D) in adult and paediatric patients 8 years of age and older with Stage 2 T1D.[1]

This infusion guidebook is funded and created by Sanofi for healthcare professionals in the UK who plan to prescribe, or already prescribe, TZIELD. Prescribing information can be accessed here.

▽ Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to the Sanofi drug safety department on Tel: 0800 0902 314. Alternatively, send via email to UK-drugsafety@sanofi.com.

T1D, Type 1 diabetes.

sanofi

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Introduction

Your guide to TZIELD infusions

The purpose of this guide

This guidebook is designed as a practical, step-by-step resource to help you and your multi-disciplinary team administer TZIELD confidently from the very first infusion, creating a positive treatment experience for both you and your patients.

Importantly, this guide has been co-created with experienced clinical experts who have successfully delivered TZIELD infusions, ensuring that you benefit from real-world experience and proven approaches to infusion management.

How to use this guide

- Sections are arranged in the order you'll encounter tasks, from patient eligibility and pre-treatment checks, to infusion administration and post-treatment monitoring
- Space has been provided for note taking at the end of every section
- At the end, you'll find concise checklists to help streamline your process

TZIELD is indicated to delay the onset of Stage 3 T1D in adult and paediatric patients aged 8 years and older with Stage 2 T1D.[1]

Please refer to the Summary of Product Characteristics (SmPC) before prescribing TZIELD.

To access the SmPC, click here.

Section 1

Clinical overview

Section 1

1.1 About TZIELD

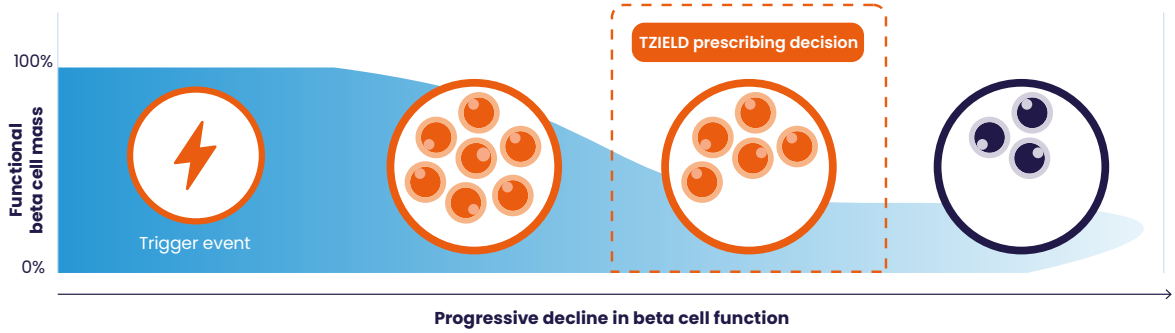
Positioning TZIELD in the autoimmune T1D continuum

Autoimmune T1D is a progressive condition characterised by the irreversible loss of pancreatic beta cells.[2-5] Beta cell loss is driven by autoreactive CD8+ T lymphocytes.[6-8]

Following a trigger event, such as a viral infection, autoimmune T1D progresses in distinct stages.[9-11]

The stages of autoimmune T1D[9-11]

	Presymptomatic		Symptomatic
	STAGE 1	STAGE 2	STAGE 3
Blood tests	**Normoglycaemia**	**Dysglycaemia**	**Hyperglycaemia**
FPG	<5.6 mmol/L	5.6–6.9 mmol/L	≥7.0 mmol/L
120-min OGTT	<7.8 mmol/L	7.8–11.0 mmol/L	≥11.1 mmol/L
HbA1c	<39 mmol/mol (<5.7%)	39–47 mmol/mol (5.7–6.4%)	≥48 mmol/mol (≥6.5%)
AAbs	**≥2**	**≥2***	**≥1**



Adapted from Haller MJ, et al. 2024, Phillip M, et al. 2024, and Breakthrough T1D. The Stages of type 1 diabetes.[9-11]

For a comprehensive overview of staging criteria, please refer to the **Resources** section at the end of this guide.

Stage 1: In children, the 5-year risk of progressing to Stage 3 T1D from Stage 1 is ~44%[9,12,13]

Stage 2: In children, the 5-year risk of progressing to Stage 3 T1D from Stage 2 is ~75%[9,12,14]

Stage 3: Symptomatic, clinical T1D (excessive thirst, frequent urination, unintentional weight loss, fatigue). **By the time clinical symptoms appear, ~60–90% of beta cells may have already been lost†[15-18]**

The lifetime risk of progressing to clinical autoimmune T1D (Stage 3) from Stages 1 and 2 approaches 100% in children.[9,12]

*Reversion to single autoantibody or negative status can occur in some people with previously confirmed multiple autoantibody positivity.[10]
†Beta cell mass is highly heterogeneous among patients with autoimmune T1D and may not correspond with severity of clinical presentation.[19]

1.1 About TZIELD

TZIELD is the first and only therapy approved to delay the onset of Stage 3 T1D in adult and paediatric patients aged 8 years and older with Stage 2 T1D.[1]

