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Teplizumab Prior Authorization Criteria Update

Date of Review: August 2026

Literature Search: 07/01/2018 – 05/15/26
Date of Last Review: Miscellaneous Antidiabetic Agents (July 2018)

Purpose of the Review: Teplizumab is a CD3-directed antibody initially approved in November of 2022 to delay the onset of Stage 3 type 1 diabetes (T1D) in adults and pediatric patients 8 years and older. Recently teplizumab has been approved for two additional indications. The purpose of this review is to update the prior authorization (PA) criteria to include these new indications.

New Indications:

Use in Stage 2 TID
Teplizumab was approved in April 2026 to delay the onset of Stage 3 T1D in pediatric patients between 1 and 8 years, previously approved in patients 8 years and older, with Stage 2 T1D.[1] Approval was based on evidence from a single arm, open-label safety and pharmacokinetic study in pediatric patients with Stage 2 T1D (**Table 1**).[2]

The diagnosis of Stage 2 T1D should be confirmed by the following before administering teplizumab:
- Document at least two positive pancreatic islet autoantibodies in those who have dysglycemia without overt hyperglycemia using an oral glucose tolerance test (OGTT) or alternative method if appropriate and OGTT is not available.
- In patients who meet criteria for a diagnosis of Stage 2 T1D, ensure the patient's diagnosis confirms an autoimmune origin and does not suggest insulin resistance due to obesity, type 2 diabetes (T2D) or dysglycemia due to other forms of diabetes.

Use in Stage 3 TID
In June 2026, teplizumab received an additional indication to delay the decline in endogenous insulin production in pediatric patients aged 8 to 17 years recently diagnosed with Stage 3 T1D.[1] Approval was granted via the accelerated approval program based on reduced C-peptide decline and may be contingent on confirmatory trials demonstrating benefit. Evidence was based on results of the PROTECT study shown in **Table 1** below. [3]

Teplizumab use in Stage 3 T1D should be confirmed by the following:
- Document at least one positive pancreatic islet cell autoantibody and peak C-peptide ≥0.2 pmol/mL on a mixed-meal tolerance test (MMTT) or alternative method if appropriate and MMTT is not available.

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Table 1. Studies used for Expanded Indications for Teplizumab

Study	Comparison	Population	Primary Outcome	Results	Notes/Limitations
Gitelman, et al[2] (PETITE-1D) MC, OL, Single arm	Teplizumab given once daily for 14-days Trial duration: 2 years	Children < 8 years with Stage 2 T1D (n=23)	Treatment-emergent adverse events (TEAE), TEAE treatment discontinuations and serious adverse events	- All participants experienced a TEAE that was mild to moderate in most cases - TEAE leading to discontinuation occurred in 3 (13%) patients (anemia, elevated liver enzymes and macro-papular rash) - Two patients (9%) had a severe adverse reaction	- Mean age 4.8 years - Safety was similar to other studies - Two patients developed Stage 3 T1D during study
Ramos, et al[3] (PROTECT) PC, Phase 3, RCT	Teplizumab given once daily as two 12-day treatment courses Vs. Placebo Trial duration: 78 weeks	Children and adolescents with newly diagnosed T1D (within 6 weeks) (n=328)	Change from baseline in beta-cell function, as measured by stimulated C-peptide levels at week 78	Teplizumab: -0.09 Placebo: -0.21 LSMD 0.13 pmol/ml; 95% CI, 0.09 to 0.17 P<0.001 -	- Mean age was 12.1 years - Baseline mean peak C-peptide level was 0.2 to 0.7 pmol/ml in 42.1% and >0.7 pmol/ml in 57.9% - Mean HbA1c was 9.0% - More patients treated with teplizumab maintained a C-peptide level of 0.2 pmol/ml or greater compared to placebo, 94.9% vs 79.2%
Abbreviations: CI = confidence interval; DB= double blind; HbA1c = hemoglobin A1C; LSMD = least square mean difference; MC = multi-center; PC = placebo controlled; RCT = randomized clinical trial; T1D = type 1 diabetes.					

