Medical Policy Bulletin

Title:
Teplizumab-mzwv (Tzield)
Policy #:
MA08.157b

The Company makes decisions on coverage based on the Centers for Medicare and Medicaid Services (CMS) regulations and guidance, benefit plan documents and contracts, and the member's medical history and condition. If CMS does not have a position addressing a service, the Company makes decisions based on Company Policy Bulletins. Benefits may vary based on contract, and individual member benefits must be verified. The Company determines medical necessity only if the benefit exists and no contract exclusions are applicable. Although the Medicare Advantage Policy Bulletin is consistent with Medicare's regulations and guidance, the Company's payment methodology may differ from Medicare.

When services can be administered in various settings, the Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition. This decision is based on the member's current medical condition and any required monitoring or additional services that may coincide with the delivery of this service.

This Policy Bulletin document describes the status of CMS coverage, medical terminology, and/or benefit plan documents and contracts at the time the document was developed. This Policy Bulletin will be reviewed regularly and be updated as Medicare changes their regulations and guidance, scientific and medical literature becomes available, and/or the benefit plan documents and/or contracts are changed.

Policy

Coverage is subject to the terms, conditions, and limitations of the member's Evidence of Coverage.

The Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition.

MEDICALLY NECESSARY

Teplizumab-mzwv (Tzield) is considered medically necessary and, therefore, covered to delay the onset of stage 3 type 1 diabetes (T1D) in adult and pediatric individuals 8 years of age and older who currently have stage 2 type 1 diabetes when all of the following criteria are met, including dosing and frequency:

- Prescribed by or in consultation with an endocrinologist
- The individual has abnormal oral glucose tolerance by oral glucose tolerance testing defined by one of the following:
    - Fasting glucose 100 to 125 milligrams per deciliter (mg/dL)/5.6 to 6.9 millimoles per liter (mmol/L)
    - Two-hour postprandial glucose 140 to 199 mg/dL/(7.8 to 11.1 mmol/L)
    - A1c 5.7 to 6.4 percent
- The individual has the presence of at least two confirmed diabetes autoantibodies detected in two samples obtained within 6 months before initiation of the treatment (e.g., 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])
- The individual does NOT have any of the following:
    - Stage 3 type 1 diabetes (e.g., excessive hunger or thirst, blurry vision, severe fatigue, frequent urination, unexplained weight loss)
    - Clinical history consistent with type 2 diabetes
- Dosing and frequency for teplizumab-mzwv (Tzield) intravenous infusion one treatment course (i.e., 14 doses) per lifetime:
    - Day one: 65 mcg/m^2
    - Day two: 125 mcg/m^2
    - Day three: 250 mcg/m^2
    - Day four: 500 mcg/m^2
    - Days five through 14: 1,030 mcg/m^2

EXPERIMENTAL/INVESTIGATIONAL

All other uses for teplizumab-mzwv (Tzield) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage for prescription drugs and biologics.

DOSING AND FREQUENCY REQUIREMENTS

The Company reserves the right to modify the Dosing and Frequency Requirements listed in this policy to ensure consistency with the most recently published recommendations for the use of teplizumab-mzwv (Tzield). Changes to these guidelines are based on a consensus of information obtained from resources such as, but not limited to: the US Food and Drug Administration (FDA); Company-recognized authoritative pharmacology compendia; or published peer-reviewed clinical research. The professional provider must supply supporting documentation (i.e., published peer-reviewed literature) in order to request coverage for an amount of teplizumab-mzwv (Tzield) outside of the Dosing and Frequency Requirements listed in this policy. For a list of Company-recognized pharmacology compendia, view our policy on off-label coverage for prescription drugs and biologics.

Accurate member information is necessary for the Company to approve the requested dose and frequency of this drug. If the member's dose, frequency, or regimen changes (based on factors such as changes in member weight or incomplete therapeutic response), the provider must submit those changes to the Company for a new approval based on those changes as part of the utilization management activities. The Company reserves the right to conduct postpayment review and audit procedures for any claims submitted for teplizumab-mzwv (Tzield).

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the service.

When coverage of teplizumab-mzwv (Tzield) is requested outside of the Dosing and Frequency Requirements listed in this policy, the prescribing professional provider must supply documentation (i.e., published peer-reviewed literature) to the Company that supports this request.

Guidelines

DRUG INFORMATION

Per the US Food and Drug Administration (FDA)–approved labeling, the recommended dosing and frequency of teplizumab-mzwv (Tzield) intravenous infusion is one treatment course (i.e., 14 doses) per lifetime.

Staging Presymptomatic Type 1 Diabetes: A Scientific Statement of JDRF, the Endocrine Society, and the American Diabetes Association

Stage 1: represents individuals who have developed two or more type 1 diabetes–associated islet autoantibodies but are normoglycemic. For children who were screened for genetic risk at birth and reach this stage, the 5-year and 10-year risks of symptomatic disease are approximately 44% and 70%, respectively, and the lifetime risk approaches 100%. The risk at this stage is quite similar in genetically at-risk children and in relatives of individuals with type 1 diabetes.

Stage 2, like stage 1, includes individuals with two or more islet autoantibodies but whose disease has now progressed to the development of glucose intolerance, or dysglycemia, from loss of functional β-cell mass. The 5-year risk of symptomatic disease at this stage is approximately 75%, and the lifetime risk approaches 100%.

