Tzield 2 mg/2 mL concentrate for solution for infusion

Summary of Product Characteristics Updated 15-Aug-2025 | SANOFI

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. Name of the medicinal product

Tzield 2 mg/2 mL concentrate for solution for infusion

2. Qualitative and quantitative composition

One mL of concentrate for solution for infusion contains 1 mg of teplizumab.

Each vial contains 2 mg of teplizumab in 2 mL of concentrate (2 mg/2 mL).

Teplizumab is a CD3-directed monoclonal antibody (humanised IgG1 kappa) expressed from a recombinant Chinese hamster ovary (CHO) cell line.

Excipient(s) with known effect

Each vial contains 7.45 mg of sodium and 0.10 mg of polysorbate 80.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Concentrate for solution for infusion.

Clear, colourless solution.

4. Clinical particulars

4.1 Therapeutic indications

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

4.2 Posology and method of administration

Patient Selection

Select adult and paediatric patients 8 years of age and older for Tzield treatment who have a diagnosis of Stage 2 type 1 diabetes.

• Confirm Stage 2 type 1 diabetes by documenting:

o At least two positive pancreatic islet cell autoantibodies

o Dysglycaemia without overt hyperglycaemia

• Ensure the clinical history of the patient does not suggest type 2 diabetes.

Laboratory Evaluation and Vaccination Prior to Initiation

• Prior to initiating Tzield obtain a complete blood count and liver enzyme tests.

• Use of Tzield is not recommended in patients with (see section 4.4):

o Lymphocyte count less than 10^9 lymphocytes/L

o Haemoglobin less than 100 g/L

o Platelet count less than 150 x 10^9 platelets/L

o Absolute neutrophil count less than 1.0 x 10^9 neutrophils/L in those of African descent and less than 1.5 x 10^9 neutrophils/L in all other groups

o 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

o Laboratory or clinical evidence of acute infection with Epstein-Barr virus (EBV) or cytomegalovirus (CMV)

o Active serious infection or chronic active infection other than localised skin infections

• Administer all age-appropriate vaccinations prior to starting Tzield (see section 4.4):

o Administer live-attenuated (live) vaccines at least 8 weeks prior to treatment.

o Administer inactivated (killed) vaccines or mRNA vaccines at least 2 weeks prior to treatment.

Premedication

Premedicate prior to Tzield 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 (see section 4.4). Administer additional doses of premedication if needed.

Posology

Administer Tzield by intravenous infusion (over a minimum of 30 minutes), using a body surface area-based dosing (BSA), once daily for 14 consecutive days as follows:

• Day 1: 65 mcg/m^2

• Day 2: 125 mcg/m^2

• Day 3: 250 mcg/m^2

• Day 4: 500 mcg/m^2

• Days 5 through 14: 1,030 mcg/m^2

Do not administer two doses on the same day.

Missed Dose(s)

If a planned Tzield infusion is missed, resume dosing by administering all remaining doses on consecutive days to complete the 14-day treatment course.

Special populations

Elderly patients

Clinical studies of Tzield did not include patients 65 years of age and older.

Paediatric patients

The safety and efficacy of Tzield in children younger than 8 years of age has not been established. No data are available.

Method of administration

Administer Tzield by intravenous infusion over a minimum of 30 minutes. Do not administer two doses on the same day.

For instructions for the preparation of Tzield before administration, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Cytokine Release Syndrome

Cytokine Release Syndrome (CRS) has been observed in patients treated with Tzield. In clinical trials, CRS was reported in 6% of patients treated with Tzield compared to 1% of patients in the control group during the treatment period and through 28 days after the last study drug administration. CRS manifestations in patients treated with Tzield included fever, nausea, fatigue, headache, myalgia, arthralgia, increased ALT, increased AST, and increased total bilirubin. These manifestations typically occurred during the first 5 days of Tzield treatment (see section 4.8).

To mitigate CRS:

• Premedicate with antipyretics, antihistamines and/or antiemetics prior to Tzield treatment (see section 4.2).

• Monitor liver enzymes and bilirubin during treatment. Discontinue Tzield treatment in patients who develop elevated ALT or AST more than 5 times the upper limit of normal (ULN) or bilirubin more than 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.

