# FOCUS ON TYPE 1 DIABETES

This resource provides practicing pharmacists with evidence-based guidance to support the early identification, risk assessment, and prevention of Type 1 Diabetes (T1D). It reviews the pathophysiology, clinical presentation, and epidemiology of T1D, along with recommended screening approaches for at-risk individuals. This resource also outlines the efficacy and safety of teplizumab to delay disease progression.

## Introduction

T1D accounts for 5% to 10% of all diabetes cases. The incidence of T1D is increasing at an estimated rate of 2% to 5% annually, suggesting that changes in environmental exposures may be contributing to this trend. In the United States, the lifetime risk of developing T1D is estimated to be approximately 1 in 300.[1]

## Pathophysiology and Epidemiology

T1D is an autoimmune disease characterized by the destruction of pancreatic ß cells, resulting in absolute insulin deficiency.[2] This autoimmune process is mediated by autoreactive T lymphocytes and typically involves the presence of multiple islet autoantibodies (e.g., glutamic acid decarboxylase antibodies [GADA], insulin autoantibodies [IAA], insulinoma-associated antigen-2 autoantibodies [IA-2A], zinc transporter 8 autoantibodies [ZnT8A]), which are detectable in approximately 90% of individuals at diagnosis.[1] T1D is an autoimmune disease that is currently not preventable or curable and eventually requires lifelong insulin dependence owing to a progressive loss of functional ß cell mass over time.[3]

## Risk Factor and Genetic Predisposition

Genetic predisposition plays a significant role in the risk of developing T1D. Key genetic markers associated with increased risk include human leukocyte antigen (HLA) class II alleles, particularly the DR and DQ haplotypes on chromosome 6 and polymorphisms in the insulin gene region and other immune-regulatory genes.[1] Despite the presence of these markers in 30% to 50% of individuals with T1D, genetic risk alone does not determine disease development.[1] In the general population, the risk is approximately 1 in 300. However, this risk increases substantially among first-degree relatives to approximately 1 in 20. More specific familial risk data include a 1 in 40 chance for offspring of mothers with T1D, 1 in 15 for offspring of fathers, 1 in 12 to 1 in 35 for siblings, 1 in 4 for HLA-identical siblings, and 1 in 3 for monozygotic twins.[2,4]

Environmental factors that may influence disease onset include viral infections (e.g., coxsackievirus, rubella), early nutritional exposures (e.g., cow's milk protein), seasonal variation, and exposure to environmental toxins.[4]

## Clinical Presentation

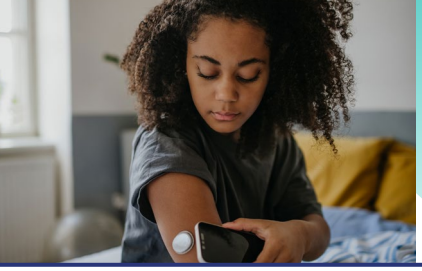
Individuals with T1D often present with classic symptoms of hyperglycemia, including excessive thirst (polydipsia), frequent urination (polyuria), increased hunger (polyphagia), unintended weight loss, and fatigue.[2] In many cases, diagnosis occurs during an episode of diabetic ketoacidosis (DKA), which is observed in 25% to 62% of new cases.[5] DKA can have long-term health consequences, including changes in brain and growth development in children and adolescents; a negative impact on attention span, cognitive function, and memory; and difficulty managing blood glucose levels, increasing the risk of future DKA occurrences.[6,7]

Disease progression is categorized into three stages (Table 1): stage 1 involves the presence of islet autoantibodies with normal blood glucose levels and no symptoms; stage 2 includes the development of abnormal glucose metabolism (dysglycemia) but remains asymptomatic; and stage 3 is marked by symptomatic hyperglycemia meeting diagnostic thresholds for diabetes.[8] Upon diagnosis of stage 3, individuals require immediate initiation of insulin therapy, regular blood glucose monitoring, and significant lifestyle adjustments, which can be burdensome for patients and families.[2]

**Table 1. Glycemia Staging Criteria[2]**

| Measure | Stage 1: Normoglycemia | Stage 2: Dysglycemia | Stage 3: Clinical Diabetes |
|---|---|---|---|
| Fasting plasma glucose | <100 mg/dL | IFG: 100–125 mg/dL | ≥126 mg/dL |
| 2-hour plasma glucose during OGTT | <140 mg/dL | IGT: 140–199 mg/dL | ≥200 mg/dL |
| A1C | <5.7% | 5.7%–6.4% | ≥6.5% |
| Random plasma glucose (in patients with hyperglycemic crisis or classic symptoms of hyperglycemia) | | | ≥200 mg/dL |

Abbreviations: A1C = hemoglobin A1C; IFG = impaired fasting glucose; IGT = impaired glucose tolerance; OGTT = oral glucose tolerance test.



