SmartPA Criteria Proposal

Drug/Drug Class:	Tzield Clinical Edit
First Implementation Date:	TBD
Proposed Date:	July 18, 2023
Prepared for:	MO HealthNet
Prepared by:	MO HealthNet/Conduent
Criteria Status:	☐Existing Criteria ☐Revision of Existing Criteria ☒New Criteria

Executive Summary

Purpose: Ensure appropriate utilization and control of Tzield™ (teplizumab-mzwv)

Why Issue Selected: On November 17, 2022, the U.S. Food and Drug Administration (FDA) approved Tzield™ (teplizumab-mzwv) the first CD3-directed antibody indicated to delay the onset of Stage 3 type 1 diabetes (T1D). Approximately 1 million to 1.5 million Americans have T1D, which is one of the most common diseases of childhood, with the annual incidence is 22.3 per 100,000 amongst children and adolescents (overall incidence is 15 per 100,000 people). Approximately 45 percent of children present with childhood-onset T1D before 10 years of age.

In genetically susceptible persons, T1D progresses through asymptomatic stages before the development of overt hyperglycemia. In stage 1, patients have normal blood glucose levels but possess beta cell autoimmunity (≥ 2 islet autoantibodies). In stage 2, metabolic responses to a glucose load are impaired and patients start to show dysglycemia. Patients remain asymptomatic in stage 2, which may lead to delay in diagnosis until stage 3 when signs and symptoms including polyuria, polydipsia, weight loss, and lethargy are recognized.

Tzield binds to CD3 (a cell surface antigen present on T lymphocytes). The mechanism may involve partial agonistic signaling and deactivation of pancreatic beta cell autoreactive T lymphocytes. Tzield leads to an increase in the proportion of regulatory T cells and of exhausted CD8+ T cells in peripheral blood.

Due to the high cost, possible adverse events, and specific approved indications, MO HealthNet will impose clinical criteria to ensure appropriate utilization of Tzield.

Program-Specific Information:

Drug	Cost per vial (WAC)	Cost per therapy course (WAC) (based on average 14 year old patient with BSA = 1.5 m^2)
TZIELD 2MG/2ML VIAL	$13,850	$193,900

Type of Criteria:

☐ **Increased risk of ADE**
☒ **Appropriate Indications**
☐ **Preferred Drug List**
☒ **Clinical Edit**

Data Sources: ☐ **Only Administrative Databases** ☒ **Databases + Prescriber-Supplied**

Setting & Population

- Drug class for review: Tzield™ (teplizumab-mzwv)
- Age range: All appropriate MO HealthNet participants aged 8 years or older

Approval Criteria

- Participant is aged 8 years or older **AND**
- Prescribed by or in consultation with an endocrinologist or an appropriate specialist for the treated disease **AND**
- Diagnosis of Stage 2 type 1 diabetes by documenting:
  - Development of least 2 of the following positive pancreatic islet cell autoantibodies within 6 months:
    - Glutamic acid decarboxylase 65 (GAD) autoantibodies
    - Insulin autoantibody (IAA)
    - Insulinoma-associated antigen 2 autoantibody (IA-2A)
    - Zinc transporter 8 autoantibody (ZnT8A)
    - Islet cell autoantibody (ICA)
  - Abnormal glucose tolerance by oral glucose tolerance test (OGTT) confirmed within 7 weeks of baseline visit using:
    - FPG greater than 100mg/dL and less than 126 mg/dL **OR**
    - 2 hour glucose greater or equal to 140 mg/dL and less than 200 mg/dL **OR**
    - 30, 60, or 90 minute value on OGTT greater than or equal to 200 mg/dL
- Documentation of complete blood count (CBC) and liver enzyme tests within the past 30 days
- Approval is for one time course of therapy (14 days)

Denial Criteria

- Participant is in Stage 1 or 3 of type 1 diabetes
- Documented history of type 2 diabetes
- Participant is currently pregnant
- Documented previous treatment with teplizumab
- Documented previous treatment with insulin
- Therapy will be denied if all approval criteria are not met

Required Documentation

Laboratory Results:	X	Progress Notes:	X
MedWatch Form:		Other:	X

Disposition of Edit

Denial: Exception code “0682” (Clinical Edit)
Rule Type: CE

Default Approval Period

3 months

References

- Tzield™ (teplizumab-mzwv) [package insert]. Red Bank, NJ: Provention Bio, Inc; November 2022
- Divers J, Mayer-Davis EJ, et.al. Trends in Incidence of Type 1 and Type 2 Diabetes Among Youths - Selected Counties and Indian Reservations, United States, 2002-2015. MMWR Morb Mortal Wkly Rep. 2020 Feb 14;69(6):161-165. doi: 10.15585/mmwr.mm6906a3. PMID: 32053581; PMCID: PMC7017961.
- 2. Sims EK, Bundy BN, et.al. Teplizumab improves and stabilizes beta cell function in antibody-positive high-risk individuals. Sci Transl Med. 2021 Mar 3;13(583):eabc8980. doi: 10.1126/scitranslmed.abc8980. PMID: 33658358; PMCID: PMC8610022.
- Nourelden AZ, Elshanbary AA, 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. doi: 10.2174/1871530320999201209222921. PMID: 33302842.
- 5. Hirsch, I. Pathogenesis of type 1 diabetes mellitus. Up To Date. Available from https://www.uptodate.com/contents/pathogenesis-of-type-1- diabetes-mellitus?search=type%201%20diabetes&topicRef=5816&source=see_link. Updated 8 June 2022. Accessed 26 January 2022.