Serious Infections

Bacterial and viral infections have occurred in patients treated with Tzield. In clinical trials, patients treated with Tzield had a higher rate of serious infections (3.5%) than patients in the control group (2%), including gastroenteritis, cellulitis, pneumonia, abscess, sepsis (see section 4.8). Use of Tzield is not recommended in patients with active serious infection or chronic 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.

Lymphopenia

In clinical trials, 80% of patients treated with Tzield developed lymphopenia compared to 17% of patients in the control group. For most patients treated with Tzield who experienced lymphopenia, lymphocyte levels began to recover after the fifth day of treatment and returned to pre-treatment values within two 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 (see section 4.8).

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.

Hypersensitivity Reactions

Acute hypersensitivity reactions including serum sickness, angioedema, urticaria, rash, vomiting and bronchospasm occurred in patients treated with Tzield (see section 4.8). If severe hypersensitivity reactions occur, discontinue use of Tzield and treat promptly.

Vaccinations

The safety of immunisation with live-attenuated vaccines in patients treated with Tzield has not been studied. Additionally, Tzield may interfere with the immune response to vaccination and decrease vaccine efficacy.

• Administer all age-appropriate vaccinations prior to starting Tzield (see section 4.2).

• Inactivated or mRNA vaccinations are not recommended within the 2 weeks prior to Tzield treatment, during treatment, or 6 weeks after completion of treatment.

• Live-attenuated vaccinations are not recommended within the 8 weeks prior to Tzield treatment, during treatment, or up to 52 weeks after treatment.

Concomitant Immunosuppressive Medication

In type 1 diabetes studies, the safety and efficacy of teplizumab in combination with immunosuppressive medication have not been evaluated (see section 4.5). Caution should be exercised when considering concomitant use of immunosuppressive medication.

Excipients

Sodium

This medicinal product contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially 'sodium-free'. Tzield is administered in 0.9% sodium chloride intravenous solution (see section 6.6).

Polysorbate 80

This medicinal product contains 0.10 mg of polysorbate 80 in each vial which is equivalent to 0.05 mg/mL.

4.5 Interaction with other medicinal products and other forms of interaction

No drug interaction studies have been performed.

4.6 Fertility, pregnancy and lactation

Pregnancy

Available case reports from clinical trials with Tzield are insufficient to identify a drug-associated risk of major birth defects, miscarriage or other adverse maternal or foetal outcomes.

An embryo-foetal toxicity study with a surrogate anti-mouse CD3 antibody in mice showed an increase in post-implantation loss in the presence of maternal toxicity.

Although there are no data on teplizumab, monoclonal antibodies can be actively transported across the placenta, and Tzield may cause immunosuppression in the utero-exposed infant. To minimise exposure to a foetus, avoid use of Tzield during pregnancy and for at least 30 days prior to planned pregnancy.

Breast-feeding

There are no data on the presence of Tzield in human milk, effects on milk production, or effects on the breastfed child.

In a pre- and postnatal development toxicity study in mice, it was suggested that the surrogate antibody was present in the milk of lactating mice (see section 5.3).

As endogenous maternal IgG and monoclonal antibodies are transferred into human milk, a lactating woman 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 child.

Fertility

There are no clinical data available for teplizumab on the effects on fertility. Fertility and reproductive performance were unaffected in female and male mice treated with a surrogate anti-mouse CD3 antibody (see section 5.3).

4.7 Effects on ability to drive and use machines

Fatigue has been reported in patients taking Tzield and this should be taken into account when driving or using machines.

For other medicinal products that are administered with teplizumab, refer to the respective current summary of product characteristics.

4.8 Undesirable effects

Summary of safety profile

Adverse reactions in patients treated with Tzield were evaluated in a pool of adult and paediatric patients who participated in five controlled clinical studies (one study in patients with Stage 2 T1D [Study TN-10], three placebo-controlled studies in an unapproved population (Stage 3 T1D), and one open-label standard-of-care controlled study of Tzield in an unapproved population (Stage 3 T1D)).

Lymphopenia, leukopenia, neutropenia, blood bicarbonate decreased, and rash were the most frequently reported adverse reactions, which occurred at a higher frequency in the teplizumab group compared to the control group.

Tabulated list of adverse reactions

The adverse reactions occurring in ≥5% of patients in the pooled safety analysis of clinical studies are shown in Table 1 per System Organ Class presented by frequency categories: very common: (≥1/10), common: (≥1/100 to <1/10), uncommon: (≥1/1000 to <1/100), rare: (≥1/10,000 to <1/1000), very rare: (<1/10,000), not known: (cannot be estimated from the available data).

