sanofi

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.

Risk minimisation material fulfils the conditions of the marketing authorisation and has been approved by the competent authority

MAT-XU-2502758 (v1.0)
MHRA Approval date: September 2025
Date of preparation: September 2025

Discover all about teplizumab.

Objectives of this guide 03

Eligibility criteria for teplizumab treatment 04–05

Staging of autoimmune Type 1 diabetes 06

Mechanism of action of teplizumab 07

Possible serious adverse reactions of teplizumab and how to mitigate them: 08–09
- Cytokine Release Syndrome
- Lymphopenia
- Serious infection
- Hypersensitivity reaction

Recommending dosing for teplizumab: 10–11
- Dosing regimen

How to use teplizumab 12–13
- Infusion preparation

Objectives of this guide

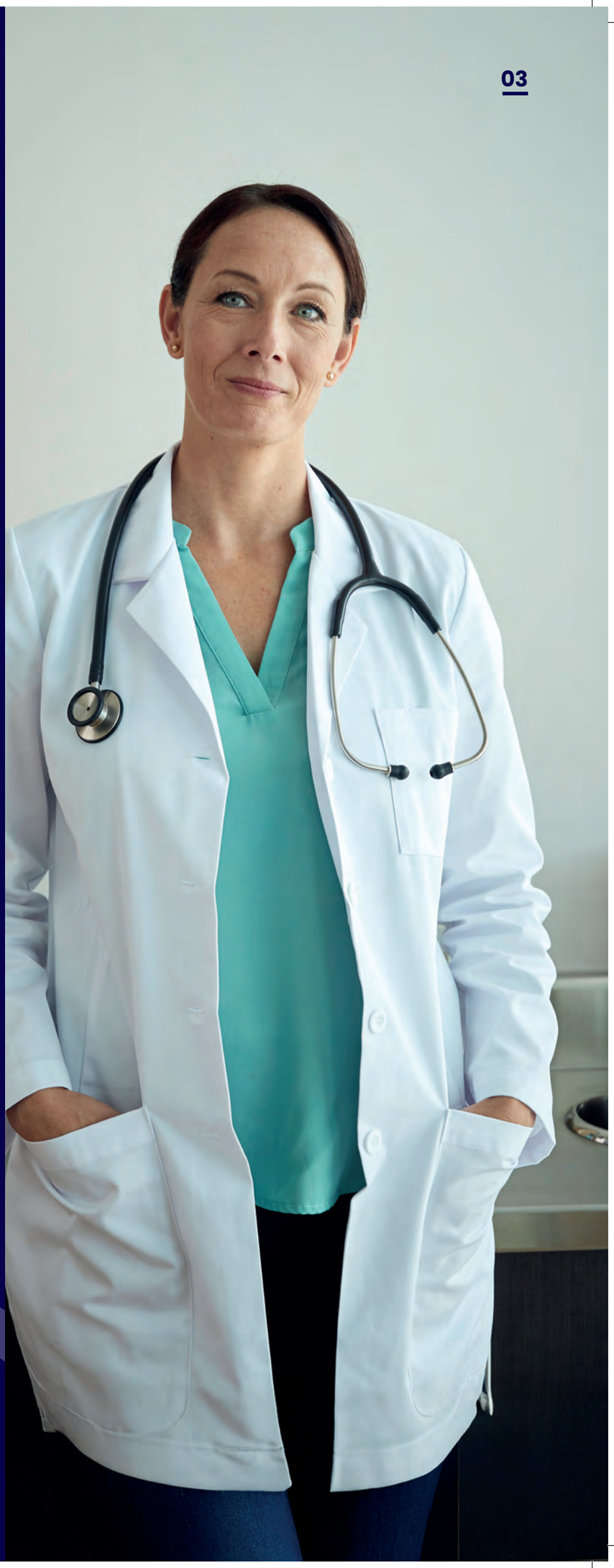
Teplizumab is indicated to delay the onset of Stage 3 Type 1 diabetes (T1D) in adults and paediatric patients patients 8 years of age and older with Stage 2 T1D.

This guide includes important information on administration of teplizumab that you should know before initiating teplizumab 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 teplizumab:

- **Cytokine Release Syndrome (CRS)**
- **Lymphopenia**
- **Serious infection**
- **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.