Patients that are candidates for teplizumab should undergo additional laboratory testing prior to administration. Prior to teplizumab use, a complete blood count, liver enzyme tests, and evaluation for active Epstein-Barr virus (EBV) and cytomegalovirus (CMV) infection, including assessment of viral load (e.g., polymerase chain reaction testing) should be performed.[1] Teplizumab should not be used in patients with certain laboratory abnormalities. The use of teplizumab is contraindicated in patients who are immunocompromised or have active viral infection (such as EBV or CMV infection). Age-appropriate vaccinations should be given prior to teplizumab administration.[1] Live-attenuated vaccines should be given at least 8 weeks prior to teplizumab and inactivated vaccines should be given at least 2 weeks prior to treatment.[1]

Administration

Teplizumab should be given intravenously once a day for 14 days (Stage 2 T1D) or 12 days (Stage 3 T1D). The dose is based on body surface area (BSA) and titrated as described in the labeling.[1] For Stage 2 TID, only one 14-day teplizumab treatment course is recommended.[1] For Stage 3 T1D, it is recommended that the initial treatment be given as soon as possible following a Stage 3 diagnosis but no later than 8 weeks from diagnosis.[1] For Stage 3 T1D, 2 treatment courses

are recommended. The second treatment course should be given 6 months after the first treatment course. If the second course is delayed, administer the second treatment course within 6 to 12 months after the first treatment course.[1]

Recommendations:

- No changes to the preferred drug list (PDL) are recommended based on the evidence for these new indications. Maintain teplizumab as nonpreferred.
- Recommend updating the PA criteria to include the new indication for teplizumab for use in Stage 3 type 1 diabetes (T1D) (**Appendix 1**).

References:

1. TZIELD (teplizumab -mzwv) [prescribing information]. Morristown, NJ; Provention Bio, Inc. April 2026.

2. Gitelman S, Simmons K, Sherr J, et al. Safety and pharmacokinetics of teplizumab in children less than 8 years of age with stage 2 type 1 diabetes. *Diabetologia* . 2026 Feb;69(2):330-342.

3. Ramos E, Dayan C, Chatenoud L, et al. Teplizumab and β-Cell Function in Newly Diagnosed Type 1 Diabetes. *N Engl J Med.* 2023;389:2151-2161.

Appendix 1: Prior Authorization Criteria

Teplizumab

Goal(s):

- To promote safe and effective use in populations with established benefit:
  - Teplizumab has benefit for *prevention* of Stage 3 type 1 diabetes mellitus (T1DM) in members with Sstage 2 T1DMdisease (defined below based on lab testing) in adult and pediatric patients 1 year of age and older.
  - Delay the decline in endogenous insulin production in pediatric patients ages 8 to 17 years recently diagnosed with Stage 3 T1D.

~~Benefit has not been established for symptomatic (stage 3) T1DM or members who do not meet the definition for stage 2 disease (defined below).~~

Length of Authorization:

- One 14-day treatment course (Stage 2) **OR**
- Two treatment courses of 12-days (Stage 3) separated by at least 6 months but not more than 12 months~~.~~

Requires PA:

- All provider-administered and pharmacy point-of-sale claims for teplizumab

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at

- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Approval Criteria		
1. Is the request for an FDA approved age? ~~(e.g. 8 years of age or older)?~~	**Yes:** Go to #2	**No:** Pass to RPh. Deny; medical appropriateness.
~~2. Has the patient previously been treated with teplizumab (use beyond the original 14 day infusion)?~~	~~**Yes:** Pass to RPh. Deny; medical appropriateness. No evidence to support additional doses.~~	~~**No:** Go to #3~~
~~6.~~2. Is the medication prescribed by or in consultation with an endocrinologist?	**Yes:** Go to #~~3~~4	**No:** Pass to RPh. Deny; medical appropriateness.
3. Has the patient previously been treated with teplizumab?	**Yes:** Go to #7	**No:** Go to #4
4. Does the patient have Stage 2 T1~~1~~D and is 1 year of age or older?	**Yes:** Go to #5	**No:** Go to #7
~~7.~~5. Does the patient meet the standard criteria for the diagnosis of type 1 diabetes as determined as having one of the following: - HbA1c of 6.5% or higher **OR** - Fasting plasma glucose (FPG) of 126 mg/dL or higher **OR** - Oral glucose tolerance test (OGTT) of 200 mg/dL or higher?	**Yes:** Pass to RPh. Deny; medical appropriateness	**No:** Go to #~~6~~5