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## Early Detection and Screening

Early detection through screening is critical to improving outcomes and reducing complications such as DKA.[5] Screening (Table 2) is recommended particularly for individuals with a family history of T1D or other autoimmune diseases. Screening protocols include testing for islet autoantibodies (e.g., GADA, IA-2A, ZnT8A, IAA) and monitoring glycemic parameters such as fasting plasma glucose, oral glucose tolerance tests, and hemoglobin A1C levels. Programs such as TrialNet and the Autoimmunity Screening for Kids (ASK) offer structured pathways for identifying at-risk individuals, especially first-degree relatives of those with T1D.[2,3]

Clinical guidelines issued by the American Diabetes Association (ADA) recommend T1D-related autoantibody testing in:[9]

- Individuals with a family history of T1D.
- Individuals with a known elevated genetic risk, especially those with certain autoimmune diseases.
  - Autoimmune diseases that may suggest an elevated genetic risk include autoimmune thyroid disorders and celiac disease.
- Adults with phenotypic risk factors that overlap with those for T1D (e.g., younger age at diagnosis, unintentional weight loss, ketoacidosis, short time to insulin treatment).

The presence of multiple autoantibodies is highly predictive of disease progression, and confirmatory testing is advised if only one autoantibody is detected. In addition to identifying risk, early screening enables health care professionals to educate patients and families, support emotional preparedness, and offer timely interventions.[9]

**Table 2. Screening Options for Type 1 Diabetes[10]**

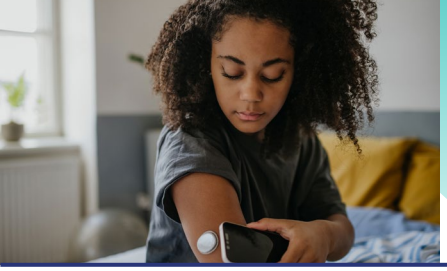
| Where to Screen | Type of Test | Cost | Autoantibodies Tested |
|---|---|---|---|
| Doctor's office or clinical lab (e.g., Labcorp, Quest Diagnostics) | Blood draw | Most insurance plans cover some or all of the cost | Varies by provider and lab (e.g., GADA, IA-2A, IAA, ZnT84, ICA) |
| Type 1 diabetes Screening Central<br><br>via screenfortype1.com | Blood draw or finger stick | Variable based on selected services | Varies depending on method (e.g., GADA, IA-2A, IAA, ZnT84) |
| Autoimmunity Screening for Kids (ASK Program) via AskHealth.org | Blood draw or finger stick | Free for all U.S. residents aged ≥1 year, with or without a family history of diabetes | Varies depending on method (e.g., GADA, IA-2A, IAA, ZnT84) |
| Online ordering via diagnostic vendors (e.g., Enable Biosciences) | Finger stick | Most insurance plans cover some or all of the cost | Varies (e.g., GADA, IA-2A, IAA) |
| TrialNet (trialnet.org/participate) | Blood draw or finger stick | Free for individuals with a first-degree relative with T1D | Comprehensive panel: GADA, IA-2A, IAA, ZnT8A, and ICA |

Abbreviations: GADA = glutamic acid decarboxylase antibodies; IA-2A = insulinoma-associated antigen-2 autoantibodies; IAA = insulin autoantibodies; ICA = islet cell antibodies; T1D = T1D; ZnT8A = zinc transporter 8 autoantibodies.