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

System Organ Class	Frequency Category		
	Very common	**Common**	**Not known**
Blood and lymphatic system disorders	Lymphopenia, Leukopenia, Neutropenia, Haemoglobin decreased, Thrombocytopenia		
Immune system disorders		Cytokine release syndrome	
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	Alanine aminotransferase increased, Aspartate aminotransferase increased,		

	Blood bicarbonate decreased, Blood calcium decreased		

Description of selected adverse reactions

Cytokine Release Syndrome (CRS)

In Study TN-10, CRS was reported in 2% of patients treated with Tzield compared to 0% of patients in the placebo group.

Of the 46 patients treated with Tzield that developed CRS (6% of all patients treated with Tzield) in the pool of 5 clinical trials, 13% of the CRS cases were serious adverse reactions (see section 4.4). Liver transaminase elevations were observed in 56% of patients treated with Tzield who experienced CRS: 64% were up to 2.5 times ULN, 32% were more than 2.5 to 5 times ULN, and 4.5% were 5-10 times ULN.

Serious Infections

In Study TN-10, serious infections (cellulitis, gastroenteritis, pneumonia, wound infection) were reported in 9% (4/44) of patients treated with Tzield compared to 0% (0/32) of patients treated with placebo any time during or after the first dose of study treatment.

Lymphopenia

In Study TN-10, lymphopenia was reported in 73% of patients treated with Tzield compared to 6% of patients in the placebo group. The average lymphocyte count nadir occurred at Day 5 of treatment, with recovery and return to baseline by Week 6 (see section 4.4).

Rash and Hypersensitivity Reactions

Hypersensitivity reactions were reported with Tzield in Study TN-10. Serum sickness was observed in 2% (1/44) of patients treated with Tzield compared to 0% (0/32) of patients in the placebo group. The patient who developed serum sickness had a prior history of positive anti-nuclear antibody and presented with arthralgias and elevated c-reactive protein and low C4 complement five days after completing their course of Tzield; illness resolved in 2.5 months.

In the pool of 5 clinical trials of patients:

• Anaphylaxis (with hypoxia and bronchospasm) was observed in one patient treated with Tzield who was hospitalised.

• Angioedema (periorbital and facial) was observed in 0.3% patients treated with Tzield, compared to 0% of patients in the control group. Peripheral and generalised oedema was reported in 1.6% of patients treated with Tzield and 0% of patients in the control group.

• Rash was observed in 35% of patients treated with Tzield compared to 10% of patients in the control group. The majority of events of rash observed with Tzield treatment were not serious and resolved without intervention; although 0.3% (2/791) of patients treated with Tzield had a serious rash compared to 0% (0/245) of patients in the placebo group.

• Urticaria was reported in 1.9% of patients treated with Tzield and in 1.2% of patients in the control group.

Other Adverse Reactions

Haemoglobin Decreased and Thrombocytopenia

In the pool of 5 clinical trials of patients, haemoglobin decreased was reported in 28% of patients treated with Tzield compared to 22% of patients in the placebo group, and thrombocytopenia was reported in 22% of patients treated with Tzield compared to 10% of patients in the placebo group during the 14-day treatment course; recovery occurred within 2 to 4 weeks of treatment. In clinical trials, 1.5% of patients treated with Tzield discontinued treatment due to haemoglobin less than 85 g/L (or a decrease of more than 20 g/L to a value less than 100 g/L), and 1% discontinued Tzield due to platelet count less than 50 x 10^9 platelets/L.

Liver Enzyme and Bilirubin Elevations

Liver enzyme and bilirubin elevations were observed in patients treated with Tzield, both in the context of CRS and in patients without CRS. On laboratory analysis, 5.1% of patients treated with Tzield experienced a peak ALT more than 3 times the ULN compared to 0.8% of patients in the control group. Most liver enzyme elevations were transient and resolved 1-2 weeks after treatment; 98% resolved by follow-up week 14.

Immunogenicity

The observed incidence of anti-drug antibodies (ADA) is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of anti-drug antibodies in the studies described below with the incidence of anti-drug antibodies in other studies, including those of Tzield or of other teplizumab products.

