**Sample Letter of Medical Necessity Template**

The following is a sample letter of medical necessity 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: Expedited review request for 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 accordance with my clinical judgment and the diagnosis above, TZIELD is medically necessary for the treatment of this patient, and I am requesting an expedited review and approval.

[Consider adding information related to the TN-10 study, the pivotal trial for TZIELD, if it is relevant to the payer's requirements for approval. A sample of potentially relevant information is provided below:]

**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.

**Please see additional Important Safety Information on next page**

**IMPORTANT SAFETY INFORMATION (cont.)**

**WARNINGS AND PRECAUTIONS (cont.)**

* **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)**.**

I am recommending TZIELD for [Patient Name] based on [his/her] diagnosis and medical records attached. The US Food & Drug Administration (FDA) approved TZIELD on 11/17/2022 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 I am requesting an expedited review and approval to treat my patient [Patient Name] with TZIELD. In my professional opinion, TZIELD is medically necessary for the treatment of this patient. Please feel free to

contact me if I can provide further information.

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

* 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.

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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