## Prevention

Teplizumab is a humanized anti-CD3 monoclonal antibody that has been shown to delay the onset of clinical T1D in high-risk individuals.[5] Teplizumab modulates the immune system by binding to the CD3 receptor on T lymphocytes, reducing the activity of autoreactive cells while promoting regulatory T-cell function. Teplizumab is indicated for delaying the onset of stage 3 T1D in individuals aged 8 years and older who are identified as having stage 2 disease.[11] This highlights the clinical importance of identifying individuals in stage 1 or stage 2, prior to the onset of symptoms, when they may be eligible for disease-modifying treatment such as teplizumab to delay progression and reduce the risk of acute complications. Teplizumab is administered as a 14-day I.V. infusion following a weight-based dose escalation schedule.[11]

The dosing regimen is based on body surface area and involves a gradual increase over the course of treatment: 65 μg/m$^2$ on day 1; 125 μg/m$^2$ on day 2; 250 μg/m$^2$ on day 3; 500 μg/m$^2$ on day 4; and 1,030 μg/m$^2$ daily on days 5 through 14. Teplizumab is supplied as a 2 mg/2 mL clear, colorless solution in a single-dose vial.[12] The product must be diluted prior to use, and each infusion should begin within 2 hours of preparation and be completed within 4 hours. Premedication with antipyretics, antihistamines, or antiemetics may be considered to mitigate the risk of infusion-related adverse reactions, such as cytokine release syndrome. Required pre-treatment tests include a complete blood count and liver function tests (alanine aminotransferase [ALT], aspartate aminotransferase [AST], bilirubin). Treatment with teplizumab is contraindicated if any of the following laboratory abnormalities





are present: absolute lymphocyte count <1,000 cells/µL, hemoglobin <10 g/dL, platelet count <150,000/µL, absolute neutrophil count <1,500/µL, ALT or AST >2 times the upper limit of normal (ULN), or total bilirubin >1.5 times ULN.[12] In addition, patients with active or chronic infections (excluding localized skin infections) or who test positive for Epstein-Barr virus or cytomegalovirus should not receive teplizumab. Live-attenuated vaccines must be administered at least 8 weeks prior to treatment or 52 weeks after treatment completion. Inactivated or mRNA vaccines should be given at least 2 weeks before or 6 weeks after therapy. Proper patient selection and monitoring are essential to ensure safety and optimize outcomes.[12]

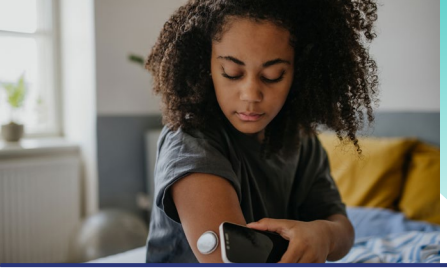
The landmark TN-10 clinical trial demonstrated that a single 14-day course of teplizumab delayed the progression from stage 2 to stage 3 T1D by a median of 48.4 months, compared with 24.4 months in the placebo group. This represents a 59% reduction in the risk of disease progression (hazard ratio: 0.41, $P = 0.0066$).[12] The ADA Standards of Care (2025) recommend that teplizumab be considered for patients aged 8 years or older with stage 2 T1D, following appropriate screening and risk assessment.[9] From a safety standpoint, teplizumab is generally well tolerated but is associated with several potential adverse effects. The most common include lymphopenia (73%), rash (36%), and leukopenia (21%). Serious adverse events, such as cytokine release syndrome and infections (e.g., gastroenteritis, pneumonia, cellulitis), occur less frequently but warrant close monitoring.[11]

## Patient-Facing Resources

- American Association of Clinical Endocrinology (AACE): Provides accessible forums for connection and shared experiences.
- American Academy of Pediatrics (AAP) – Type 1 Diabetes in Children: Features parent-focused articles and videos available in English and Spanish.
- American Diabetes Association (ADA) – Patient Resources: Provides tools, advocacy information, and links to support groups.
- Association of Diabetes Care & Education Specialists (ADCES): Includes blood glucose monitoring tools and diabetes self-management education and support resources.
- Beyond Type 1 – Thrive: Delivers community-based education, virtual events, and support networks.
- Breakthrough T1D: Organizes family-friendly engagement and advocacy events across the country.
- Centers for Disease Control and Prevention (CDC) – National Diabetes Education Program: Offers culturally tailored educational materials and ongoing support.
- DiaTribe: Provides evidence-based, accessible information on diabetes management, lifestyle strategies, and emerging technologies.
- Take Control of Your Diabetes (TCOYD): Hosts educational programs and interactive events for individuals living with diabetes.