In the placebo-controlled study in patients aged 8 years of age and older with Stage 2 type 1 diabetes (Study TN-10) (see section 5.1), approximately 57% of patients treated with Tzield developed anti-teplizumab antibodies, 46% of whom developed neutralising antibodies. There was a higher incidence of rash in patients treated with Tzield who developed anti-teplizumab antibodies (39%) compared to those who did not develop anti-teplizumab antibodies (33%). There is insufficient information to characterise the effects of ADA on pharmacokinetics, pharmacodynamics, or effectiveness of Tzield.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Signs and Symptoms

There is no clinical experience with overdose with teplizumab.

Management

In the event of taking more than the recommended dose of Tzield, monitor the patient for signs or symptoms of adverse effects and take all appropriate measures immediately. Clinical judgement should be applied.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: other drugs in diabetes, ATC Code: A10XX01

Mechanism of action

Teplizumab binds to CD3 (a cell surface antigen present on T lymphocytes) and delays the onset of Stage 3 type 1 diabetes in adults and paediatric patients aged 8 years and older with Stage 2 type 1 diabetes. The mechanism may involve partial agonistic signalling and deactivation of pancreatic beta cell autoreactive T lymphocytes. Teplizumab leads to an increase in the proportion of regulatory T cells and of exhausted CD8+ T cells in peripheral blood.

Pharmacodynamic effects

Clinical studies have shown that teplizumab binds to CD3 molecules on the surface of both CD4+ and CD8+ T cells during treatment, with internalisation of the teplizumab/CD3 complex from the surface of T cells. Pharmacodynamic effects include lymphopenia in the absence of depletion of T cells with a nadir on the 5^{th} day of dosing, during a 14-day course of TZIELD treatment (see section 4.4). Teplizumab exposure-response relationship and time course of pharmacodynamic response for the safety and effectiveness of teplizumab have not been fully characterised.

Clinical efficacy and safety

The effectiveness of Tzield was investigated in a randomised, double-blind, event-driven, placebo-controlled study (Study TN-10) in 76 patients, 8 to 49 years of age with Stage 2 type 1 diabetes. Stage 2 type 1 diabetes was defined as having both of the following:

1. Two or more of the following pancreatic islet autoantibodies:

o Glutamic acid decarboxylase 65 (GAD) autoantibodies

o Insulin autoantibody (IAA)

o Insulinoma-associated antigen 2 autoantibody (IA-2A)

o Zinc transporter 8 autoantibody (ZnT8A)

o Islet cell autoantibody (ICA)

2. Dysglycaemia on oral glucose tolerance testing

In this study, patients were randomised to receive Tzield or placebo once daily by intravenous infusion for 14 days. Patients in the Tzield group had a total drug exposure that was comparable to the total drug exposure achieved with the recommended total Tzield dosage (see section 4.2*).* The primary efficacy endpoint in this study was the time from randomisation to development of Stage 3 type 1 diabetes diagnosis.

Baseline Patient Characteristics

In this study, 45% were female; 97% White, 1% Asian, and 1% reported multiracial background; 3% were Hispanic or Latino ethnicity; and 95% were from the United States. The median age was 14 years (72% were <18 years old) (Table

2).

Table 2. Baseline age characteristics of adult and paediatric patients 8 years of age and older with Stage 2 Type 1 Diabetes (Study TN-10)[1]

	Tzield N=44	Placebo N=32
Age Group		
≥ 18 Years	34%	19%
< 18 years	66%	81%
Paediatric Age Group Quartiles		
8 to <11 years	21%	25%
11 to <14 years	27%	31%
14 to <18 years	18%	25%

[1] Intent to treat (ITT) population

Baseline Disease Characteristics

Table 3 displays the baseline disease characteristics in Study TN-10.

Table 3. Baseline disease characteristics of adult and paediatric patients 8 years of age and older with Stage 2 Type 1 Diabetes (Study TN-10)[1]

	Tzield N=44	Placebo N=32
Glucose, mg/dL[2]		
median (min, max)	165 (115, 207)	154 (103, 200)
HbA1c, %		
median (min, max)	5.2 (4.6, 6.1)	5.3 (4.3, 5.6)
HLA-DR3/DR4		
Both DR3 and DR4	25%	22%
DR3 only	23%	25%
DR4 only	36%	44%
Missing	5%	0
Neither DR3 nor DR4	11%	9%
Autoantibodies Positive (N)		
1	2%	0
2	27%	22%
3	25%	16%
4	27%	44%
5	18%	19%