Eligibility checklist for teplizumab treatment

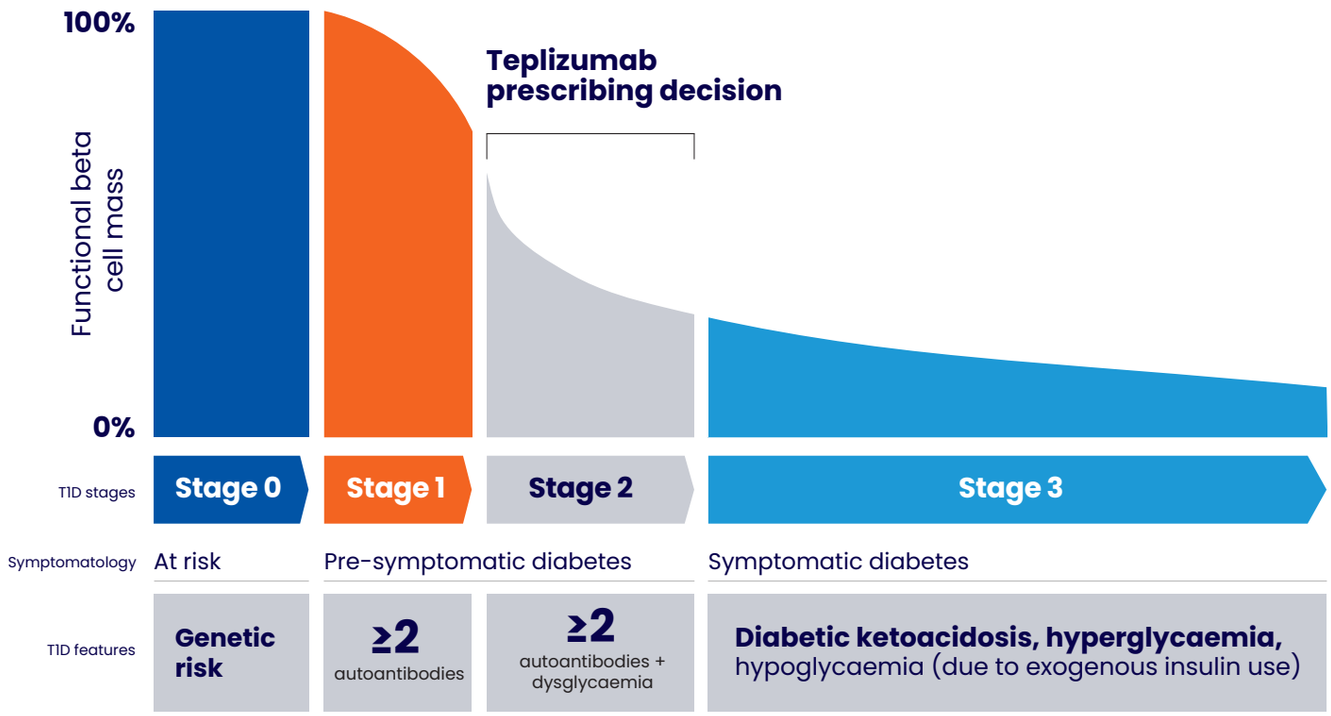
Prior to treatment	**Age 8yrs and above**
	Confirmed Stage 2 T1D
	Clinical history of the patient does not suggest Type 2 diabetes
	At least two positive pancreatic islet cell autoantibodies • Glutamic acid decarboxylase 65 (GAD) autoantibodies • Insulinoma-associated antigen 2 autoantibody (IA-2A) • Zinc transporter 8 autoantibody (ZnT8A) • Insulin autoantibody (IAA)
	Confirm dysglycaemia without overt hyperglycaemia
	Hepatic function • Total bilirubin equal to or less than 1.5 times upper limit of normal (ULN) • Aspartate aminotransferase (AST) equal to or less than 2 times ULN • Alanine aminotransferase (ALT) equal to or less than 2 times ULN
	Bone marrow function • Haemoglobin equal to or more than 100 g/L • Lymphocyte count equal to or more than 1 x 10^9 lymphocytes/L • Absolute neutrophil count (ANC) equal to or more than 1.5 x 10^9/L (For African descent: ANC equal to or more than 1.0 x 10^9/L) • Platelet count equal to or more than 150 x 10^9/L
	Vaccinations Administer all age-appropriate vaccinations prior to starting teplizumab • Administer live-attenuated vaccines at least 8 weeks prior to treatment • Administer inactivated (killed) or mRNA vaccines at least 2 weeks prior to treatment
	Premedication Consider premedication prior to teplizumab infusion for the first 5 days of dosing with: • nonsteroidal anti-inflammatory drug (NSAID) or paracetamol • antihistamines, and/or • antiemetics Administer additional doses of premedication beyond Day 5 if needed.
	General Consideration • Caution should be exercised when considering concomitant use of immunosuppressive medication