## Communicating with Patients

Pharmacists are uniquely positioned to support early identification and management of T1D. The approaches in Table 3 can help guide conversations with patients and caregivers, promote awareness, and improve understanding of T1D in the community.



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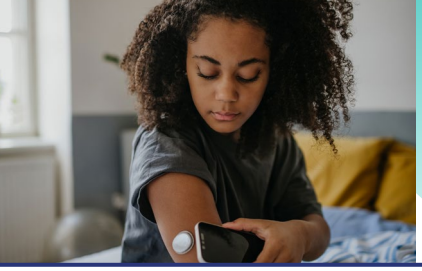
| Table 3. Conversation Starters | |
|---|---|
| Did you know that T1D is an autoimmune condition and not caused by diet or weight? | T1D is not caused by sugar consumption, poor diet, or lifestyle. It occurs when the immune system mistakenly attacks the insulin-producing ß cells in the pancreas. As a result, the body produces little or no insulin, a hormone essential for glucose metabolism. Explaining this distinction helps reduce stigma and guilt that families or patients may feel, particularly when a child is newly diagnosed.[1,2,3,4] |
| Has anyone in your family ever been diagnosed with T1D? | Family history is a known risk factor for T1D. Siblings and children of people with T1D have an increased risk due to genetic predisposition.[1]<br><br>Although most people with T1D have no family history, identifying those at higher risk may prompt early symptom awareness or even autoantibody testing in research or specialist settings.[1,2]<br><br>When a primary family member is diagnosed, information on available screening options should be provided, such as autoantibody testing, and support should be given to families to understand the benefits of early identification. Early-stage diagnosis may allow eligibility for disease-modifying therapies such as teplizumab, which can delay the onset of symptomatic disease. Additionally, addressing concerns about diagnosis through clear, empathetic communication may help reduce fear and promote timely action.[9,11,12] |
| Would you like help understanding the difference between T1D and T2D? | Type 1 diabetes, sometimes referred to as T1D, is an autoimmune condition where the body's immune system mistakenly attacks and destroys the insulin-producing ß cells in the pancreas.[2]<br><br>T1D usually develops in children, adolescents, or young adults, but it can occur at any age. The exact cause is unknown, but it's believed to involve genetic predisposition and environmental triggers.[2]<br><br>Type 2 diabetes, also called T2D, is primarily characterized by insulin resistance, where the body's cells don't respond effectively to insulin. Although insulin is initially produced, the pancreas becomes unable to maintain adequate levels to overcome resistance.[2]<br><br>T2D is most common in adults over 40, but it is increasing in younger people due to obesity and sedentary lifestyles.[2] |
| Living with T1D means daily routines, but there are lots of tools to help. Want to see a few options? | This opens a supportive discussion about self-management technologies, such as:[13]<br>▪ Continuous glucose monitors<br>▪ Insulin pumps or pens<br>▪ Mobile apps for carb counting or glucose tracking<br><br>Demonstrating or recommending tools empowers patients and caregivers, improves adherence, and reduces the daily burden of care.[13] |
| Have you heard of any support groups or online resources? I can help point you to a few. | Support groups provide emotional reassurance, community learning, and encouragement, especially for newly diagnosed patients and families. Organizations like DiabetesSisters, American Diabetes Association, Beyond Type 1 and Beyond Type 2, Defeat Diabetes, and Breakthrough T1D all offer national and local programs that can help direct patients to resources and support groups.<br><br>Additionally, patients may speak with their local diabetes education team to identify in-person support options if preferred. These connections can help patients and caregivers build resilience and gain practical, lived-experience insights into daily T1D management.[9] |
| Have you ever considered screening for T1D before symptoms start? | Screening for T1D autoantibodies in high-risk individuals (such as first-degree relatives) can identify those at risk before clinical onset. Early detection enables proactive monitoring and, where eligible, participation in research or preventive treatment programs.[1,9] |
| There's now a medication that may delay the onset of T1D. Would you like to hear about it? | Teplizumab (Tzield) is the first treatment approved by FDA to delay the onset of stage 3 T1D in patients aged 8 years and older with stage 2 T1D. Teplizumab is ideal for use in screened, high-risk individuals.[11,12] |



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