Preemptive policy: This is a P&T approved policy and can be used after the drug is FDA approved until it is superseded by an updated policy

Clinical Policy: Teplizumab (PRV-031)

Reference Number: ERX.SPA.405
Effective Date: FDA Approval Date
Last Review Date: 08.22
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Teplizumab (PRV-031) is an anti-CD3 monoclonal antibody.

FDA Approved Indication(s) [Pending]
Teplizumab is indicated for the prevention or delay of type 1 diabetes mellitus (T1DM) in patients at high risk of developing the disease, as indicated by the presence of two or more T1DM-related autoantibodies.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that teplizumab is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria*
**Criteria will mirror the clinical information from the prescribing information once FDA-approved*

A. Prevention of Type 1 Diabetes Mellitus (must meet all)**:**
1. Prescribed for the prevention of T1DM;*
2. Prescribed by or in consultation with an endocrinologist;
3. Age ≥ 8 years;*
4. Member does not have a diagnosis of T1DM;
5. Member is at high risk for developing T1DM as evidenced by all of the following (a, b, and c):*
   a. Member has a first, second, or third degree relative who was diagnosed with T1DM before age 40 and started on insulin therapy within one year of diagnosis;
   b. Presence of two or more diabetes-related autoantibodies detected in two samples obtained within the last 6 months: anti-insulin autoantibodies (mIAA), islet cell antibodies (ICA), anti-glutamic acid decarboxylase(GAD)65ab, anti-ICA512ab;
   c. Abnormal glucose tolerance during an oral glucose-tolerance test (OGTT) confirmed within the last 7 weeks (i, ii, or iii) (*two confirmatory tests are required for members age ≥ 18 years*):
      i. Fasting plasma glucose ≥ 110 mg/dL, and < 126 mg/dL;
      ii. 2 hour plasma glucose ≥ 140 mg/dL, and < 200 mg/dL;
      iii. 30, 60, or 90 minute value on OGTT ≥ 200 mg/dL;
6. Dose does not exceed a total dose of 9,034 μg/m^2 administered over a 14-day treatment course.*

Approval duration: 3 months (one 14-day treatment course only)

B. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy*

**Criteria will mirror the clinical information from the prescribing information once FDA-approved*

A. Prevention of Type 1 Diabetes Mellitus

1. Continued therapy will not be authorized as teplizumab is indicated to be dosed one time only.

Approval duration: Not applicable

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents;

B. Treatment of T1DM.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
GAD: glutamic acid decarboxylase
ICA: islet cell antibodies
mIAA: anti-insulin autoantibodies
MMTT: mixed meal tolerance test
OGTT: oral glucose tolerance test
T1DM: type 1 diabetes mellitus

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings [Pending]

- Contraindication(s): pending
- Boxed warning(s): pending

Appendix D: General Information

- In 2010, teplizumab failed to meet the primary efficacy endpoint (a composite of total daily insulin usage and HbA1c level at 12 months) in the phase 3 Protégé study, demonstrating no difference compared to placebo for the treatment of patients with early-onset T1DM; as a result, clinical programs were suspended. In 2018, Provention Bio acquired teplizumab from MacroGenics/Lilly. A new phase 3 study for the treatment of early-onset T1DM is now ongoing (PROTECT, NCT03875729). Results from this study are not yet available.

V. Dosage and Administration [Pending]

Indication	Dosing Regimen	Maximum Dose
Prevention of T1DM*	14 day treatment course administered IV:* • Day 1: 51 µg/m^2 • Day 2: 103 µg/m^2 • Day 3: 207 µg/m^2 • Day 4: 413 µg/m^2 • Days 5-14: 826 µg/m^2	9,034 µg/m^2/ treatment course* .

VI. Product Availability [Pending]

Pending

VII. References

Prevention of T1DM

1. Herold KC et al. An anti-CD3 antibody, teplizumab, in relatives at risk for type 1 diabetes. New Engl J Med. 2019; 381(7): 603-613. doi: 10.1056/NEJMoa1902226. Epub 2019 Jun 9.
2. Provention Bio, Inc. Teplizumab for prevention of type 1 diabetes in relatives "at-risk". Available at: https://clinicaltrials.gov/ct2/show/NCT01030861. Accessed March 30, 2022.
3. Sims EK et al. Teplizumab improves and stabilizes beta cell function in antibody-positive high-risk individuals. Science Translational Medicine. 2021; 13(583): eabc8980.

Treatment of T1DM

4. Sherry N et al. Teplizumab for treatment of type 1 diabetes (Protégé study): 1-year results from a randomized, placebo-controlled trial. Lancet. 2011; 378(9790): 487-497.
5. Hagopian W et al. Teplizumab preserves C-peptide in recent-onset type 1 diabetes: two-year results from the randomized, placebo-controlled Protégé trial. Diabetes. 2013; 62(11): 3901-3908.
6. Herold KC et al. Teplizumab (anti-CD3 mAb) treatment preserves C-peptide responses in patients with new-onset type 1 diabetes in a randomized controlled trial: Metabolic and immunologic features at baseline identify a subgroup of responders. Diabetes. 2013; 62: 3766-3774.
7. Provention Bio, Inc. Recent-onset type 1 diabetes trial evaluating efficacy and safety of teplizumab (PROTECT). Available at: https://clinicaltrials.gov/ct2/show/NCT03875729. Accessed March 30, 2022.
8. Nourelden AZ et al. Safety and efficacy of teplizumab for treatment of type one diabetes mellitus: A systematic review and meta-analysis. Endocr Metab Immune Disord Drug Targets. 2021; 21(10): 1895-1904.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	05.19.20	08.20
3Q 2021 annual review: no significant changes; references reviewed and updated.	03.17.21	08.21
3Q 2022 annual review: no significant changes as drug is not yet FDA-approved; references reviewed and updated.	03.30.22	08.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.