Prior to treatment	**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 inform their healthcare provider of a known or suspected pregnancy as they should not receive teplizumab during pregnancy and at least 30 days before a planned pregnancy • Lactation: Advise a lactating woman that she may interrupt breastfeeding and pump and discard breast milk during treatment and for 20 days after teplizumab administration in order to minimise drug exposure to a breastfed infant
During	**Throughout the treatment course, monitor:** • White blood cell counts for prolonged lymphopenia (<0.5 x 10^9 cells/L lasting 1 week or longer) • Liver enzymes ALT, AST, and bilirubin • For signs and symptoms of infection or hypersensitivity reactions If CRS, serious infections, lymphopenia, and/or hypersensitivity reactions were to occur, see the Prescribing Information and next pages for management considerations
After	**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

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 T1D-associated islet autoantibodies but are normoglycaemic.

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 dysglycaemia, 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]

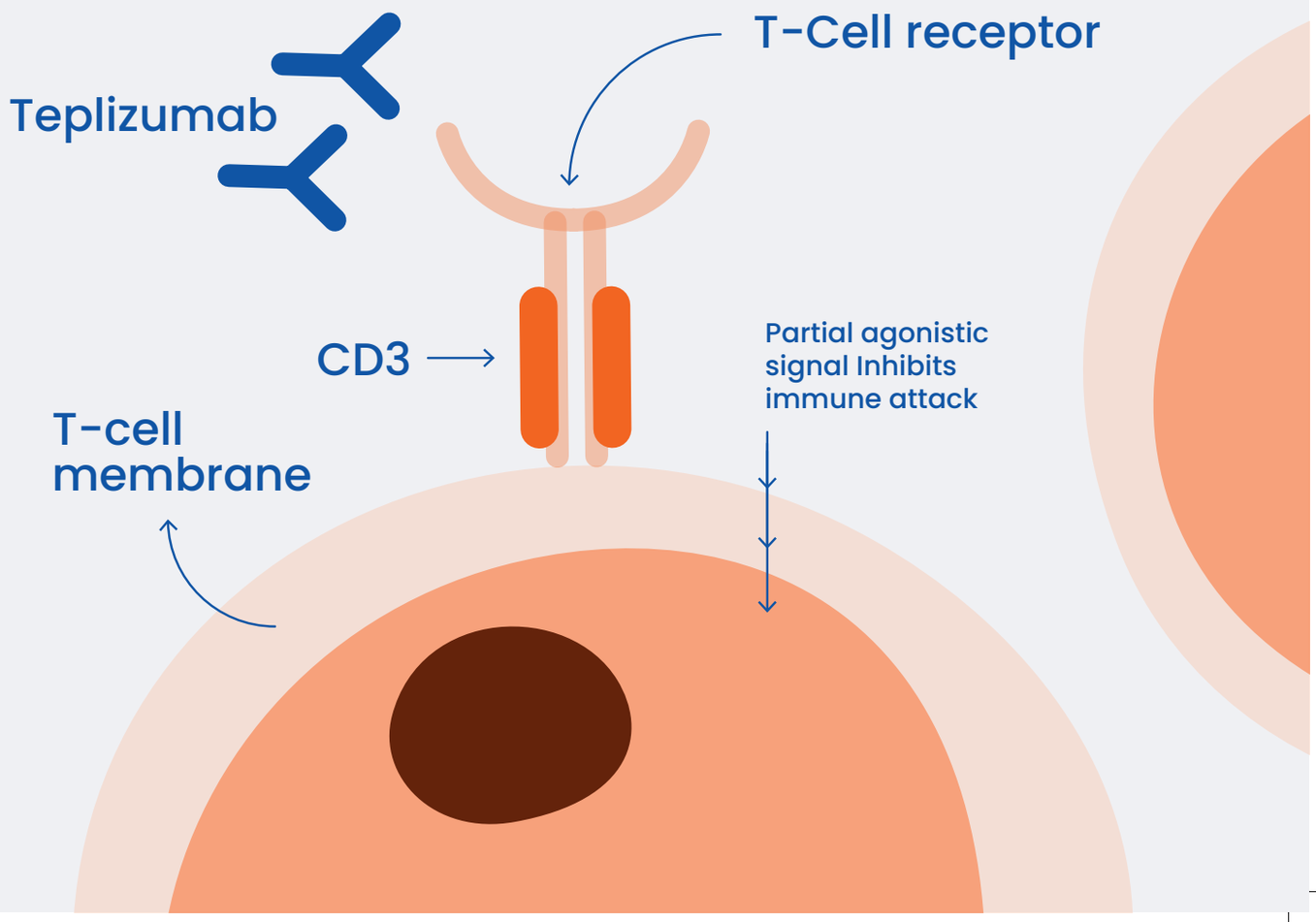
1. Insel RA, et al. Diabetes Care. 2015; 38(10): 1964–1974
2. Herold, KC, Diabetologia 2013; 56(2): 391–400
3. Ramos, E.L. et al. N Engl J Med. 2023; 389:2151–61
4. Long SA, et al. Sci Immunol. 2016; 1(5):eaai7793

