Tzield® (Teplizumab-Mzwv)

Policy Number: 2026D0117J
Effective Date: October 1, 2026

➲ Instructions for Use

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Community Plan Policy

- Tzield® (Teplizumab-Mzwv)

Application

UnitedHealthcare Commercial

This Medical Drug Policy applies to UnitedHealthcare Commercial benefit plans.

UnitedHealthcare Individual Exchange

This Medical Drug Policy applies to Individual Exchange benefit plans.

Coverage Rationale

➲ See Benefit Considerations

Delay Onset of Stage 3 Type 1 Diabetes (T1D) in Adult and Pediatric Patients Aged 1 Year and Older With Stage 2 T1D

Tzield is proven to delay the onset of stage 3 T1D in pediatric and adult patients with stage 2 T1D when all of the following criteria are met:

- Patient is 1 year of age or older; **and**
- Diagnosis of stage 2 type 1 diabetes confirmed by **all** of following:
  - Presence of at least two positive pancreatic islet autoantibodies
  - Dysglycemia without overt hyperglycemia using an oral glucose tolerance test (OGTT)
  - Clinical history of patient does not suggest insulin resistance due to obesity, type 2 diabetes (T2D), or dysglycemia due to other forms of diabetes [e.g., genetic forms of diabetes, maturity-onset diabetes of the young (MODY), latent autoimmune diabetes in adults (LADA), diabetes secondary to medications or surgery]

  and
- Dosing is in accordance with the U.S. Food and Drug Administration (FDA)–approved labeling; **and**
- Patient has not been previously treated with Tzield; **and**
- Authorization will be issued for no more than one 14-dose treatment course per lifetime

Tzield is medically necessary to delay the onset of stage 3 T1D in pediatric and adult patients with stage 2 T1D when all of the following criteria are met:

- Patient is 1 year of age or older; **and**
- Diagnosis of stage 2 type 1 diabetes confirmed by **all** of the following:
  - Presence of at least **two** of the following pancreatic islet autoantibodies:

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        - 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)

      and
    - Presence of dysglycemia without overt hyperglycemia defined by **one** of the following:
        - Fasting plasma glucose ≥ 100 mg/dL and < 126 mg/dL; **or**
        - 2-hour post-prandial plasma glucose level ≥ 140 mg/dL and < 200 mg/dL; **or**
        - A1C ≥ 5.7 and < 6.5% or ≥ 10% increase in A1C

      and
    - Patient does not have symptoms associated with stage 3 type 1 diabetes (e.g., increased urination, excessive thirst, weight loss); **and**
    - Clinical history of patient does not suggest insulin resistance due to obesity, type 2 diabetes (T2D), or dysglycemia due to other forms of diabetes [e.g., genetic forms of diabetes, maturity-onset diabetes of the young (MODY), latent autoimmune diabetes in adults (LADA), diabetes secondary to medications or surgery]

  and
- Prescribed by or in consultation with an endocrinologist; **and**
- Dosing is in accordance with the FDA-approved labeling; **and**
- Patient has not been previously treated with Tzield; **and**
- Authorization will be issued for no more than one 14-dose treatment course per lifetime

Delay Decline in Beta Cell Function in Pediatric Patients Aged 8 to 17 Years With Recently Diagnosed Stage 3 T1D

Tzield is proven to delay the decline in beta cell function in pediatric patients with recently diagnosed stage 3 T1D when all of the following criteria are met:

- Patient is aged 8 to 17 years; **and**
- Recent diagnosis (i.e., within the last 8 weeks) of stage 3 T1D; **and**
- Diagnosis of stage 3 T1D confirmed by **all** of the following:
    - Presence of at least one positive pancreatic islet cell autoantibody; **and**
    - Peak C-peptide ≥ 0.2 pmol/mL on a mixed-meal tolerance test (MMTT); **and**
    - Clinical history of patient does not suggest insulin resistance due to obesity, type 2 diabetes (T2D), or dysglycemia due to other forms of diabetes [e.g., genetic forms of diabetes, maturity-onset diabetes of the young (MODY), latent autoimmune diabetes in adults (LADA), diabetes secondary to medications or surgery]

  and
- Dosing is in accordance with the FDA-approved labeling; **and**
- Patient has not been previously treated with Tzield; **and**
- Authorization will be issued for no more than two 12-dose treatment courses per lifetime

