CENTENE® Corporation

Clinical Policy: Teplizumab (PRV-031)

Reference Number: CP.PHAR.492
Effective Date: FDA Approval Date
Last Review Date: 08.22
Line of Business: Commercial, HIM, Medicaid

Coding Implications
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.

It is the policy of health plans affiliated with Centene Corporation® 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 the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid 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. Erratum in: N Engl J Med. 2020 Feb 6; 382(6): 586.
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.

Coding Implications [Pending]
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
Pending	Pending

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 as drug is not yet FDA-approved; references to HIM.PHAR.21 revised to HIM.PA.154; 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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan

retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.