The mechanism of action of TZIELD

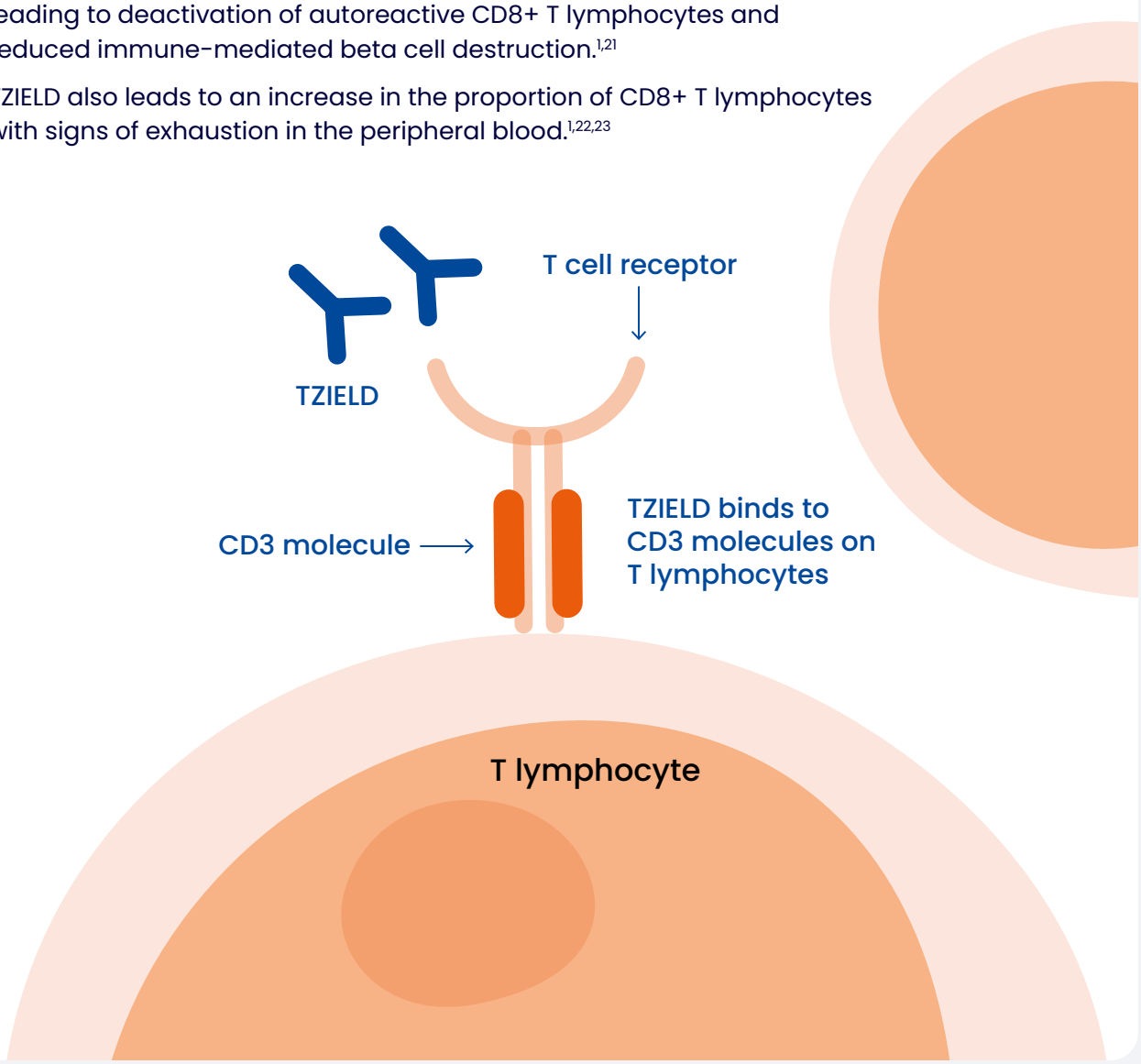
TZIELD is a humanised anti-CD3 monoclonal antibody designed to modulate the autoimmune process that drives beta cell destruction in T1D.[20] Although the mechanism of action is not yet fully defined, evidence indicates that TZIELD is not broadly immunosuppressive; instead, it primarily acts as an immune modulator, restoring balance between effector and regulatory T-cell populations.[20]

By targeting the underlying immune attack and helping slow the loss of insulin-producing beta cells, TZIELD can delay progression from Stage 2 to Stage 3 T1D, providing valuable time before insulin replacement therapy becomes necessary.[2,20]

TZIELD binds to CD3 (a cell surface antigen present on T lymphocytes).[1,21]

The mechanism of action may involve partial agonistic signalling leading to deactivation of autoreactive CD8+ T lymphocytes and reduced immune-mediated beta cell destruction.[1,21]

TZIELD also leads to an increase in the proportion of CD8+ T lymphocytes with signs of exhaustion in the peripheral blood.[1,22,23]



Clinical efficacy data

The clinical safety and efficacy of TZIELD was tested in the TrialNet-10 (TN-10) clinical trial.[24]

TN-10 was a randomised, double-blind, placebo-controlled Phase II trial evaluating the efficacy and safety of TZIELD in individuals deemed at high risk‡ for developing clinical autoimmune T1D.[24]

Primary endpoint:
Time to diagnosis of Stage 3 T1D.[24]

Eligibility criteria:

Individuals aged 8–45 years who were:[24]

- relatives of people with autoimmune T1D
- positive for ≥2 diabetes-related AAbs
- demonstrating dysglycaemia on OGTT

Note: The above outlines the patient eligibility criteria for TN-10. TZIELD is indicated to delay the onset of Stage 3 T1D in adult and paediatric patients 8 years of age and older with Stage 2 T1D.[1]

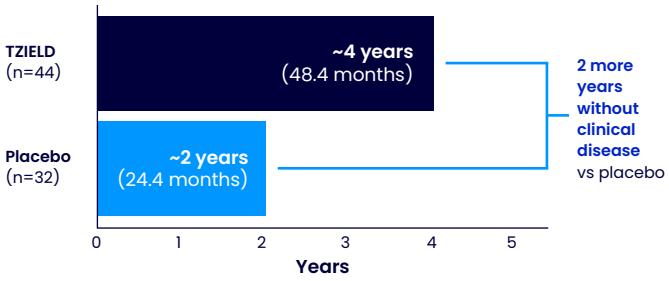
TN-10 primary and extended analysis:

TN-10 primary analysis (median follow-up time: ~2 years)§[24]

In the TN-10 trial in patients with Stage 2 T1D (N=76), those treated with TZIELD took a median of 2 more years to progress to clinical disease (Stage 3) vs placebo.

(HR 0.41; 95% CI, 0.22–0.78; *P*=0.0066 by an adjusted Cox proportional-hazards model stratified by age and OGTT status at randomisation).

Primary endpoint: Median time to Stage 3 T1D onset



Median follow-up time was 745 days (range: 74 days–2,683 days).

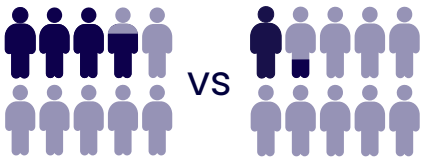
Stage 3 T1D was diagnosed in 20 (45%) patients treated with TZIELD and 23 (72%) patients treated with placebo.[1]

Extended analysis (median follow-up time: ~7 years)‖[22]

The median time to Stage 3 T1D was ~4 years in the TZIELD group vs ~2 years in the placebo group (*P*=0.0026).

After a median follow-up of ~7 years (80.46 months):

36.4% of TZIELD-treated patients (n=16/44)



12.5% of patients on placebo (n=4/32)

had not progressed to Stage 3 T1D (*P*=0.03; Fisher's exact test)

Extended follow-up analysis limitations: The TN-10 trial was relatively small (N=76) and therefore the estimated power was limited.[22,24] Definitive conclusions cannot be derived from these extended follow-up data. Patient results may vary.

‡Consensus guidance endorsed by ISPAD considers individuals with single or transient single AAb status to be at risk for developing autoimmune T1D.[10]
§In the primary analysis of the TN-10 trial, 76 patients aged 8–49 years with Stage 2 T1D received either a single 14-day course of TZIELD or placebo and were followed in a blinded fashion until 40 patients had developed Stage 3 T1D.[24]
‖In an extended analysis of the TN-10 trial, after a median follow-up of 80.46 months, median time to Stage 3 T1D onset was 52.2 months (95% CI: 30.5–86.7) in the TZIELD group vs 27.3 months (95% CI: 9.5–48.4) in the placebo group (*P*=0.0026, log-rank test).[22]

Safety profile

TZIELD is an immunomodulator with a well-documented safety profile.[1]

The safety of TZIELD was assessed in a pooled analysis of five clinical trials.[1]

Adverse reactions occurring in ≥5% of patients in the pooled safety analysis of clinical studies[1]