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 (MoA)	The mechanism may involve partial agonistic signalling and deactivation of autoreactive T cells that attack and destroy pancreatic beta cells.

Teplizumab:

- Delivers a partial agonistic signal at the CD3 molecule and inhibits autoimmune attack on beta cells
- Increases regulatory T cell function
- Induces expansion of partially exhausted CD8+ T cells that are linked to preserved beta cell function in recently-diagnosed T1D patients[3] associated with slower loss of C-peptide following T1D diagnosis[2,4]
- Partial agonistic signal leads to transient cytokine release and is responsible for the mechanism-based side effects



Possible serious adverse reactions of teplizumab and how to mitigate them

Possible infusion-related adverse reactions	How to mitigate these adverse reactions
Cytokine release syndrome (CRS) CRS has been observed in teplizumab treated patients. In clinical trials, CRS was reported in 6% of teplizumabtreated patients compared to 1% of control-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, increased AST and increased 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 treating HCPs to receive adequate treatment.	**Consider to 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. consider use of 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 1-2 days** (and administer the remaining doses to complete the full 14-day course on consecutive days) or **discontinuing treatment** • Follow strictly the instructions on the infusion preparation and the dosing regimen
Lymphopenia Teplizumab-related effects included lymphopenia. In clinical trials, 80% of teplizumab-treated patients developed lymphopenia compared to 17% of control-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 (<0.5 x 10^9 cells/L lasting one week or longer) develops, **discontinue** teplizumab • 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 teplizumab may have to be discontinued. 

Serious infections
Bacterial and viral infections have occurred in teplizumab-treated patients.

In clinical trials, teplizumab-treated patients had a higher rate of serious infections (3.5%) than control-treated patients (2%), including:
- Gastroenteritis
- Cellulitis
- Pneumonia
- Abscess and sepsis

- **Use of teplizumab is not recommended in patients with active serious infection or chronic active infection other than localised skin infections**
- **Monitor patients for signs and symptoms of infection during and after teplizumab treatment**
- **If serious infection develops, treat appropriately, and discontinue teplizumab**

In case of infection symptoms inform patients to urgently seek medical advice/contact their treating HCPs to receive adequate treatment.