Stage 3 represents manifestations of the typical clinical symptoms and signs of diabetes, which may include polyuria, polydipsia, weight loss, fatigue, diabetic ketoacidosis (DKA), and others.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, teplizumab-mzwv (Tzield) is covered under the medical benefits of the Company's products when the medical necessity criteria including dosing and frequency requirements listed in this medical policy are met.

US FOOD AND DRUG ADMINISTRATION (FDA) STATUS

Teplizumab-mzwv (Tzield) was approved by the FDA on November 17, 2022, to delay the onset of stage 3 type 1 diabetes in adults and pediatric patients 8 years of age and older who currently have stage 2 type 1 diabetes.

PEDIATRIC USE

The safety and effectiveness of teplizumab-mzwv (Tzield) have been established in adults and pediatric patients aged eight years and older with Stage 2 T1D.

Description

Type 1 diabetes is a disease that occurs when the immune system attacks and destroys the cells that make insulin. The autoimmune attack directed against β cells occurs for about 5 years or more before the clinical presentation of diabetes. Even after the diagnosis of diabetes, there is still significant β-cell function and after treatment of the acute presentation there is a period of clinical remission—the "honeymoon phase." The remaining functional cells try to maintain an adequate insulin secretion to prevent complications such as hyperglycemia, ketoacidosis, retinopathy, nephropathy, and neuropathy. The remission is usually temporary and β-cell function declines so that many individuals require full replacement doses of insulin within a few months. Immunological interventions have been directed both before the development of diabetes and after diagnosis in order to prevent decline in residual β-cell function.

Although type 1 diabetes (T1D) can appear at any age, it is usually diagnosed in children and young adults. A person is at higher risk for type 1 diabetes if they have a parent, brother, or sister with type 1 diabetes, although most individuals with type 1 diabetes do not have a family history.

Teplizumab (Tzield) is an Fc receptor (FcR)-nonbinding humanized anti-CD3 monoclonal antibody, disease-modifying agent that delays the progression of clinical T1D in presymptomatic individuals with detected islet autoantibodies who are at high risk of developing this condition, such as having direct family members with the disease. In the Phase 2 "At-Risk" trial (TN10), a single 14-day course of intravenous teplizumab delayed the onset of clinical T1D by 32.5 months compared to placebo, and one-half of the study participants were still free from clinical T1D after 5 years compared to 20 percent in the placebo group.

Teplizumab (Tzield) binds to certain immune system cells and delays progression to stage 3 T1D. Teplizumab (Tzield) may deactivate the immune cells that attack insulin-producing cells, while increasing the proportion of cells that help moderate the immune response.

PEER-REVIEWED LITERATURE

The safety and efficacy of teplizumab-mzwv (Tzield) were evaluated in a randomized, double-blind, event-driven, placebo-controlled trial with 76 individuals with stage 2 T1D. In the trial, individuals randomly received teplizumab-mzwv (Tzield) or a placebo once daily via intravenous infusion for 14 days. The primary measure of efficacy was the time from randomization to development of stage 3 T1D diagnosis. The trial results showed that over a median follow-up of 51 months, 45% of the 44 individuals who received teplizumab-mzwv (Tzield) were later diagnosed with stage 3 T1D, compared to 72% of the 32 individuals who received a placebo. The mid-range time from randomization to stage 3 T1D diagnosis was 50 months for the individuals who received teplizumab-mzwv (Tzield) and 25 months for those who received a placebo.

The most common adverse reactions (>10%) were lymphopenia, rash, leukopenia, and headache. Warnings and precautions include premedication and monitoring for symptoms of cytokine release syndrome, risk of serious infections, decreased levels of a type of white blood cell called lymphocytes, and hypersensitivity reactions.

OFF-LABEL INDICATIONS

There may be additional indications contained in the Policy section of this document due to the evaluation of criteria highlighted in the Company's off-label policy, and/or review of clinical guidelines issues by leading professional organizations and government entities.

References

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Coding

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

CPT Procedure Code Number(s)

N/A

ICD - 10 Procedure Code Number(s)

N/A

ICD - 10 Diagnosis Code Number(s)

E10.A2 Type 1 diabetes mellitus, presymptomatic, Stage 2
R73.01 Impaired fasting glucose
R73.02 Impaired glucose tolerance (oral)
R73.03 Prediabetes
R73.09 Other abnormal glucose
R76.0 Raised antibody titer
Z83.3 Family history of diabetes mellitus

HCPCS Level II Code Number(s)

J9381 Injection, teplizumab-mzwv, 5 mcg

Revenue Code Number(s)

N/A

Policy History

Revisions From MA08.157b:

12/16/2024	This version of the policy will become effective 12/16/2024. This policy has been updated to communicate removal of the medical necessity criteria for individuals who have a first-degree (e.g., brother, sister, parent, offspring) **or** second-degree (e.g., niece, nephew, aunt, uncle, grandchild, cousin) relative with type 1 diabetes.

Revisions From MA08.157a:

10/01/2024	This policy has been identified for the ICD-10 code update, effective 10/01/2024. The following ICD-10 code has been **added** to this policy: E10.A2 Type 1 diabetes mellitus, presymptomatic, Stage 2

MA08.157

05/07/2024	The policy has been developed to communicate the Company's coverage position for teplizumab-mzwv (Tzield).

Version Effective Date:
12/16/2024
Version Issued Date:
12/16/2024
Version Reissued Date:
N/A