	Frequency		
System organ class	**Very common** (≥1/10)	**Common** (1/100 to <1/10)	**Not known**¶
Blood and lymphatic system disorders	Lymphopenia Leukopenia Neutropenia Decreased haemoglobin Thrombocytopenia		
Immune system disorders		CRS	
Nervous system disorders	Headache		
Respiratory, thoracic and mediastinal disorders		Nasopharyngitis	
Gastrointestinal disorders	Nausea	Diarrhoea	Vomiting
Skin and subcutaneous tissue disorders	Rash Pruritus	Urticaria	Rash Pruritic
General disorders and administration site conditions	Pyrexia	Chills	Fatigue Pain Illness
Investigations	Increased ALT, Increased AST, Decreased blood bicarbonate, Decreased blood calcium		

Adapted from TZIELD (teplizumab) UK SmPC. 2025.[1]

The most frequently reported adverse reactions were:[1]

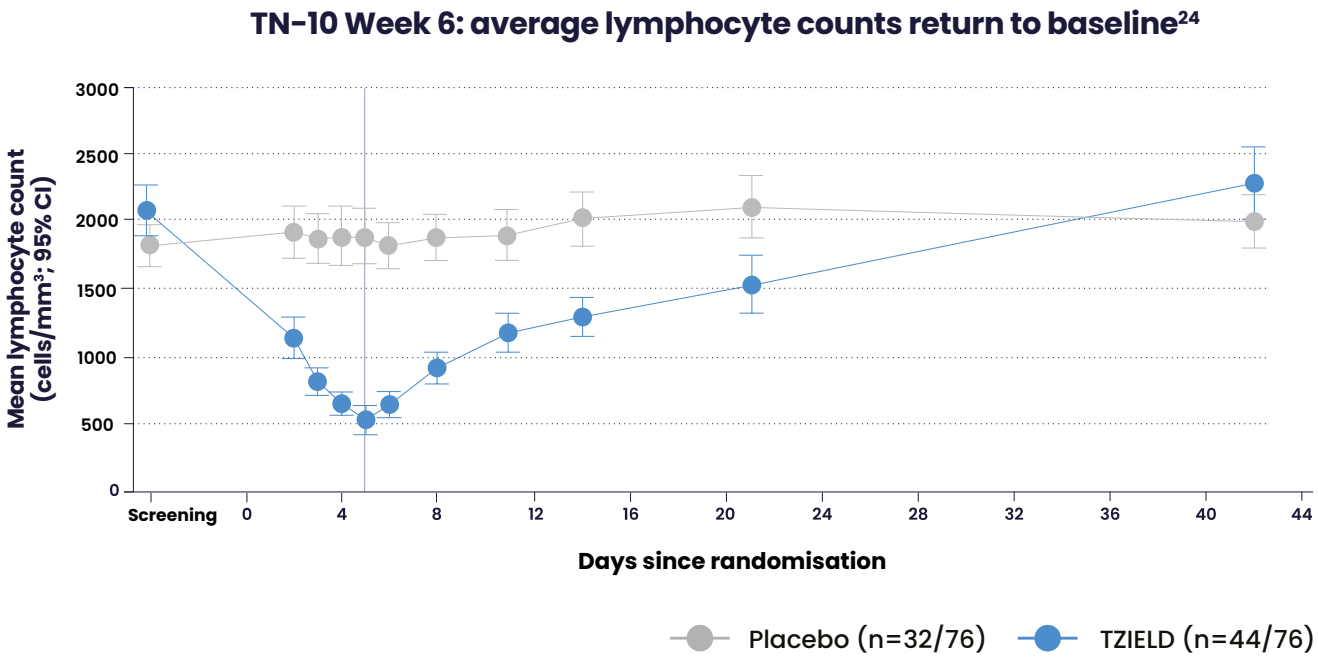
- lymphopenia
- leukopenia
- neutropenia
- decreased blood bicarbonate
- rash

Importantly, TZIELD is not an immunosuppressant; it is an immunomodulator designed to target and modulate T lymphocyte activity rather than broadly suppress immune function.[1,25] Some laboratory changes, such as lymphopenia, can be expected and are consistent with those seen with other immunomodulatory therapies used for autoimmune conditions such as multiple sclerosis and rheumatoid arthritis. While TZIELD is the first therapy of its kind in autoimmune T1D, its safety profile is not unusual within this therapeutic class.[26,27]

¶Cannot be estimated from available data.

1.1 About TZIELD

Lymphopenia is an expected and very common adverse reaction to TZIELD that is often resolved by Week 6.[1,24]