Hypersensitivity reactions

Acute hypersensitivity reactions have occurred in teplizumab-treated patients, including:

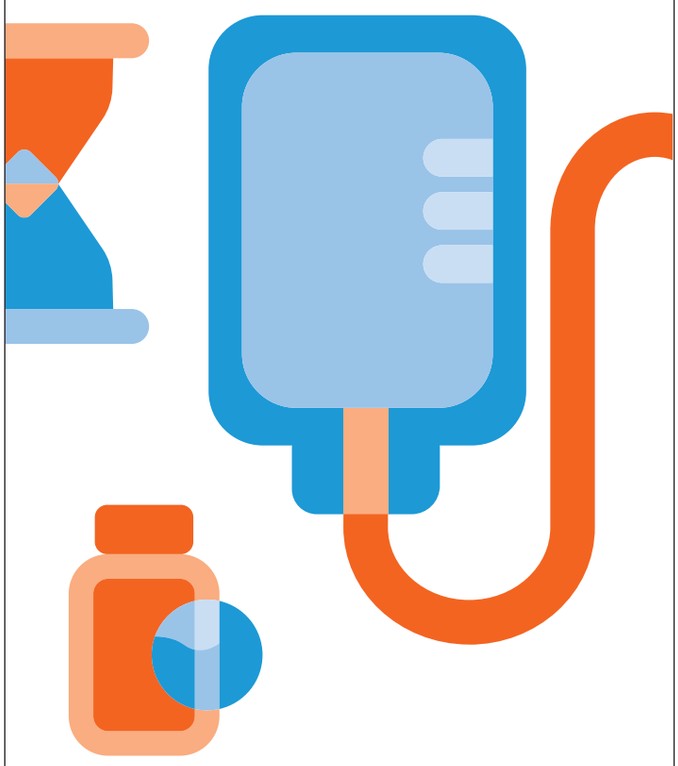
- Serum sickness
- Angioedema
- Urticaria
- Rash
- Vomiting
- Bronchospasm

In the TN-10 trial, serum sickness was observed in 2% (1/44) of teplizumab-treated patients compared to 0% (≠0/32) of placebo-treated patients.

In the pool of 5 clinical trials of patients:
- Anaphylaxis (with hypoxia and bronchospasm) was observed in one teplizumab-treated patient who was hospitalised
- Angioedema (periorbital and facial) was observed in 0.3% teplizumab-treated patients, compared to 0% in control-treated patients. Peripheral and generalised edema was reported in 1.6% of teplizumab-treated patients and 0% of control-treated patients
- Rash was observed in 35% of teplizumab-treated patients compared to 10% in control-treated patients, with 33 excess cases of rash per 100 patients. The majority of rashes observed with teplizumab treatment were not serious and resolved without intervention; although 0.3% (2/791) of teplizumab-treated patients had a serious rash compared to 0% (0/245) of placebo treated patients
- Urticaria was reported in 1.9% of teplizumab-treated patients and in 1.2% of control-treated patients

- Teplizumab is **contraindicated** inpatients who have had severe hypersensitivity reactions, including anaphylaxis, to teplizumab or any of its excipients
- If severe hypersensitivity reactions occur, **discontinue** use of teplizumab and **treat promptly**

If such symptoms occur inform patients to seek medical attention promptly/contact their treating HCPs to receive adequate treatment.



Recommended dosing for teplizumab

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

Once daily, consecutive 14-day course[1]

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[1]

Administer teplizumab by IV infusion for a minimum of 30 minutes, using body surface area based dosing*

*Patient monitoring time will be required post administration

The recommended teplizumab 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:

Dosing regimen

Calculation

How to calculate Body Surface Area (BSA) using the Mosteller formula:[2]

BSA EQUATION

$$\text{BSA } (m^2) = \sqrt{\frac{[\text{height (cm)} \times \text{weight (kg)}]}{3600}}$$

EXAMPLE
Male, 8 years old, 120 cm, 26kg

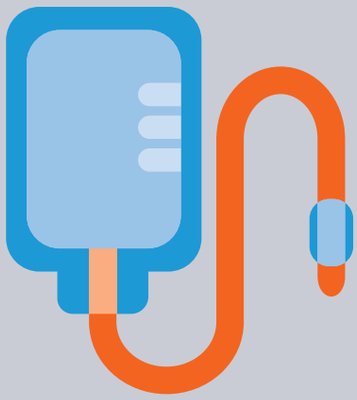
$$\text{BSA } (m^2) = \sqrt{\frac{(120)(26)}{3600}} = 0.931 m^2$$

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

How to use teplizumab: infusion preparation

Teplizumab is supplied as a sterile, preservative-free, clear, and colourless solution in a 1 mg/1 ml, single-dose vial.