Tzield is medically necessary to delay the decline in beta cell function in pediatric patients with recently diagnosed stage 3 T1D when all of the following criteria are met:

- Patient is aged 8 to 17 years; **and**
- Recent diagnosis (i.e., within the last 8 weeks) of stage 3 T1D; **and**
- Diagnosis of stage 3 T1D confirmed by **all** of the following:
    - Presence of at least **one** of the following pancreatic islet autoantibodies:
        - 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)

      and
    - Peak C-peptide ≥ 0.2 pmol/mL on a mixed-meal tolerance test (MMTT); **and**
    - Clinical history of patient does not suggest insulin resistance due to obesity, type 2 diabetes (T2D), or dysglycemia due to other forms of diabetes [e.g., genetic forms of diabetes, maturity-onset diabetes of the young (MODY), latent autoimmune diabetes in adults (LADA), diabetes secondary to medications or surgery]

  and
- Prescribed by or in consultation with an endocrinologist; **and**
- Dosing is in accordance with the FDA-approved labeling; **and**
- Patient has not been previously treated with Tzield; **and**

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- Authorization will be issued for no more than two 12-dose treatment courses per lifetime

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other policies and guidelines may apply.

HCPCS Code	Description
J9381	Injection, teplizumab-mzwv, 5 mcg

Diagnosis Code	Description
E10.10	Type 1 diabetes mellitus with ketoacidosis without coma
E10.11	Type 1 diabetes mellitus with ketoacidosis with coma
E10.21	Type 1 diabetes mellitus with diabetic nephropathy
E10.22	Type 1 diabetes mellitus with diabetic chronic kidney disease
E10.29	Type 1 diabetes mellitus with other diabetic kidney complication
E10.311	Type 1 diabetes mellitus with unspecified diabetic retinopathy with macular edema
E10.319	Type 1 diabetes mellitus with unspecified diabetic retinopathy without macular edema
E10.3211	Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, right eye
E10.3212	Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, left eye
E10.3213	Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, bilateral
E10.3219	Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, unspecified eye
E10.3291	Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, right eye
E10.3292	Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, left eye
E10.3293	Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, bilateral
E10.3299	Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, unspecified eye
E10.3311	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, right eye
E10.3312	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, left eye
E10.3313	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, bilateral
E10.3319	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, unspecified eye
E10.3391	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, right eye
E10.3392	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, left eye
E10.3393	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, bilateral
E10.3399	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, unspecified eye

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Diagnosis Code	Description
E10.3411	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, right eye
E10.3412	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, left eye
E10.3413	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, bilateral
E10.3419	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, unspecified eye
E10.3491	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, right eye
E10.3492	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, left eye
E10.3493	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, bilateral
E10.3499	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, unspecified eye
E10.3511	Type 1 diabetes mellitus with proliferative diabetic retinopathy with macular edema, right eye
E10.3512	Type 1 diabetes mellitus with proliferative diabetic retinopathy with macular edema, left eye
E10.3513	Type 1 diabetes mellitus with proliferative diabetic retinopathy with macular edema, bilateral
E10.3519	Type 1 diabetes mellitus with proliferative diabetic retinopathy with macular edema, unspecified eye
E10.3521	Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, right eye
E10.3522	Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, left eye
E10.3523	Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, bilateral
E10.3529	Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, unspecified eye
E10.3531	Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, right eye
E10.3532	Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, left eye
E10.3533	Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, bilateral
E10.3539	Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, unspecified eye
E10.3541	Type 1 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, right eye
E10.3542	Type 1 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, left eye
E10.3543	Type 1 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, bilateral
E10.3549	Type 1 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, unspecified eye
E10.3551	Type 1 diabetes mellitus with stable proliferative diabetic retinopathy, right eye
E10.3552	Type 1 diabetes mellitus with stable proliferative diabetic retinopathy, left eye
E10.3553	Type 1 diabetes mellitus with stable proliferative diabetic retinopathy, bilateral
E10.3559	Type 1 diabetes mellitus with stable proliferative diabetic retinopathy, unspecified eye
E10.3591	Type 1 diabetes mellitus with proliferative diabetic retinopathy without macular edema, right eye
E10.3592	Type 1 diabetes mellitus with proliferative diabetic retinopathy without macular edema, left eye