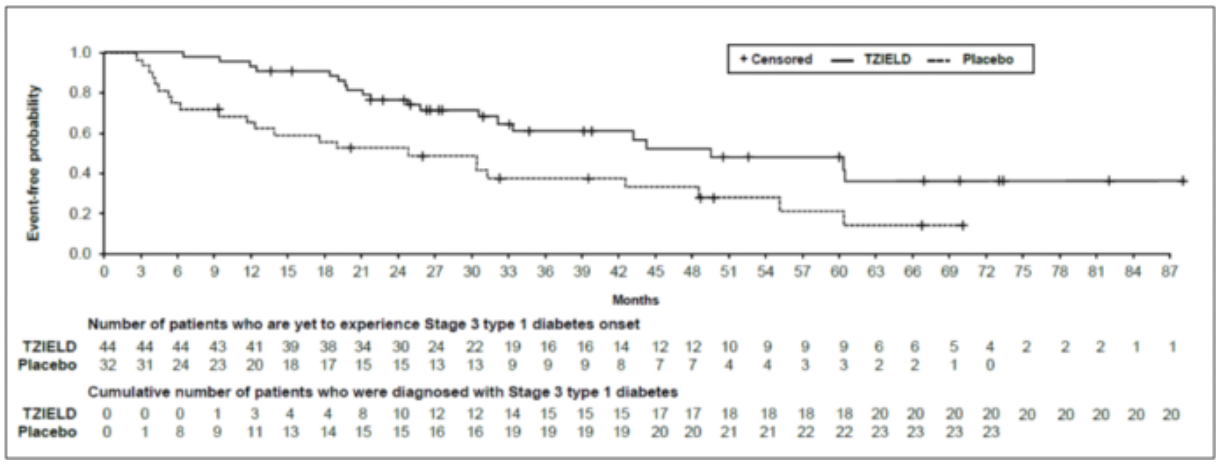
[1] Intent to treat (ITT) population [2] The glucose data are area under the time-concentration curve (AUC) values from the oral glucose tolerance test. Abbreviations: HbA1c=haemoglobin A1c, SD=standard deviation, HLA = human leukocyte antigen.

Efficacy Results

In Study TN-10, Stage 3 type 1 diabetes was diagnosed in 20 (45%) of the patients treated with Tzield and in 23 (72%) of the patients treated with placebo. A Cox proportional hazards model, stratified by age and oral glucose tolerance test status at randomisation, demonstrated that the median time from randomisation to Stage 3 type 1 diabetes diagnosis was 50 months in the Tzield group and 25 months in the placebo group, for a difference of 25 months. With a median follow-up time of 51 months, therapy with Tzield resulted in a statistically significant delay in the development of Stage 3 type 1 diabetes, hazard ratio 0.41 (95% CI: 0.22 to 0.78; p=0.0066) (Figure 1).

Study TN-10 was not designed to assess whether there were differences in the effectiveness between subgroups based on demographic characteristics or baseline disease characteristics.

Figure 1: Kaplan-Meier curve of time to diagnosis of Stage 3 Type 1 Diabetes in adult and paediatric patients 8 years of age and older with Stage 2 Type 1 Diabetes by treatment group (Study TN-10)[1]



[1] ITT population

5.2 Pharmacokinetic properties

Steady state concentrations of teplizumab are not expected to be achieved during the 14-day course of Tzield.

Absorption

There is no information about absorption since Tzield is administered intravenously.

Distribution

The central volume of distribution (Vd) of teplizumab was 2.27 L in a 60 kg subject.

Metabolism

Teplizumab is expected to be metabolised into small peptides by catabolic pathways.

Elimination

Teplizumab showed saturable binding and elimination. The population clearance (SD) of teplizumab is 2.7 (1.04) L/day in a 60 kg subject, respectively.

Special populations

Age

No clinically significant differences in the pharmacokinetics of teplizumab were observed based on age (8 to 35 years old).

Gender

No clinically significant differences in the pharmacokinetics of teplizumab were observed based on biologic sex.

Race

No clinically significant differences in the pharmacokinetics of teplizumab were observed based on racial groups (White, Asian).

Weight

BSA-based dosing normalises the exposure to teplizumab across body weight.

Paediatric

No clinically significant differences in the pharmacokinetics of teplizumab were observed in paediatric patients 8 years of age and older.