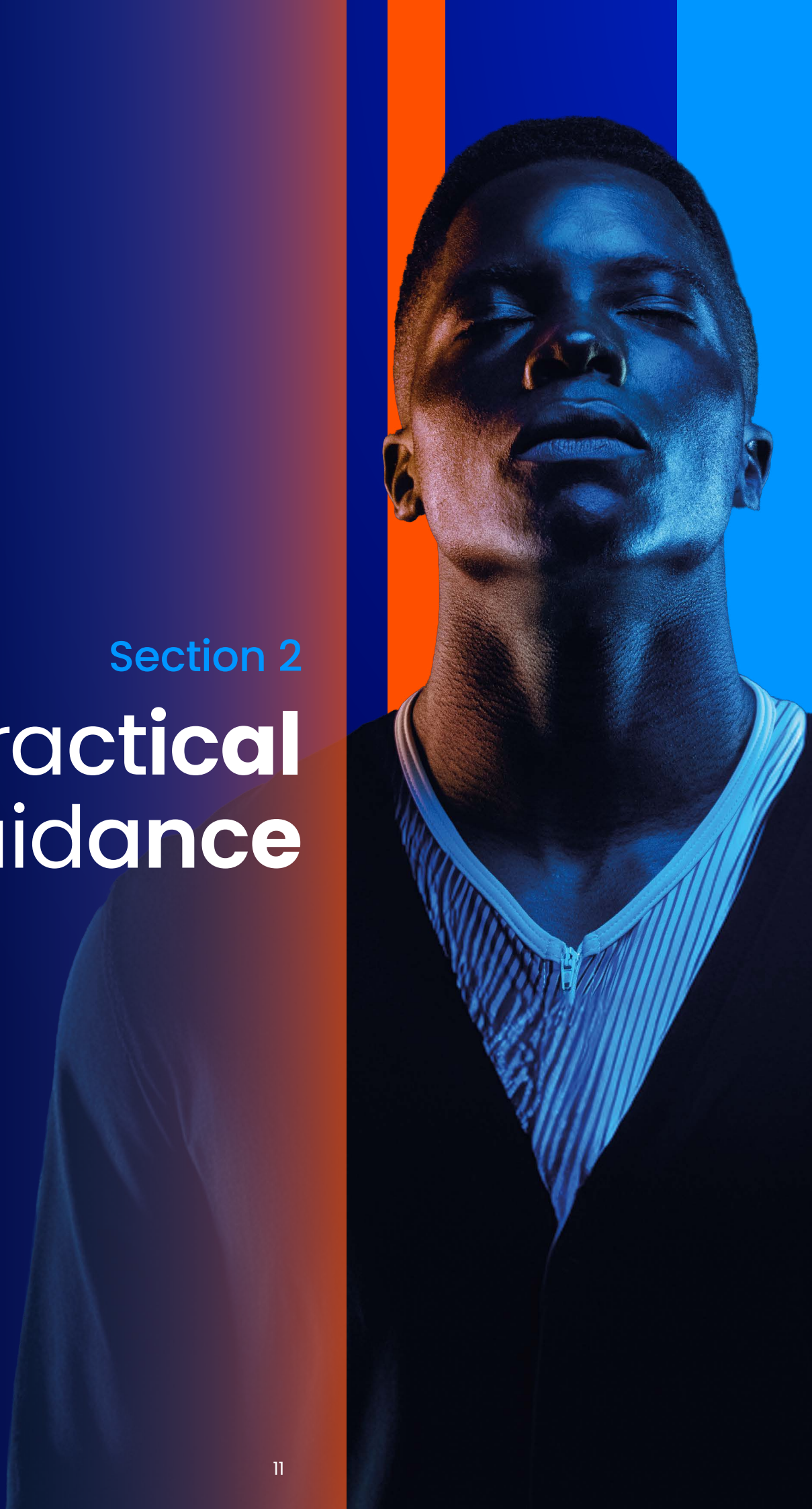


Adapted from Herold KC, et al. 2019.[24]

Notes

Section 2

Practical guidance



Section 2

2.1 Prescribing TZIELD

Patient eligibility criteria

To be eligible for TZIELD, patients must:[1]

be aged 8 years or above

have Stage 2 T1D confirmed by:

- the presence of ≥2 pancreatic islet-specific AAbs
- dysglycaemia without overt hyperglycaemia

not have Type 2 diabetes or secondary dysglycaemia related to a condition other than autoimmune T1D

A TZIELD eligibility checklist is provided in the **Resources** section at the end of this guide.

Pre-treatment requirements

Before initiating treatment with TZIELD, it is essential to complete all baseline evaluations and pre-treatment checks.

Ensure patients receive the Patient Guide and understand the potential risks associated with TZIELD. Take time to counsel patients on what to expect during and after treatment, including the follow-up requirements. Explain monitoring plans and when to return for review. Reassure that care continues beyond the last infusion and outline ongoing responsibilities (i.e. blood glucose monitoring, symptom reporting).

See **pages 39 and 40** for more information on how to prepare and support patients throughout their treatment with TZIELD.

2.1 Prescribing TZIELD

Laboratory evaluations

Prior to initiating TZIELD, you must obtain a complete blood count and liver enzyme tests.[1]

Use of TZIELD is **not recommended** in patients with:[1]

Lymphocyte count	<10^9 lymphocytes/L
Haemoglobin	<100 g/L
Platelet count	<150 x 10^9 platelets/L
Absolute neutrophil count	<1.0 x 10^9 or <1.5 x 10^9 neutrophils/L*
Elevated ALT or AST or bilirubin	>2 x ULN >1.5 x ULN
Laboratory or clinical evidence of acute infection with Epstein-Barr virus or cytomegalovirus	
Active serious infection or chronic active infection other than localised skin infections	

Vaccinations

TZIELD may interfere with the immune response to vaccination and decrease vaccine efficacy.[1]

Prior to initiating TZIELD, you must administer all age-appropriate vaccinations.[1]

Administer live-attenuated (live) vaccines at least **8 weeks prior** to treatment[1]

Administer inactivated (killed) vaccines or mRNA vaccines at least **2 weeks prior** to treatment[1]

Individuals should be up-to-date on all vaccines including influenza and COVID-19 prior to treatment initiation.[20]

*Absolute neutrophil count <1.0 x 10^9 neutrophils/L in those of African descent and <1.5 x 10^9 neutrophils/L in all other groups.[1]

Premedications

Cytokine release syndrome (CRS) is a systemic inflammatory response caused by the release of large amounts of cytokines.[28,29]

To mitigate CRS, premedicate prior to TZIELD infusion for the first 5 days of dosing with:[1]

1. a nonsteroidal anti-inflammatory drug (NSAID) or paracetamol
2. an antihistamine
3. an antiemetic (if required)

Additional doses of premedication can be administered if needed.

For more information about managing adverse reactions including CRS, see **pages 30–32**.

Take-home medications

Please ensure take-home medications are prescribed **in advance** so patients can manage mild symptoms at home, with clear instructions on how and when to use them.

Considerations for women of childbearing potential

Fertility

There are no clinical data available for the effects of TZIELD on fertility.[1]

Pregnancy

There are insufficient data to assess the risk of adverse maternal or foetal outcomes as a result of TZIELD treatment.[1]

To minimise exposure to a foetus, avoid prescribing TZIELD during pregnancy and for at least 30 days prior to planned pregnancy.[1]

Breastfeeding

There are no data on the presence of TZIELD in human milk, effects on milk production, or effects on the breastfed child.[1]

To minimise drug exposure to a breastfed child, lactating patients may interrupt breastfeeding and pump and discard breast milk during treatment with TZIELD, and for 20 days after TZIELD.[1]

To support readiness and streamline the infusion process, a TZIELD infusion checklist is provided in the **Resources** section at the end of this guide.

Notes

Section 2

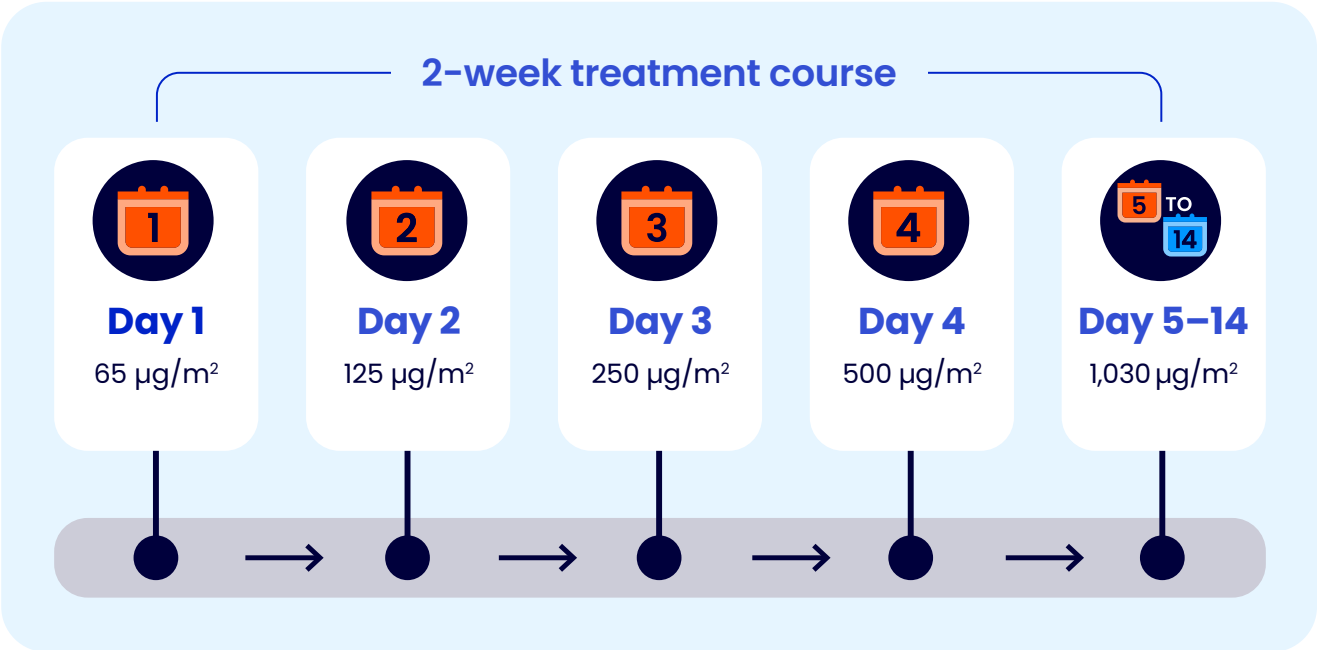
2.2 Dosing

TZIELD is administered by intravenous (IV) infusion over a minimum of 30 minutes once daily for 14 consecutive days.[1]

