

Health Technology Briefing

October 2024

Tirzepatide for treating type 2 diabetes in children and adolescents aged 10 to 18 years

Company/Developer

Eli Lilly and Company Ltd

New Active Substance

Significant Licence Extension (SLE)

NIHRI ID: 34863

NICE ID: Not Available

UKPS ID: Not Available

Licensing and Market Availability Plans

Currently in phase III clinical development.

Summary

Tirzepatide is currently in clinical development for treating type 2 diabetes (T2D) in children and adolescents aged 10 to 18 years when their conditions are not being controlled with metformin and/or insulin. T2D is a lifelong condition where the body's cells become resistant to, or stop producing enough insulin, a hormone that helps to control the levels of glucose (sugar) in the blood. T2D is increasingly seen in younger people who are at a much higher risk of developing diabetes complications such as heart disease or damage to the kidneys, eyes or nerves, compared to older adults. Symptoms of T2D often include increased thirst, frequent urination, and fatigue. Some current treatment options for younger people have produced temporary therapeutic effect or the need for frequent dose adjustments which could result in poor adherence, hence the need for more effective longer acting therapies for this age group.

Tirzepatide is a long-acting medicine that acts in the same way as hormones produced in the gut and bind to specific receptors (targets) in the body, such as, among others, the pancreas and brain. This increases the amount of insulin that the pancreas releases in response to food and helps lower blood glucose levels in people with T2D. Tirzepatide is administered by weekly subcutaneous (under the skin) injections. If licensed, tirzepatide would provide an additional treatment option for patients aged 10 to 18 years with T2D that is inadequately controlled with metformin and/or insulin.

Proposed Indication

Treatment of type 2 diabetes in paediatric and adolescent populations aged 10 to 18 years whose conditions are inadequately controlled with metformin or basal insulin or both.¹

Technology

Description

Tirzepatide (LY3298176; Mounjaro) is a long-acting dual glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptor agonist². Both receptors are present on the pancreatic α and β endocrine cells, heart, vasculature, immune cells (leukocytes), gut and kidney, with GIP receptors also presenting on adipocytes. Tirzepatide lowers body weight and body fat mass by decreased food intake through the regulation of appetite and modulation of fat utilization. Tirzepatide also improves glycaemic control by lowering fasting and postprandial glucose concentrations in patients with type 2 diabetes through several mechanisms. It has also been shown to increase pancreatic β -cell glucose sensitivity as it enhances first- and second-phase insulin secretion in a glucose dependent manner³.

Tirzepatide is currently in clinical development for the treatment of type 2 diabetes mellitus in paediatric and adolescent populations aged 10 to 18 years inadequately controlled with metformin or basal insulin or both. In the phase III clinical trial (SURPASS-PEDS, NCT05260021) participants receive 5 mg or 10 mg tirzepatide through a weekly subcutaneous (SC) injection starting with a low dose then increased to a higher dose every four weeks until maintenance dose level is reached.^{1,4}

Key Innovation

Despite adolescent type 2 diabetes becoming more prevalent there are currently fewer glucose-lowering treatment options that have been approved for use in the treatment of adolescent type 2 diabetes in the UK when compared to adult populations.⁵ Many current treatments for type 2 diabetes have produced temporary therapeutic effects or the need for frequent dose adjustments.⁵

In a previous phase III study (NCT03987919), the glycated haemoglobin level target of less than 5.7% (normoglycaemia) was met in 27 to 46% of the patients who received tirzepatide.^{6,7} In addition, many patients who received tirzepatide were noted to have an improved lipid profile as well as improved blood pressure, biomarkers of insulin sensitivity, and liver-enzyme levels.⁶ Tirzepatide is approved for the treatment of adults with insufficiently controlled type 2 diabetes and provides an alternative treatment option in cases where metformin is considered inappropriate.³

If licensed, tirzepatide will offer an additional treatment option for children and adolescents aged 10 to 18 years with type 2 diabetes, following previous treatment with metformin and/or basal insulin.

Regulatory & Development Status

Tirzepatide has Marketing Authorisation in the EU/UK for the following indications:³

- treatment of adults with insufficiently controlled type 2 diabetes as an adjunct to diet and exercise:
 - as monotherapy when metformin is considered inappropriate due to intolerance or contraindications
 - in addition to other medicinal products for the treatment of diabetes
- for weight management, including weight loss and weight maintenance, as an adjunct to a reduced-calorie diet and increased physical activity in obese (Body Mass Index, BMI ≥ 30 kg/ m²) or overweight (BMI ≥ 27 kg/m² to < 30 kg/m²) adults in the presence of at least one weight-related

comorbid condition (for example, hypertension, dyslipidaemia, obstructive sleep apnoea, cardiovascular disease, prediabetes, or type 2 diabetes)

Tirzepatide is also in phase II and III clinical development for the treatment obesity.⁸