5.3 Preclinical safety data

In single-dose toxicology studies in chimpanzees using teplizumab, expected target-mediated pharmacology was observed. Repeated-dose toxicity studies in mice were conducted using surrogate anti-mouse CD3 antibody. In these studies, expected target-mediated pharmacology was also observed.

No studies have been performed to assess the genotoxic, including mutagenic, potential of teplizumab. As an antibody, teplizumab is not expected to interact directly with DNA. No long-term studies have been performed to assess the carcinogenic potential of teplizumab.

In an embryo-foetal developmental toxicity study, pregnant mice were administered a murine surrogate anti-mouse CD3 antibody by subcutaneous injection at dose levels of 0, 0.03, 0.3, or 20 mg/kg on gestation days 6, 10, and 14. Increase in post-implantation loss occurred in the 20 mg/kg group, in the presence of maternal toxicity.

In a pre- and postnatal development toxicity study in pregnant mice, in which the murine surrogate antibody was administered every 3 days from gestation day 6 through lactation day 19 at doses of 0, 0.3, 3, or 20 mg/kg, no maternal toxicity or increased incidence of post-implantation loss was observed. Reductions in T cell populations and increases in B cells, and a reduction in the adaptive immune response to keyhole limpet hemocyanin (KLH) were observed in the offspring on postnatal days 35 and 84 at 20 mg/kg. The surrogate antibody was present in the offspring serum at level less than 1.5% that of maternal serum at the high dose. A trend towards reduction in fertility was observed in the offspring of dams administered the murine surrogate antibody at 20 mg/kg.

Fertility and reproductive performance were unaffected in female and male mice that received a murine surrogate anti-mouse CD3 antibody administered by the subcutaneous route at doses up to 20 mg/kg.

6. Pharmaceutical particulars

6.1 List of excipients

Dibasic sodium phosphate (E339)

Monobasic sodium phosphate (E339)

Polysorbate 80 (E433)

Sodium chloride

Water for injection

6.2 Incompatibilities

In the absence of compatibility studies, Tzield should not be mixed with other medicinal products. Do not add or simultaneously infuse other medicinal products through the same intravenous line. This medicinal product should be prepared and administered as instructed in section 4.2 and section 6.6.

6.3 Shelf life

Unopened Vial

3 years

After dilution

If not used immediately, store the diluted solution at room temperature (15°C to 30°C) and complete infusion within 4 hours of the start of preparation. Discard the diluted solution if not administered within 4 hours of preparation (see section 6.6).

6.4 Special precautions for storage

Store in a refrigerator (2°C to 8°C). Do not freeze or shake the vials.

Keep the vial in the outer carton in order to protect from light. Store upright.

For storage conditions after dilution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

Tzield is supplied in a 2 mL Type 1 borosilicate glass vial with a butyl rubber stopper and an aluminum seal with a coloured polypropylene flip-off cap. Pack sizes of 1, 10 or 14 vials.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Preparation for intravenous administration

• Must dilute Tzield prior to use (see section 4.2).

• In preparation for dilution, inspect Tzield visually before use (the supplied solution is clear and colourless). Do not use Tzield if particulate matter or colouration is seen.

• Prepare Tzield using aseptic technique. Each vial is intended for single dose only.

• Prepare a:

o Sterile glass vial with 18 mL of 0.9% sodium chloride solution for injection or

o Polyvinylchloride (PVC) infusion bag with 18 mL of 0.9% sodium chloride solution for injection.

• Remove 2 mL of Tzield 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 mcg/mL of teplizumab.

• Using an appropriately sized syringe (e.g., 5 mL), withdraw the volume of diluted Tzield solution required for that day's calculated dose from the 100 mcg/mL solution (see section 4.2).

• Slowly add contents of the syringe containing the Tzield 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.

Important:

Based on BSA dosing requirements (e.g., >1.94 m^2), 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:

o Prepare 2 dilution solutions

o Add the cumulative volume for the calculated dose to a single infusion bag

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

• Start the Tzield infusion within 2 hours of preparation. If not used immediately, store the infusion solution at room temperature (15°C to 30°) and complete infusion within 4 hours of the start of preparation. Discard the infusion solution if not administered within 4 hours of preparation.

Disposal

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

7. Marketing authorisation holder

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8. Marketing authorisation number(s)

PLGB 04425/0908

9. Date of first authorisation/renewal of the authorisation

Date of first authorisation: 14/08/2025

10. Date of revision of the text

14/08/2025

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