Once daily, consecutive 14-day course

≥30-minute administration

The recommended TZIELD dosage for adults and paediatric patients aged 8 years and older uses body surface area (BSA)-based dosing and is administered according to the following regimen[1]:



How to calculate BSA using the Mosteller formula

There are a number of mathematical formulas you can use to calculate BSA,[30] as well as online resources to help you perform these calculations.[31]

In the TN-10 trial, the Mosteller formula was used to calculate BSA.[32]

BSA equation:

$$\text{BSA } (m^2) = \sqrt{\frac{[\text{height (cm)} \times \text{weight (kg)}]}{3{,}600}}$$

The Mosteller formula[30]

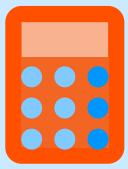
1. **Measure** the height (cm) and weight (kg) of your patient
2. **Multiply** their height and weight
3. **Divide** the product **by 3,600**
4. **Calculate** the **square root** of that number
5. **Result =** BSA in m^2

Worked example BSA calculation:

Example patient:
male, 8 years old, 118 cm, 24 kg

$$\text{BSA } (m^2) = \sqrt{\frac{(118)(24)}{3{,}600}} = \mathbf{0.89\ m^2}$$

Not actual patient.



To access the online TZIELD dosing calculator, click here.

Based on BSA dosing requirements, multiple vials may be needed for some individuals (for example, in patients with a BSA >1.94 m^2).[1]

Notes

Section 2

2.3 Preparing TZIELD for infusion

Supplies

Before you start preparing the infusion, ensure that you have all the essential supplies.

Administration supplies

Ensure availability of the following:[1]

- ☐ Vials of TZIELD†
- ☐ Sterile glass vial OR sterile PVC infusion bags
- ☐ Sterile diluent (0.9% sodium chloride injection)
- ☐ Sterile syringe
- ☐ IV catheter
- ☐ Routine infusion supplies (e.g., needles, gauze, tape, alcohol wipes and tourniquet)

In case of emergency

Ensure age-appropriate emergency medications, equipment and trained personnel are present for every TZIELD infusion.[20]

- ☐ Adrenaline
- ☐ Oxygen
- ☐ Bronchodilators
- ☐ Dexamethasone (or equivalent glucocorticoid)
- ☐ Antihistamines
- ☐ Resuscitation equipment and other supplies for the emergency management of an allergic/adverse reaction

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Next, inspect TZIELD visually.[1] The solution should be clear and colourless. Do not use TZIELD if particulate matter or colouration is seen.[1]

TZIELD must be diluted prior to use, this involves a two-step process.[1]

TZIELD should be prepared using standard aseptic non-touch technique (ANTT)[1]

Each vial is intended for a single dose only[1]

†A patient may need more than one vial (e.g., if BSA >1.94 m^2).[1]

2.3 Preparing TZIELD for infusion

Preparing an IV infusion bag[1]

Step 1

Initial dilution

Prepare 18 mL of sodium chloride 0.9% solution in a -

- Sterile glass vial (shown), **OR**
- Sterile PVC infusion bag

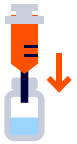
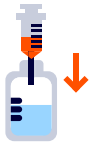
1. Remove the cap from the vial – **this is the preparation start time**

2. Remove 2 mL of TZIELD from the vial

TZIELD	2 mL	

3. Slowly add to the 18 mL of 0.9% sodium chloride

4. Mix gently by slowly swirling the vial or rocking the infusion bag

	Vessel	Vial	IV Infusion Bag
TZIELD	2 mL		
Saline solution	18 mL		
Initial dilution (1/10)	20 mL	 **10x**	 **10x**

The resulting 20 mL diluted solution contains 100 µg/mL of TZIELD

5. Calculate your patient's BSA, e.g., by using the Mosteller formula

$$\text{BSA } (m^2) = \sqrt{\frac{[\text{height (cm)} \times \text{weight (kg)}]}{3{,}600}}$$

6. Using your patient's BSA, calculate the required dose needed for the treatment day

$$\text{Dose } (\chi\ \mu g) = \text{Daily dosage level } \left(\frac{\chi\ \mu g}{m^2}\right) \times \text{BSA } (m^2)$$

7. Calculate the volume of 100 µg/mL diluted TZIELD solution (prepared in Step 1) to be further diluted in Step 2

$$\text{Volume of initial dilution, 1:10 (mL)} = \frac{\text{Dose } (\chi\ \mu g)}{100}$$

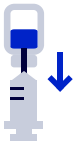
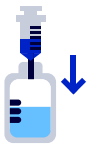
2.3 Preparing TZIELD for infusion

Preparing an IV infusion bag[1]

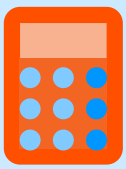
Step 2

Final dilution

Infusion bag for IV infusion

		Vessel	Vial	IV Infusion Bag
1. Using an appropriately sized syringe (e.g., 5 mL), withdraw the volume of diluted solution required for that day's calculated dose	**Initial dilution (1/10)**	2 mL		
		Intermediate volume		
2. Slowly add contents of the syringe containing the dose to a PVC infusion bag containing 25 mL 0.9% sodium chloride solution for injection	**Initial dilution (1/10)**	Intermediate volume		
	Saline solution	25 mL		
3. Gently rock the infusion bag to ensure that the solution mixes sufficiently. Do not shake	**Final dilution**	Total infusion volume		

Infusion administration has a minimum duration of 30 minutes.



To access the online TZIELD dosing calculator, click here.

