**Sample Letter of Appeal Template**

If treatment with TZIELD™ (teplizumab-mzwv) is denied by your patient’s health plan, you may appeal this decision by phone or letter. The following is a sample letter of appeal that can be customized based on your patient’s medical history and demographic information. Please note that some health plans may have specific forms that must be completed in order to request prior authorization or to document medical necessity. It is important to ensure that this letter is tailored to the requirements of the health plan.

This sample letter and related information are provided for informational purposes only. It is the responsibility of the healthcare provider and/or their office staff, as appropriate, to determine the appropriate diagnosis, treatment protocol, and content of all such letters and related forms for each individual patient. Provention Bio does not guarantee coverage or reimbursement for any product.

[Date]

Re: [Patient Name], [DOB], [Parent/Legal Guardian’s Name]

Policy Number: [Policy Number]

Group Number: [Group Number]

Medicaid Number (if applicable): [Medicaid Number]

**Subject: Appeal for coverage denial of TZIELD™ (teplizumab-mzwv)**

Dear [Medical Director],

I am writing to request authorization for TZIELD™ (teplizumab-mzwv) for my patient, [Patient Name], [DOB], [patient weight, height], who has Stage 2 type 1 diabetes (T1D) and is at risk of developing Stage 3 (clinical) T1D. [Patient Name] was diagnosed on [diagnosis date], based on documentation of at least two positive pancreatic islet autoantibodies and dysglycemia without overt hyperglycemia using an oral glucose tolerance test (OGTT) [or alternative method if appropriate and OGTT is not available; provide clinical rationale for alternative method]. The clinical history of [Patient Name] does not suggest type 2 diabetes.

In a letter dated [date of denial letter], [insurance company name] stated that TZIELD is not covered for [Patient Name] due to [reason(s) for denial]. I have reviewed this letter and, based on my medical expertise, ask that you reconsider this decision with regard to the following clinical information. I believe TZIELD is medically necessary for my patient, [Patient Name], based on their diagnosis of Stage 2 T1D and [add other clinically relevant criteria].

**[Include the following information if it is relevant to your patient and** **the health plan’s reason for denial]**

My patient, [Patient Name], meets the TZIELD patient selection criteria1 and the American Diabetes Association (ADA) diagnostic criteria for Stage 2 T1D2 based on the following:

**Documentation of ≥2 positive pancreatic islet cell autoantibodies** as evidenced by lab results on [date]:

[Select which of the below apply to your patient and provide supporting evidence (e.g., lab work or chart notes where applicable)]

* Glutamic acid decarboxylase (GAD) autoantibodies
* Tyrosine phosphatase autoantibodies (IA-2A)
* Zinc transporter 8 autoantibodies (ZnT8A)
* Insulin autoantibodies (IAA)
* Islet-cell autoantibodies (ICA)

**AND**

**Dysglycemia** without overt hyperglycemia using an oral glucose tolerancetest (OGTT): 2-hour plasma glucose (2-h PG) level of [140-199 mg/dL (7.8-11.0 mmol/L)] during a 75-g OGTT. [Provide supporting evidence (e.g., lab work or chart notes where applicable)]

[If an OGTT is not available, an alternative method for diagnosing dysglycemia without overt hyperglycemia may be appropriate. Include the rationale for utilizing and alternative method. Include the following information if it is relevant to your patient and the health plan’s reason for denial]

According to the ADA’s guidelines, dysglycemia may be diagnosed based on plasma glucose criteria, either the fasting plasma glucose (FPG) value ***or*** the 2-h plasma glucose (PG) value during a 75-g OGTT, ***or*** A1C criteria.2

**Additional information regarding [Patient Name]’s diagnosis and disease progression:**

[Include additional information about your patient’s disease progression and the need to prescribe TZIELD, if it is relevant to the payer’s reason for denial]

[Consider adding information related to the TN-10 study, the pivotal trial for TZIELD, if it is relevant to the payer’s reason for denial:]

**TZIELD Clinical Trial Overview**

TZIELD is a CD3-directed antibody indicated to delay the onset of Stage 3 type 1 diabetes (T1D) in adults and pediatric patients aged 8 years and older with Stage 2 T1D.1