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Diagnosis Code	Description
E10.3593	Type 1 diabetes mellitus with proliferative diabetic retinopathy without macular edema, bilateral
E10.3599	Type 1 diabetes mellitus with proliferative diabetic retinopathy without macular edema, unspecified eye
E10.36	Type 1 diabetes mellitus with diabetic cataract
E10.37X1	Type 1 diabetes mellitus with diabetic macular edema, resolved following treatment, right eye
E10.37X2	Type 1 diabetes mellitus with diabetic macular edema, resolved following treatment, left eye
E10.37X3	Type 1 diabetes mellitus with diabetic macular edema, resolved following treatment, bilateral
E10.37X9	Type 1 diabetes mellitus with diabetic macular edema, resolved following treatment, unspecified eye
E10.39	Type 1 diabetes mellitus with other diabetic ophthalmic complication
E10.40	Type 1 diabetes mellitus with diabetic neuropathy, unspecified
E10.41	Type 1 diabetes mellitus with diabetic mononeuropathy
E10.42	Type 1 diabetes mellitus with diabetic polyneuropathy
E10.43	Type 1 diabetes mellitus with diabetic autonomic (poly)neuropathy
E10.44	Type 1 diabetes mellitus with diabetic amyotrophy
E10.49	Type 1 diabetes mellitus with other diabetic neurological complication
E10.51	Type 1 diabetes mellitus with diabetic peripheral angiopathy without gangrene
E10.52	Type 1 diabetes mellitus with diabetic peripheral angiopathy with gangrene
E10.59	Type 1 diabetes mellitus with other circulatory complications
E10.610	Type 1 diabetes mellitus with diabetic neuropathic arthropathy
E10.618	Type 1 diabetes mellitus with other diabetic arthropathy
E10.620	Type 1 diabetes mellitus with diabetic dermatitis
E10.621	Type 1 diabetes mellitus with foot ulcer
E10.622	Type 1 diabetes mellitus with other skin ulcer
E10.628	Type 1 diabetes mellitus with other skin complications
E10.630	Type 1 diabetes mellitus with periodontal disease
E10.638	Type 1 diabetes mellitus with other oral complications
E10.641	Type 1 diabetes mellitus with hypoglycemia with coma
E10.649	Type 1 diabetes mellitus with hypoglycemia without coma
E10.65	Type 1 diabetes mellitus with hyperglycemia
E10.69	Type 1 diabetes mellitus with other specified complication
E10.8	Type 1 diabetes mellitus with unspecified complications
E10.9	Type 1 diabetes mellitus without complications
E10.A0	Type 1 diabetes mellitus, presymptomatic, unspecified
E10.A1	Type 1 diabetes mellitus, presymptomatic, Stage 1
E10.A2	Type 1 diabetes mellitus, presymptomatic, Stage 2

Background

Type 1 diabetes (T1D) is a chronic autoimmune disease that leads to destruction of insulin-producing beta cells and dependence on exogenous insulin for survival. Approximately 1 to 1.5 million Americans have TD1, which is one of the most common diseases of childhood. Although it can appear at any age, TD1 is usually diagnosed in children and young adults. A person is at higher risk for T1D if they have a parent, brother, or sister with T1D, although most patients do not have a family history. Type 1 diabetes progresses through asymptomatic stages before the development of overt hyperglycemia. These stages are characterized by the appearance of autoantibodies (stage 1) and then dysglycemia (stage 2). In stage 2, metabolic responses to a glucose load are impaired but the level of glycosylated hemoglobin remains normal. Insulin therapy and glucose monitoring are currently the standard of care for treating the clinical stage, Stage 3 T1D.

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Teplizumab-mzwv is a CD3-directed monoclonal antibody which binds CD3 on the surface of T lymphocytes. Teplizumab-mzwv may deactivate the T lymphocytes that attack pancreatic insulin-producing beta cells, while increasing the proportion of regulatory T lymphocytes that help moderate the immune response.

Benefit Considerations

Some Certificates of Coverage allow for coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the benefit document or in the medical or drug policy.