2.3 Preparing TZIELD for infusion

Worked example for a complete dosing schedule

Infusion bag

BSA: **0.89m²** Age: **8** Weight: **24 kg** Height: **118 cm**	**Stage 2**		Dosing method **IV infusion bag**		
	DAY 1	DAY 2	DAY 3	DAY 4	DAYS 5–14
Dosing Regimen (µg)	57.9 (65 x 0.89)	111.3 (125 x 0.89)	222.5 (250 x 0.89)	445.0 (500 x 0.89)	916.7 (1,030 x 0.89)
Volume of intermediate TZIELD dilution to add to infusion bag (mL)	0.58 (57.9 ÷ 100)	1.1 (111.3 ÷ 100)	2.2 (222.5 ÷ 100)	4.5 (445.0 ÷ 100)	9.2 (916.7 ÷ 100)
Volume of saline (mL)	25.0	25.0	25.0	25.0	25.0
Total infusion volume (mL)	25.6 (25 + 0.58)	26.1 (25 + 1.1)	27.2 (25 + 2.2)	29.5 (25 + 4.5)	34.2 (25 + 9.2)
Number of daily vials needed	1	1	1	1	1

Total number of vials for the 14-day treatment course: 14

If two vials of TZIELD are needed, make sure the complete dose for each day is contained in one infusion bag:[1]

- Prepare two dilution solutions
- Add the cumulative volume for the calculated dose to a single 25 mL 0.9% saline infusion bag

Choosing an infusion line

TZIELD is compatible with a number of different infusion lines:‡[20]

IV peripheral catheter (the method used in the TN-10 trial)

Midline catheter

Peripherally inserted central catheter (PICC) line

To help determine the choice of infusion line, healthcare professionals should consider patient preferences, presence of trained personnel and local hospital policies.[20] Individuals and their caregivers should be presented with all access options.

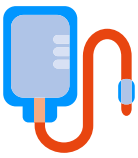
‡Sanofi does not endorse a particular method of infusion line placement; this is at the discretion of the healthcare provider.

Notes

Section 2

2.4 Administering the TZIELD infusion

Timing of the infusion



The infusion should be initiated within 2 hours of preparation and completed within 4 hours of preparation[1]

If not used immediately, store the infusion solution at room temperature (15–30°C). Discard the solution if not administered within 4 hours of preparation.[1]

The infusion should be administered over a minimum of 30 minutes[1]

Administering the infusion at the same time every day will maintain a dosing interval close to every 24 hours

Missed or interrupted doses

If a planned infusion is missed, resume dosing on the following day and administer all remaining doses on consecutive days to complete the 14-day treatment course.[1]

Do not administer two doses on the same day.[1]

Flushing

Flushing with a small amount of additional saline at the end of the infusion will help ensure the complete dose of TZIELD has been administered and cleared from the infusion tubing.[20,33]

Disposing of TZIELD

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.[1]

No solutions other than 0.9% sodium chloride may be run through the same IV line when TZIELD is being administered.[1]

Notes

Section 2

2.5 Monitoring patients during and after each TZIELD infusion

Vital signs:

Assess vital signs every 15 minutes and for an additional 60 minutes after infusion.[20]

Immediate reactions:

Monitor for signs and symptoms of infusion reactions both during and immediately after the infusion.[1,20]

These include but are not limited to the following:[1,20]

- Fever
- Chills
- Headache
- Nausea
- Vomiting
- Infusion-site pain
- Anaphylaxis
- Urticaria
- Rash

For detailed information on adverse reactions with TZIELD and how to mitigate them, see **pages 30–32**.

Notes

Section 2

2.6 Managing adverse reactions

Special warnings and precautions for use

Like all medicines, TZIELD may cause adverse reactions. Throughout the course of treatment, monitor for:[1]

Possible infusion-related adverse reaction	How to mitigate
CRS • CRS has been observed in TZIELD treated patients • In clinical trials, CRS was reported in 6% of TZIELD-treated patients during the treatment period and through 28 days after the last study drug administration **Symptoms included:** • Fever • Nausea • Fatigue • Headache • Myalgia • Arthralgia • Increased ALT, AST and total bilirubin • These symptoms typically occurred during the first 5 days of treatment • Inform patients on such signs and symptoms and if they occur, to urgently seek medical advice/contact their care team	• Premedicate prior to the TZIELD infusion for the first 5 days of dosing with: 1. an NSAID or paracetamol 2. an antihistamine 3. an antiemetic (if required) • Administer additional doses of premedication if needed • Monitor liver enzymes ALT, AST and bilirubin during treatment • Discontinue treatment in patients who develop elevated ALT or AST >5 x ULN or bilirubin >3 x ULN • Treat symptoms of CRS with antipyretics, antihistamines, and/or antiemetics • If severe CRS develops, consider temporarily pausing dosing for 1–2 days (and administer the remaining doses to complete the full 14-day course on consecutive days) or discontinuing treatment • Because symptoms may appear after the patient has left the infusion centre, on call or cross-covering providers should be made aware of ongoing infusion therapy and ensure contact information is provided to patients/their family

2.6 Managing adverse reactions

Possible infusion-related adverse reaction	How to mitigate
Lymphopenia • In clinical trials, 80% of TZIELD-treated patients developed lymphopenia • For most patients treated with TZIELD who experienced 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 • Severe lymphopenia ($<0.5 \times 10^9$ cells/L) lasting 1 week or longer occurred in 0.9% of patients treated with TZIELD and 0.5% of patients treated with TZIELD permanently discontinued TZIELD because of lymphopenia • Inform patients that you will be monitoring their white blood cell counts, and if these are too low for a prolonged period of time TZIELD may have to be discontinued	• Monitor white blood cell counts during the treatment period • If prolonged severe lymphopenia ($<0.5 \times 10^9$ cells/L lasting 1 week or longer) develops, discontinue TZIELD

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 an active serious infection or chronic active infection other than localised skin infections
	• Monitor patients for signs and symptoms of infection during and after TZIELD treatment
	• If serious infection develops, treat appropriately, and discontinue TZIELD

Hypersensitivity reactions
• Acute hypersensitivity reactions have occurred in TZIELD-treated patients, including:
  • Serum sickness
  • Angioedema
  • Urticaria
  • Rash
  • Vomiting
  • Bronchospasm
	• If severe hypersensitivity reactions occur, discontinue use of TZIELD and treat promptly

Discontinuing TZIELD

Treatment should be permanently discontinued in the case of:[1]

Elevated ALT or AST Elevated bilirubin	>5 x ULN >3 x ULN
Prolonged severe lymphopenia	<0.5 x 10^9 lymphocytes/L lasting 1 week or longer
A serious infection or hypersensitivity reaction develops	

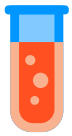
Notes

Section 2

2.7 Monitoring your patients after treatment with TZIELD

It is important that patients and caregivers understand that care does not end after the last infusion.