The effectiveness of TZIELD was investigated in a randomized, 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. Patients were randomized to receive TZIELD (N=44) or placebo (N=32) once daily by intravenous infusion for 14 days. The primary efficacy endpoint in this study was the time from randomization to development of Stage 3 type 1 diabetes diagnosis. In this study, Stage 3 type 1 diabetes was diagnosed in 20 (45%) of the TZIELD-treated patients and in 23 (72%) of the placebo-treated patients. A Cox proportional hazards model, stratified by age and oral glucose tolerance test status at randomization, demonstrated that the median time from randomization 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).1

In Study TN-10, common (≥10%) adverse reactions that occurred during treatment and through 28 days after the last study drug administration were lymphopenia, rash, leukopenia and headache.1

**IMPORTANT SAFETY INFORMATION**

**WARNINGS AND PRECAUTIONS**

* **Cytokine Release Syndrome (CRS):** CRS occurred in TZIELD-treated patients during the treatment period and through 28 days after the last drug administration. Prior to TZIELD treatment, premedicate with antipyretics, antihistamines and/or antiemetics, and treat similarly if symptoms occur during treatment. If severe CRS develops, consider pausing dosing for 1 day to 2 days and administering the remaining doses to complete the full 14-day course on consecutive days; or discontinue treatment. Monitor liver enzymes during treatment. Discontinue TZIELD treatment in patients who develop elevated alanine aminotransferase or aspartate aminotransferase more than 5 times the upper limit of normal (ULN) or bilirubin more than 3 times ULN.
* **Serious Infections:** Use of TZIELD is not recommended in patients with active serious infection or chronic infection other than localized skin infections. Monitor patients for signs and symptoms of infection during and after TZIELD administration. If serious infection develops, treat appropriately, and discontinue TZIELD.
* **Lymphopenia:** Lymphopenia occurred in most patients. For most patients, lymphocyte levels began to recover after the fifth day of treatment and returned to pretreatment values within two weeks after treatment completion and without dose interruption. Monitor white blood cell counts during the treatment period. If prolonged severe lymphopenia develops (<500 cells per mcL lasting 1 week or longer), discontinue TZIELD.
* **Hypersensitivity Reactions:** Acute hypersensitivity reactions including serum sickness, angioedema, urticaria, rash, vomiting and bronchospasm occurred in TZIELD-treated patients. If severe hypersensitivity reactions occur, discontinue TZIELD and treat promptly.
* **Vaccinations:** The safety of immunization with live-attenuated (live) vaccines in TZIELD-treated patients has not been studied. TZIELD may interfere with immune response to vaccination and decrease vaccine efficacy. Administer all age-appropriate vaccinations prior to starting TZIELD.
	+ Administer live vaccines at least 8 weeks prior to treatment. Live vaccines are not recommended during treatment, or up to 52 weeks after treatment.
	+ Administer inactivated (killed) vaccines or mRNA vaccines at least 2 weeks prior to treatment. Inactivated vaccines are not recommended during treatment, or 6 weeks after completion of treatment.

**ADVERSE REACTIONS:** Most common adverse reactions (>10%) were lymphopenia, rash, leukopenia, and headache.

**USE IN SPECIFIC POPULATIONS**

* **Pregnancy:** May cause fetal harm.
* **Lactation:** A lactating woman may consider pumping and discarding breast milk during and for 20 days after TZIELD administration.

**Before prescribing TZIELD, please read the accompanying** [**Prescribing Information**](https://proventionbio.com/s/tzield-prescribing-information.pdf)**, including** [**Medication Guide**](https://proventionbio.com/s/tzield-medication-guide.pdf)**.**

Based upon my clinical judgment, I request that you reconsider the previous denial. If further information is required for approval of this request, please contact my office at [physician phone number/email address].

Thank you for your attention to this very important matter.

**Enclosures:** [suggested but additional, different documents may be required by individual plans]

* Original denial letter
* TZIELD Prescribing Information
* TZIELD FDA Approval Letter
* Relevant medical records and/or laboratory results
* Relevant clinical guidelines and clinical data

Sincerely,

[Physician Name]

[Health Care Practice Name]

[PO Box or Street Address]

[City], [State] [Zip Code]

**References: 1.** TZIELD Prescribing Information. Provention Bio, Inc. **2.** American Diabetes Association Professional Practice Committee; 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes—2022. Diabetes Care 1 January 2022; 45 (Supplement\_1): S17–S38.

The information contained in this template letter is provided by Provention Bio for patients who have been prescribed TZIELD. There is no requirement that any patient or healthcare provider use any Provention Bio product in exchange for this information, and this template is not meant to substitute for a prescriber’s independent medical decision-making.

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