Clinical Evidence

Proven

Delay Onset of Stage3 T1D in Adult and Pediatric Patients Aged 8 Years and Older With Stage 2 Type 1D

The efficacy of teplizumab-mzwv was established in a randomized double-blind, event-driven, placebo-controlled study in 76 patients, 8 to 49 years of age with Stage 2 T1D. Patients were randomized to receive teplizumab-mzwv or placebo once daily by intravenous (IV) infusion for 14 days. The primary efficacy endpoint was the time from randomization to development of Stage 3 T1D was diagnosed in 20 (45%) of the teplizumab-treated patients and in 23 (72%) of the placebo-treated patients. A Cox proportional hazards model, stratified by age and oral glucose tolerance test status at randomization, demonstrated that the median time from randomization to Stage 3 T1D diagnosis was 50 months in the teplizumab-mzwv group and 25 months in the placebo group, for a difference of 25 months. With a median follow-up time of 51 months, therapy with Tzield resulted in a statistically significant delay in the development of Stage 3 T1D (hazard ratio 0.41, 95% CI: 0.22, 0.78; p = 0.0066). The most common adverse reactions (> 10%) with teplizumab-mzwv use were lymphopenia, rash, leukopenia, and headache. Lymphocyte count decreased to a nadir on day 5 (total decrease, 72.3%; interquartile range, 82.1 to 68.4; p < 0.001) and resolved by day 45 in all participants except one; in that participant, the lymphocyte counts returned to the normal range on day 105. A spontaneously resolving rash occurred in 16 (36%) of participants who received teplizumab-mzwv.

The expanded indication to include pediatric patients as young as 1 year of age with stage 2 T1D was supported by 1-year interim data from the PETITE-1D phase 4 study. PETITE-1D is an ongoing, a single-arm, nonrandomized, open-label, multicenter trial designed to evaluate the safety and pharmacokinetics of teplizumab-mzwv in young children. The trial enrolled 23 children under the age of 8 years with stage 2 type 1 diabetes, each receiving a 14-day course of IV teplizumab-mzwv once daily. Primary endpoints included treatment-emergent adverse events (TEAEs), TEAEs causing treatment discontinuation, and serious adverse events (SAEs). Other endpoints assessed immunogenicity, pharmacokinetics, pharmacodynamics and time from study treatment to stage 3 type 1 diabetes. Mean participant age was 4.8 years (range 1.7-6.8). Median follow-up duration was 51.9 weeks (range 3.9-77.1). All participants experienced one or more TEAE, with most being mild to moderate. No grade 4 or 5 TEAEs were reported. Three participants (13%) had TEAEs leading to teplizumab-mzwv discontinuation: anaemia, elevated liver enzymes and maculo-papular rash. Two participants (9%) each had two SAEs. Serum teplizumab-mzwv concentrations peaked at day 14. Two participants progressed to stage 3 type 1 diabetes. The estimated probability of lack of progression to stage 3 was 89.6% (95% CI 64.3%, 97.3%) at the time of interim analysis.

Delay Decline in Beta Cell Function in Pediatric Patients Aged 8 to 17 Years With Recently Diagnosed Stage 3 T1D

The efficacy of teplizumab-mzwv to delay the decline in endogenous insulin production in patients recently diagnosed with Stage 3 T1D was evaluated in a randomized double-blind, placebo-controlled study (PROTECT Study; NCT03875729) in 328 patients aged 8 to 17 years recently diagnosed with Stage 3 T1D (within 6 weeks of diagnosis). The trial enrolled patients with residual beta cell function, as indicated by peak stimulated C-peptide > 0.2 pmol/mL on a mixed-meal stimulation test. Patients were randomized to receive teplizumab-mzwv or placebo once daily by intravenous infusion for a 12-day course followed by another 12-day course 6 months later (or at approximately 12 months for a subset of 28 patients). The primary efficacy endpoint was change from baseline in stimulated C-peptide at Week 78, a marker of beta cell function. Teplizumab-mzwv demonstrated a statistically significant reduction in decline versus placebo. The least squares mean change in C-peptide AUC was −0.09 pmol/mL with Tzield compared to −0.22 pmol/mL with placebo (difference 0.13; 95% CI, 0.08–0.17; p < 0.0001).

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Professional Societies

American Diabetes Association (ADA)

In 2026, the ADA published "Standards of Care in Diabetes-2026" which includes current clinical practice recommendations and is intended to provide the components of diabetes care, general treatment goals and guidelines, and tools to evaluate quality of care. The ADA differentiates type 1 diabetes from type 2 diabetes through clinical presentation and laboratory findings as summarized below:

- Type 1 diabetes is due to autoimmune b-cell destruction, usually leading to absolute insulin deficiency, including latent autoimmune diabetes of adulthood while type 2 diabetes is due to a non-autoimmune progressive loss of adequate b-cell insulin secretion frequently on the background of insulin resistance.
- Children with type 1 diabetes often present with the hallmark symptoms of polyuria/polydipsia, and approximately half present with diabetic ketoacidosis (DKA).
- The onset of type 1 diabetes may be more variable in adults; they may not present with the classic symptoms seen in children and may progress to insulin replacement more slowly.
- The features most useful in determination of type 1 diabetes include younger age at diagnosis (< 35 years) with lower BMI (< 25 kg/m^2), unintentional weight loss, ketoacidosis, and plasma glucose > 360 mg/dL at presentation.
- Three distinct stages of type 1 diabetes have been identified:
  - Stage 1:
    - Characteristics: Autoimmunity, normoglycemia, presymptomatic
    - Diagnostic Criteria: Multiple islet autoantibodies, no dysglycemia
  - Stage 2:
    - Characteristics: Autoimmunity, dysglycemia, presymptomatic
    - Diagnostic Criteria:
      - Islet autoantibodies (usually multiple)
      - Dysglycemia
        - Fasting plasma glucose 100-125 mg/dL
        - 2-hour post prandial plasma glucose 140-199 mg/dL
        - A1C 5.7-6.4% or ≥ 10% increase in A1C
  - Stage 3:
    - Characteristics: Autoimmunity, overt hyperglycemia, symptomatic
    - Diagnostic Criteria: Autoantibodies may become absent, diabetes by standard criteria

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Tzield is a CD3-directed antibody indicated to delay the onset of Stage 3 type 1 diabetes (T1D) in adults and pediatric patients aged 1 year of age or older with Stage 2 T1D.

It is also indicated to delay the decline in endogenous insulin production in pediatric patients aged 8 to 17 years recently diagnosed with Stage 3 T1D. This indication is approved under accelerated approval based on evidence of reduced C-peptide decline. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

Limitations of Use

There is limited evidence of safety and effectiveness in patients aged 45 years and older with Stage 2 T1D. Tzield is not effective as a disease modifying therapy in non-autoimmune dysglycemic conditions.

References

1. Tzield® [package insert]. Morristown, NJ: Provention Bio Inc.; June 2026.
2. Herold KC, Bundy BN, Long SA, et al. An Anti-CD3 Antibody, Teplizumab, in Relatives at Risk for Type 1 Diabetes n Engl J Med. 2019;381(7):603-613.
3. Gitelman SE, Simmons K, Sherr JL, et al. Safety and pharmacokinetics of teplizumab in children less than 8 years of age with stage 2 type 1 diabetes. Diabetologia. 2026;69(2):330-342.
4. Ramos EL, Dayan CM, Chatenoud L, et al. Teplizumab and β-Cell Function in Newly Diagnosed Type 1 Diabetes. n Engl J Med. 2023;389(23):2151-2161.

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5. American Diabetes Association Professional Practice Committee for Diabetes. 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes-2026. Diabetes Care. 2026;49(Supplement_1):S27-S49.