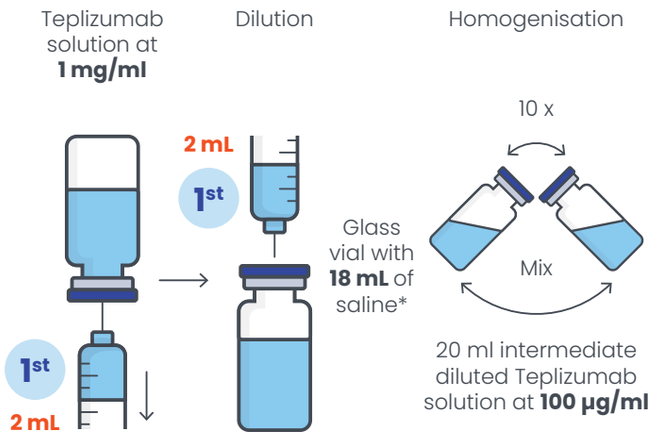
For detailed information regarding storage conditions refer to the product label.



Teplizumab must be diluted prior to use

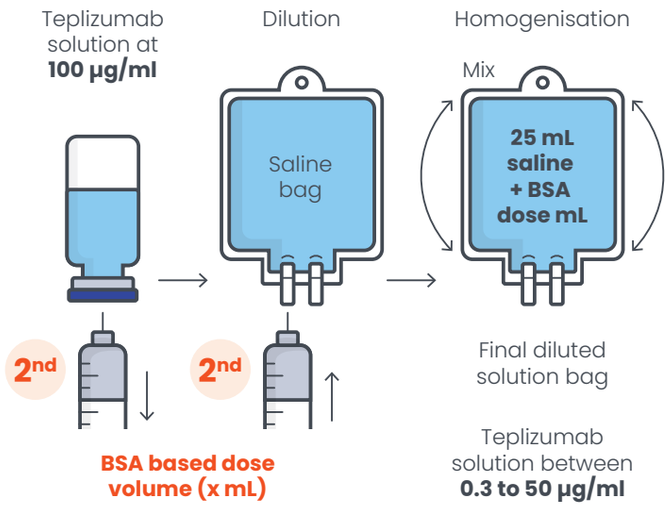
Dilution Method A

Step 1: Intermediate dilution in glass vial



*18 mL can be obtained by removing saline from an IV bag

Step 2: Final dilution in IV bag



Step 1

Inspect teplizumab visually before use (the supplied solution is clear and colourless).

- Do not use teplizumab if particulate matter or colouration is seen.

Step 2

Prepare teplizumab using aseptic technique.

Each vial is intended for single dose only. Prepare a sterile glass vial with 18 mL of 0.9% sodium chloride solution for Injection (Dilution method A) or polyvinylchloride (PVC) infusion bag with 18 mL of 0.9% sodium chloride solution for Injection (Dilution method B).

Step 3

Remove 2 mL of teplizumab from the vial and slowly add to the 18 mL of 0.9% sodium chloride solution for Injection.

Mix gently by slowly inverting the vial or rocking the infusion bag. The resulting 20 mL diluted solution contains 100 µg/mL of teplizumab.

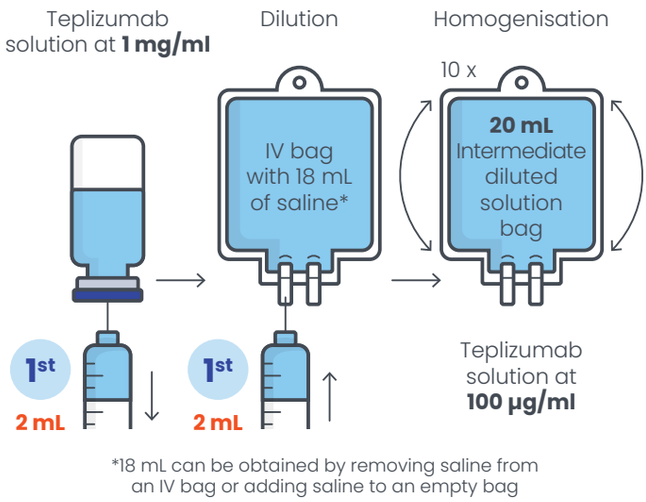
Important:

Based on BSA dosing requirements (e.g., >1.94 m²), 2 vials may be needed for days 5 through 14. To make sure the complete dose for each day is contained in 1 infusion bag:

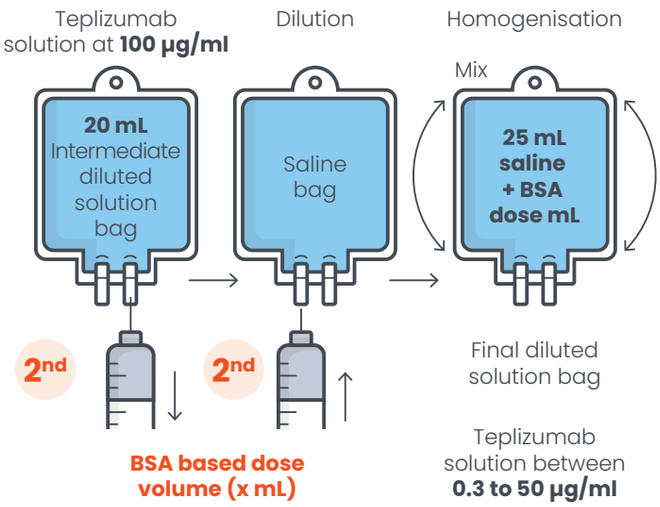
- Prepare 2 diluted teplizumab solutions
- Add the cumulative volume for the calculated dose to a single infusion bag

Dilution Method B

Step 1: Intermediate dilution in IV bag



Step 2: Final dilution in IV bag



Step 4

Using an appropriately sized syringe (e.g., 5 mL), withdraw the volume of diluted teplizumab solution required for that day's calculated dose from the 100 µg/mL solution

Step 5

Slowly add contents of the syringe containing the teplizumab dose to a PVC infusion bag containing 25 mL 0.9% sodium chloride solution for injection.
Gently rock the infusion bag to ensure that the solution mixes sufficiently.

- Do not shake.

Step 6

Discard unused portion of remaining diluted teplizumab solution in the sterile glass vial or PVC infusion bag.

- The unused solution should not be used for another patient

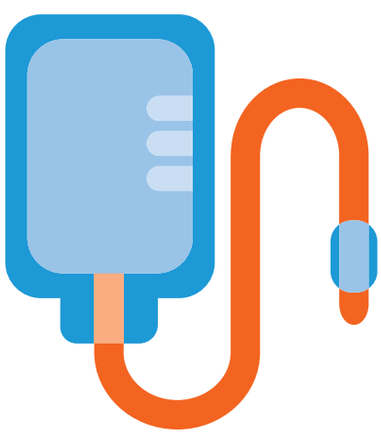
Step 7

Start the teplizumab 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.

- Discard the infusion solution if not administered within 4 hours of preparation.

Step 8

When the teplizumab infusion solution has been completely administered, infuse an additional volume of 0.9% sodium chloride solution for injection (i.e., normal saline) equal to the volume contained in the infusion tubing at the same constant rate as teplizumab infusion to ensure that all the medication has been given.



Notes

▼ This Medicinal Product is subject to additional monitoring. This will allow quick identification of new safety information.

Please report suspected adverse drug reactions (ADRs) to the MHRA through the Yellow Card scheme, via the Yellow Card website www.mhra.gov.uk/yellowcard, the free Yellow Card app available in Apple App Store or Google Play Store, and also some clinical IT systems for healthcare professionals. Alternatively, you can call 0800 731 6789 for free, Monday to Friday between 9am and 5pm.

When reporting please provide as much information as possible. By reporting adverse drug reactions, you can help provide more information on the safety of this medicine.

Adverse drug reactions can also be reported to Sanofi: Tel: 0800 0902314. email: uk-drugsafety@sanofi.com

If you have any enquiries or wish to request extra hard copies of any of these materials please contact Sanofi Medical Information: Telephone: 0800 035 2525 Email: UK-medicalinformation@sanofi.com Additionally, electronic versions of these materials are available to download on the following website: www.medicines.org.uk/emc/