Post-treatment care



Laboratory evaluations

Follow up with laboratory tests 1–4 weeks post treatment depending on the severity of any abnormalities at end of infusion and then periodically until abnormalities are resolved.[20]

Blood glucose monitoring

Advise patients that regular blood glucose checks are critical after completing TZIELD therapy. This supports timely initiation of insulin and helps prevent DKA.[10]

Consider instituting a surveillance protocol of trending OGTT or continuous glucose monitoring (CGM) results at least every 6 months using threshold values diagnostic for Stage 3 T1D.[20]

Continue to set expectations

Reinforce that TZIELD delays progression but is not a definitive cure.[1]

Educate on the signs and symptoms of Stage 3 T1D

Patients should remain vigilant for symptoms of Stage 3 T1D and report them promptly.[20]

2.7 Monitoring your patients after treatment with TZIELD

Symptoms of Stage 3 T1D – the four Ts[10]

Toilet
Going for a wee more often (especially at night)

Thirsty
Being constantly thirsty and not being able to quench it

Tired
Feeling incredibly tired and lacking energy

Thinner
Losing weight without trying to or looking thinner than usual

Diabetic ketoacidosis (DKA)

Explain that dangerously low insulin levels can lead to ketone accumulation in the blood, causing the blood to become acidic and resulting in a serious, potentially life-threatening condition that often requires hospitalisation. Ensure patients are aware that DKA can occur suddenly and is sometimes the first indication of Stage 3 T1D.[34,35]

Symptoms of DKA[34]

- Nausea and/or vomiting
- Abdominal pain
- Confusion
- Rapid, deep breathing
- Fruity-smelling breath

Ensure patients and caregivers know these warning signs and understand the need for urgent medical attention if they occur.

Vaccinations

Inactivated or mRNA vaccinations may be administered **6 weeks after** completion of treatment.[1]

Live-attenuated vaccinations may be administered **52 weeks after** completion of treatment.[1]

Notes

Section 2

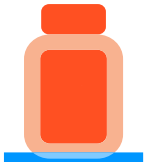
2.8 Supply details and storage guidance

How TZIELD is supplied

TZIELD is supplied as a sterile, clear and colourless solution in a 2 mg/2 mL single-dose vial. Pack sizes range from 1 to 10 to 14 vials.[1]

How to store and handle TZIELD[1]

Store in a refrigerator (2 to 8°C)



Store upright

Do not freeze or shake

Keep the TZIELD vial in the original packaging to protect from light

Notes

Section 2

2.9 Preparing your patients for TZIELD

What to expect

Providing patients with a clear understanding of what to expect helps reduce anxiety and promotes a smooth infusion experience.[36,37]

Patients may experience anxiety related to:

- fear of needles[38,39]
- worry about fainting or feeling faint[38,39]
- general nervousness about the infusion process[36]
- potential side effects[1]

Acknowledge and normalise feelings of anxiety

Reassure patients that feeling anxious is common and that your team is experienced in administering infusions and helping individuals feel relaxed and comfortable throughout the process.

Set expectations clearly

Explain to your patients that treatment with TZIELD can delay, but not prevent, the onset of Stage 3 T1D, and patients will eventually require insulin therapy.[1,10] TZIELD can help the pancreas to produce insulin on its own for a bit longer, providing patients more time to look out for the symptoms of Stage 3 T1D.[10,40]

Let your patients know that while the infusion itself takes at least 30 minutes,[1] the full appointment may last around 4 hours including prep and monitoring. Be sure to walk them through what to anticipate before, during and after the infusion.

Infusion centres can feel cool, and sitting still can cause discomfort. Suggest patients wear comfortable clothing and bring an extra layer.

2.9 Preparing your patients for TZIELD

Other helpful coping strategies

Beyond setting expectations, you can equip patients with tips to help overcome needle phobia and have a more comfortable experience.[38,39]

Applied tension techniques
For patients who might feel faint when faced with needles, it can be helpful to explain the applied tension technique.[38,39]

Breathing exercises
For patients who feel panicky but not necessarily faint, simple breathing exercises can promote relaxation.[38,39]

Distractions
It's also a good idea to suggest bringing additional items to the infusion centre, such as headphones, books, snacks and something to drink. These comforts can help patients stay occupied and relaxed during their infusion.[38,39]

Reassure patients
Be sure to let patients know that, with your and your team's support, most people adapt quickly and are able to establish a routine that works well for them.[38]

Home infusion options

It may be possible to administer TZIELD at your patient's home on some days, via a homecare programme. Eligibility is determined by the prescribing clinician.

- Home infusions offer convenience for your patients and caregivers and may provide a more comfortable environment for patients to access their treatment.[41]
- If at-home infusions are arranged, ensure clear communication is set-up between your patient and the Homecare provider to help create a smooth infusion experience for your patient.

For information surrounding the availability of a Sanofi-funded homecare programme please contact your Sanofi NHS Engagement Manager or email NEMGenMed@Sanofi.com.

Notes

Resources

Resources

Staging criteria for AAb-positive individuals[10]

	Stage	Pancreatic islet AAb status	Glycaemic status	Symptoms
Presymptomatic T1D	Stage 1	≥2	**Normoglycaemia** • FPG <5.6 mmol/L • 120-min OGTT <7.8 mmol/L • HbA1c <39 mmol/mol (<5.7%)	None
	Stage 2	≥2*	**Glucose intolerance or dysglycaemia not meeting diagnostic criteria for Stage 3 T1D, with at least two of the following, or meeting the same single criteria at two time points within 12 months:** • FPG 5.6–6.9 mmol/L • 120-min OGTT 7.8–11.0 mmol/L • OGTT values ≥11.1 mmol/L at 30, 60, and 90 min • HbA1c 39–47 mmol/mol (5.7–6.4%) or longitudinal ≥10% increase in HbA1c from the first measurement with Stage 2 T1D • CGM values >7.8 mmol/L for 10% of time over 10 days' continuous wear† and confirmed by at least one other non-CGM glucose measurement test listed	None
Clinical T1D	Stage 3	≥1	**Persistent hyperglycaemia with or without symptoms, as measured and confirmed by one or more of the following:** • One random venous glucose ≥11.1 mmol/L with overt symptoms • 120-min OGTT ≥11.1 mmol/L and/or • Two random venous glucose ≥11.1 mmol/L and/or • FPG ≥7.0 mmol/L and/or • Laboratory-tested HbA1c ≥48 mmol/mol (≥6.5%) • CGM values >7.8 mmol/L for 20% of time over 10 days' continuous wear† and confirmed by at least one other non-CGM glucose measurement test listed	May include‡: Polyuria Polydipsia Weight loss Fatigue DKA

Adapted from Phillip M, et al. *Diabetes Care*. 2024;47(8):1276-1298.[10]

*Reversion to single AAb or negative status can occur in some people with previously confirmed multiple AAb positivity.[10]
†CGM is ideally blinded and must be applied and interpreted by a trained healthcare professional. Note, CGM metrics are not part of current ISPAD guidelines on staging criteria in T1D.[10]
‡Stage 3 might not include symptoms.[10]

Patient eligibility checklist

This checklist provides a quick, structured way for you to review the key requirements for treatment with TZIELD. It brings together the main clinical and safety criteria to help guide informed decision-making and ensure safe, appropriate treatment initiation.