Policy History/Revision Information

Date	Summary of Changes
10/01/2026	**Coverage Rationale** ***Delay Onset of Stage 3 Type 1 Diabetes (T1D) in Adult and Pediatric Patients Aged 1 Year and Older with Stage 2 T1D*** • Replaced language indicating: ○ "Tzield, *administered as a one-time 14-day course of therapy*, is proven to delay the onset of stage 3 type 1 diabetes in pediatric and adult patients that meet the [listed] criteria" with "Tzield is proven to delay the onset of stage 3 T1D in pediatric and adult patients *with stage 2 T1D* when all of the [listed] criteria are met" ○ "Tzield is medically necessary when all of the [listed] criteria are met" with "Tzield is medically necessary *to delay the onset of stage 3 T1D in pediatric and adult patients with stage 2 T1D* when all of the [listed] criteria are met" • Revised coverage criteria: Proven ○ Replaced criterion requiring: ▪ "Clinical history of patient does not suggest type 2 diabetes (T2D)" with "clinical history of patient does not suggest *insulin resistance due to obesity*, T2D, *or dysglycemia due to other forms of diabetes [e.g., genetic forms of diabetes, maturity-onset diabetes of the young (MODY), latent autoimmune diabetes in adults (LADA), diabetes secondary to medications or surgery]*" ▪ "Authorization will be issued for no more than *14 doses*" with "authorization will be issued for no more than *one 14-dose treatment course per lifetime*" Medically Necessary ○ Added criterion requiring clinical history of patient does not suggest insulin resistance due to obesity, type 2 diabetes (T2D), or dysglycemia due to other forms of diabetes [e.g., genetic forms of diabetes, maturity-onset diabetes of the young (MODY), latent autoimmune diabetes in adults (LADA), diabetes secondary to medications or surgery] ○ Removed criterion requiring diagnosis of T2D has been ruled out ○ Replaced criterion requiring "authorization will be issued for no more than one treatment course *(i.e., 14 doses)* per lifetime" with "authorization will be issued for no more than one *14-dose* treatment course per lifetime" ***Delay Decline in Beta Cell Function in Pediatric Patients Aged 8 to 17 Years with Recently Diagnosed Stage 3 T1D*** • Added language to indicate: ○ Tzield is proven to delay the decline in beta cell function in pediatric patients with recently diagnosed stage 3 T1D when all of the following criteria are met: ▪ Patient is aged 8 to 17 years ▪ Recent diagnosis (i.e., within the last 8 weeks) of stage 3 T1D ▪ Diagnosis of stage 3 T1D confirmed by all of the following: – Presence of at least one positive pancreatic islet cell autoantibody – Peak C-peptide ≥ 0.2 pmol/mL on a mixed-meal tolerance test (MMTT) – Clinical history of patient does not suggest insulin resistance due to obesity, T2D, or dysglycemia due to other forms of diabetes (e.g., genetic forms of diabetes, MODY, LADA, diabetes secondary to medications or surgery) ▪ Dosing is in accordance with the U.S. Food and Drug Administration (FDA)–approved labeling ▪ Patient has not been previously treated with Tzield ▪ Authorization will be issued for no more than two 12-dose treatment courses per lifetime ○ Tzield is medically necessary to delay the decline in beta cell function in pediatric patients with recently diagnosed stage 3 T1D when all of the following criteria are met: ▪ Patient is aged 8 to 17 years ▪ Recent diagnosis (i.e., within the last 8 weeks) of stage 3 T1D ▪ Diagnosis of stage 3 T1D confirmed by all of the following:

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Date	Summary of Changes
	– Presence of at least one of the following pancreatic islet autoantibodies: • 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) – Peak C-peptide ≥ 0.2 pmol/mL on a MMTT – Clinical history of patient does not suggest insulin resistance due to obesity, T2D, or dysglycemia due to other forms of diabetes (e.g., genetic forms of diabetes, MODY, LADA, diabetes secondary to medications or surgery) ▪ Prescribed by or in consultation with an endocrinologist ▪ Dosing is in accordance with the FDA-approved labeling ▪ Patient has not been previously treated with Tzield ▪ Authorization will be issued for no more than two 12-dose treatment courses per lifetime **Applicable Codes** • Added ICD-10 diagnosis codes E10.10, E10.11, E10.21, E10.22, E10.29, E10.311, E10.319, E10.3211, E10.3212, E10.3213, E10.3219, E10.3291, E10.3292, E10.3293, E10.3299, E10.3311, E10.3312, E10.3313, E10.3319, E10.3391, E10.3392, E10.3393, E10.3399, E10.3411, E10.3412, E10.3413, E10.3419, E10.3491, E10.3492, E10.3493, E10.3499, E10.3511, E10.3512, E10.3513, E10.3519, E10.3521, E10.3522, E10.3523, E10.3529, E10.3531, E10.3532, E10.3533, E10.3539, E10.3541, E10.3542, E10.3543, E10.3549, E10.3551, E10.3552, E10.3553, E10.3559, E10.3591, E10.3592, E10.3593, E10.3599, E10.36, E10.37X1, E10.37X2, E10.37X3, E10.37X9, E10.39, E10.40, E10.41, E10.42, E10.43, E10.44, E10.49, E10.51, E10.52, E10.59, E10.610, E10.618, E10.620, E10.621, E10.622, E10.628, E10.630, E10.638, E10.641, E10.649, E10.65, E10.69, E10.8, E10.9, E10.A0, E10.A1, and E10.A2 • Removed ICD-10 diagnosis codes E10.8 and E10.9 **Supporting Information** • Updated *Clinical Evidence*, *FDA*, and *References* sections to reflect the most current information • Archived previous policy version 2026D0117I

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its policies and guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

This Medical Benefit Drug Policy may also be applied to Medicare Advantage plans in certain instances. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS allows a Medicare Advantage Organization (MAO) to create its own coverage determinations, using objective evidence-based rationale relying on authoritative evidence (Medicare IOM Pub. No. 100-16, Ch. 4, §90.5).

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

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