Approval Criteria		
6. Is the person at high risk of developing T1DM (e.g. Stage 2 diabetes) as determined by having the following: - Presence of two or more diabetes-related autoantibodies (e.g. insulin autoantibodies (IAA), islet cell antibodies (ICA), glutamic acid decarboxylase 65 (GAD) autoantibodies, insulinoma-associated antigen 2 autoantibody (IA-2A), zinc transporter 8 autoantibody (ZnT8A)) **AND** - Abnormal glucose confirmed within the last 2 months as determined by: - An abnormal glucose during an OGTT (140-199 mg/dL) **OR** - FPG 100-125 mg/dL **OR** - HbA1c 5.7-6.4% or ≥10% increase in HbA1c **OR** - 2-hour plasma glucose 140-199 mg/dL	**Yes: Go to** #8	**No:** Pass to RPh. Deny; medical appropriateness.
7. Is the patient aged 8 to 17 years and recently diagnosed with **Stage 3** T1D (within in the previous **8 weeks**) by documentation of: - at least one positive pancreatic islet cell autoantibody **AND** - peak C-peptide > 0.2 pmol/mL on a mixed-meal tolerance test (MMTT) or alternative method if appropriate and MMTT is not available	**Yes:** Go to #8	**No:** Pass to RPh. Deny; medical appropriateness.
8. Have baseline liver function tests, ~~and~~ complete blood panel and evaluation for active EBV and CMV infection ~~been~~ assessed ~~evaluated~~ in the past 2 months?	**Yes:** Go to #96	**No:** Pass to RPh. Deny; medical appropriateness

Approval Criteria		
9. Has the patient received, or have contraindications to, all routine immunizations recommended for their age based on provider attestation of immunization history? Note: - Teplizumab labeling recommends administration of live-attenuated vaccines at least 8 weeks prior to treatment and inactivated (killed) vaccines or mRNA vaccines at least 2 weeks prior to treatment. - Routine vaccinations for patients at least 8 years of age typically include hepatitis B, hepatitis A, diphtheria, tetanus, pertussis, pneumococcal conjugate, inactivated poliovirus, influenza, and at least 2 doses of measles, mumps, rubella, and varicella.	**Yes:** Approve for a 14-day course (**Stage 2**) **OR** for up to two 12-day treatment courses (**Stage 3**) separated by 6 months but not more than 12 months~~Go to #7~~ Document provider attestation of immunization history.	**No:** Pass to RPh. Deny; medical appropriateness
~~Is the person at high risk of developing T1DM (e.g. Stage 2 diabetes) as determined by having the following:~~ ~~Presence of two or more diabetes-related autoantibodies (e.g. insulin autoantibodies (IAA), islet cell antibodies (ICA), glutamic acid decarboxylase 65 (GAD) autoantibodies, insulinoma-associated antigen 2 autoantibody (IA-2A), zinc transporter 8 autoantibody (ZnT8A)) **AND**~~ ~~Abnormal glucose confirmed within the last 2 months as determined by:~~ ~~An abnormal glucose during an OGTT (140-199 mg/dL) **OR**~~ ~~FPG 100-125 mg/dL **OR**~~ ~~HbA1c 5.7-6.4% or ≥10% increase in HbA1c **OR**~~ ~~2-hour plasma glucose 140-199 mg/dL~~ ~~Note: Teplizumab is preventative therapy and not approved at this time for people diagnosed with symptomatic T1DM (e.g. Stage 3)~~	~~**Yes:** Approve for one 14-day course.~~	~~**No:** Pass to RPh. Deny; medical appropriateness.~~