Patient Group

Disease Area and Clinical Need

Type 2 diabetes is a lifelong condition that develops when the cells of the body become resistant to insulin, or the pancreas stops producing enough insulin.⁹ Insulin is a hormone produced in the pancreas that helps to regulate the levels of glucose in the blood.⁹ The symptoms of type 2 diabetes often develop gradually over time and commonly include; increased thirst, frequent urination, unintended weight loss, fatigue, blurred vision, slow healing of cuts or wounds.¹⁰ There are several risk factors associated with type 2 diabetes, including being overweight or obese, an inactive lifestyle, and a family history of type 2 diabetes.¹¹ Developing type 2 diabetes also increases the risk of developing serious problems of the eyes, feet, heart and nerves.¹¹ In the last couple of decades, there has been an increase in the number of children and adolescents being diagnosed and treated for type 2 diabetes.¹² Type 2 diabetes in adolescents has been seen to be more aggressive than in adults, with a higher treatment failure rate and standardised mortality.¹³ Younger people diagnosed with type 2 diabetes are at a much higher risk of developing diabetes complications as the condition is more aggressive compared to older adults. These complications can come on more quickly in children and young adults than in older adults such as a faster rate of deterioration of β -cell function and greater extent of insulin resistance and a decreased response to insulin sensitisers^{5,14}.

In UK, about 35,000 children and young people under the age of 19 years have diabetes, of which about 10% have type 2 diabetes.^{15,16} From a surveillance study conducted between April 2015 and April 2016, the UK incidence of type 2 diabetes was estimated at 0.72 per 100,000 children and young people per year.¹⁶ In 2023-24, in England, there were 219 finished consultant episodes (FCE) for type 2 diabetes (ICD10 code E11) with individuals between 10-17 years of age. This accounted for around 0.34% of all recorded cases, from which it can be estimated that there were around 22 day cases and 962 FCE bed days¹⁷.

Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) recommend the following interventions for children and young people with type 2 diabetes:¹⁸

- Insulin therapy
- Metformin
- Liraglutide
- Dulaglutide
- Empagliflozin
- Dietary and lifestyle changes
- Surgery

Clinical Trial Information

Trial	<p>SURPASS-PEDS; NCT05260021; A Randomised, Double-Blind, Placebo-Controlled, Phase 3 Study With an Open-Label Extension Assessing the Efficacy, Safety, and Pharmacokinetics/Pharmacodynamics of Tirzepatide in Paediatric and Adolescent Participants With Type 2 Diabetes Mellitus Inadequately Controlled With Metformin, or Basal Insulin, or Both</p> <p>Phase III – Active, not recruiting</p> <p>Location(s): Two EU countries, UK, USA and other countries</p> <p>Primary completion date: July 2024</p>
Trial Design	Randomised, double-blinded, parallel assignment
Population	N=99; aged 10 to below 18 years of age with type 2 diabetes, treated with diet and exercise and metformin and/or basal insulin. HbA1c >6.5% to ≤11% and a body weight ≥50 kilogram (kg) 110 pounds and BMI of >85th percentile of the general age and gender-matched population for that country or region
Intervention(s)	Tirzepatide weekly 5 mg or 10 mg SC injection, starting with a low dose then increased to a higher dose every four weeks until maintenance dose level is reached. ⁴
Comparator(s)	Placebo
Outcome(s)	Change from baseline in haemoglobin A1c (HbA1c) [Time frame: Baseline, Week 30]
Results (efficacy)	-
Results (safety)	-

Estimated Cost

Tirzepatide is already marketed in the UK;¹⁹

- a 5mg (8.333mg/ml) solution for injection 2.4ml pre-filled pen costs £92
- a 10mg (16.667mg/ml) solution for injection 2.4ml pre-filled pen costs £107

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Dulaglutide for treating type 2 diabetes (ID1451). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Canagliflozin for treating type 2 diabetes in people 10 to 17 years (TS ID 11888). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Semaglutide for treating type 2 diabetes (ID1450). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Insulin icodec for treating type 2 diabetes (ID6175). Expected May 2025.
- NICE technology appraisal. Empagliflozin in combination therapy for treating type 2 diabetes (TA336). March 2015.

- NICE clinical guideline. Diabetes (type 1 and type 2) in children and young people: diagnosis and management (NG18). August 2015. Last updated: May 2023.
- NICE quality standard. Diabetes in children and young people (QS125). Last updated: March 2022.

NHS England (Policy/Commissioning) Guidance

- NHS England. Action for Diabetes. January 2014.
- NHS England. 2013/14 NHS Standard contract. Paediatric medicine: endocrinology and diabetes. E03/S/e.

Other Guidance

- Scottish Intercollegiate Guidelines Network (SIGN). Pharmacological management of glycaemic control in people with type 2 diabetes. 2017.²⁰
- Scottish Intercollegiate Guidelines Network (SIGN). Management of diabetes. 2017.²¹

Additional Information

Eli Lilly and Company Ltd did not enter information about this technology onto the UK PharmaScan database; the primary source of information for UK horizon scanning organisations on new medicines in development. As a result, the NIHR Innovation Observatory has had to obtain data from other sources. UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective decision making and faster uptake of innovative new medicines for patients who could benefit. We urge pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate and comprehensive information on new medicines.

References

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