Age[1]

- [ ] Eight years of age or older

Autoantibodies[1]

- [ ] ≥2 T1D relevant AAbs (GAD-65 antibody, ICA, IA-2A, IAA, ZnT8A)

Circle and date:

- GAD-65 antibody – YES/NO, Date(s): _____
- IA-2A – YES/NO, Date(s): _____
- IAA – YES/NO, Date(s): _____
- ZnT8A – YES/NO, Date(s): _____
- ICA – YES/NO, Date(s): _____

Glucose testing[§20]

- [ ] **1.** OGTT with impaired dysglycaemia within the preceding 6 months[‖]
  - OGTT 30 min: ____ mmol/L
  - OGTT 60 min: ____ mmol/L
  - OGTT 90 min: ____ mmol/L
  - OGTT 2 hours: ____ mmol/L

OGTT 30–90 min postprandial glucose	>11.0 mmol/L
OGTT 2-hour postprandial glucose	7.8–11.0 mmol/L

- [ ] **2.** FPG between 5.6–6.9 mmol/L
  - FPG: _____ mmol/L

- [ ] **3.** HbA1c 5.7–6.4% or ≥10% increase in HbA1c even in the normal range[¶]

§Monitoring guidance, endorsed by ISPAD, recommends measurement of two dysglycaemic parameters or one abnormal parameter repeated within 12 months.[10]
‖Consider repeating OGTT on a separate date if there are no other signs of dysglycaemia.[20]
¶Consider HbA1c change >10% even if under 5.7%.[20]

Additional resources

TZIELD infusion checklist[1]

This checklist provides a quick reference for all key steps, from confirming eligibility and completing baseline assessments to monitoring throughout the infusion course and planning post-treatment care.

Pre-treatment

- [ ] Age 8 years or above
- [ ] Confirmed Stage 2 T1D
- [ ] Clinical history of the patient is not suggestive of Type 2 diabetes

At least two positive pancreatic islet cell AAbs

- [ ] GAD-65 autoantibody
- [ ] IA-2A
- [ ] IAA
- [ ] ZnT8A
- [ ] ICA

- [ ] **Confirmed dysglycaemia without overt hyperglycaemia**

Hepatic function

- [ ] AST ≤2 x ULN
- [ ] ALT ≤2 x ULN
- [ ] Total bilirubin ≤1.5 x ULN

Bone marrow function

- [ ] Haemoglobin ≥100 g/L
- [ ] Lymphocyte count ≥1 x 10^9 lymphocytes/L
- [ ] Absolute neutrophil count ≥1.0 x 10^9 or ≥1.5 x 10^9 neutrophils#
- [ ] Platelet count ≥150 x 10^9/L

Vaccinations

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

#TZIELD is not recommended in patients with absolute neutrophil count <1.0 x 10^9 neutrophils/L in those of African descent and <1.5 x 10^9 neutrophils/L in all other groups.[1]

Additional resources

Exclusion criteria

- [ ] Laboratory or clinical evidence of acute infection with Epstein-Barr virus or cytomegalovirus
- [ ] Active serious infection or chronic active infection other than localised skin infections
- [ ] Pregnancy: Patients should not receive TZIELD during pregnancy
- [ ] Lactation: Advise a lactating woman that she may interrupt breastfeeding and pump and discard breast milk during treatment and for 20 days after TZIELD administration to minimise drug exposure to a breastfed infant

Premedication and take-home medications

- [ ] Ensure premedications and take-home medications are prescribed before the infusion is started

Premedicate prior to the TZIELD infusion for the first 5 days of dosing with:

- NSAID or paracetamol
- an antihistamine
- an antiemetic (if required)

Administer additional doses of premedication if needed

Equipment

- [ ] Ensure availability of all equipment needed for the chosen administration method

During treatment

Throughout the treatment course, monitor:

- [ ] Vital signs
- [ ] Liver enzymes ALT, AST and bilirubin for signs of CRS
- [ ] White blood cell counts for prolonged lymphopenia (<0.5 x 10^9 cells/L lasting 1 week or longer)
- [ ] For signs and symptoms of infection or hypersensitivity reactions

If CRS, lymphopenia, serious infection and/or hypersensitivity reactions were to occur, see the SmPC and previous pages for management considerations

Additional resources

After treatment

Vaccination after the treatment

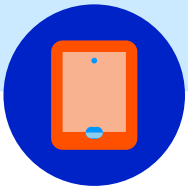
- Inactivated or mRNA vaccines are not recommended for up to 6 weeks after treatment
- Live-attenuated vaccines are not recommended for up to 52 weeks after treatment
- Monitor blood glucose as well as signs and symptoms of hypoglycaemia or hyperglycaemia and manage according to current practice guidelines[10,42]

Additional information

A suite of further materials has been developed to help you feel comfortable and confident prescribing and administering TZIELD.

Online TZIELD Dosing Calculator

TZIELD Campus Website



TZIELD Leave Behind

Infusion Readiness Checklist

The following materials may also be provided to patients:

Paediatric Treatment Handbook

Risk Management Guide for Patients

Adult Treatment Handbook

Patient Website

Homecare Guide

For more information about dosing and administration of TZIELD or to arrange a visit by a local Sanofi representative please contact ContactUKaT1D@sanofi.com

Notes

Glossary

Autoantibody
An antibody reactive to self-antigens. IAA, GAD-65 antibody, IA-2A and ZnT8A are currently used in the detection of autoimmune T1D.[16]

Autoreactive
Reactive to self-antigens, e.g., those expressed on pancreatic islet cells.[43]

CD3 complex
A component of the T-cell receptor (TCR) found on all T lymphocytes. It anchors the TCR to the cell membrane and contains immunoreceptor tyrosine-based activation motifs that initiate intracellular signalling when the TCR recognises an antigen presented by a major histocompatibility complex.[44]

Regulatory T lymphocyte
A specialised subset of T lymphocyte that maintains immune tolerance and prevents excessive immune responses by secreting anti-inflammatory cytokines and direct cell-cell contact inhibition.[45]

Exhausted T lymphocyte
A T lymphocyte that has become functionally impaired after prolonged exposure to persistent antigen stimulation. Exhausted T lymphocytes exhibit poor proliferative potential, high inhibitory receptor expression and reduced effector function.[46]

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Abbreviations

ADA, American Diabetes Association; **ALT,** alanine aminotransferase; **ANTT,** aseptic non-touch technique; **AST,** aspartate aminotransferase; **BSA,** body surface area; **CD3,** cluster of differentiation 3; **CD8,** cluster of differentiation 8; **CGM,** continuous glucose monitor; **CI,** confidence interval; **CRS,** cytokine release syndrome; **DEHP,** di-(2-ethylhexyl)phthalate; **DKA,** diabetic ketoacidosis; **FPG,** fasting plasma glucose; **GAD,** glutamic acid decarboxylase; **HbA1c,** haemoglobin A1c; **HR,** hazard ratio; **IA-2A,** insulinoma-associated antigen 2 antibody; **IAA,** insulin autoantibody; **ICA,** islet cell autoantibody; **ISPAD,** International Society of Pediatric and Adolescent Diabetes; **IV,** intravenous; **NSAID,** non-steroidal anti-inflammatory drug; **OGTT,** oral glucose tolerance test; **PICC,** peripherally inserted central catheter; **PVC,** polyvinylchloride; **SmPC,** Summary of Product Charactereistics; **T1D,** Type 1 diabetes; **TCR,** T-cell receptor; **TN10,** TrialNet-10; **ULN,** upper limit of normal; **ZnT8A,** zinc transporter type 8 autoantibody.

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