

Health Technology Briefing September 2022

Tirzepatide for treating obese or overweight adults

Company/Developer

Eli Lilly and Company Ltd

New Active Substance

Significant Licence Extension (SLE)

NIHRIO ID: 29596

NICE ID: 10641

UKPS ID: 661601

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Tirzepatide is in clinical development for the treatment of obesity or overweight individuals with weight-related comorbidities (e.g., sleep apnoea, cardiovascular disease). Excess weight can place stress on both mental and physical health, leading to complications such as depression, low self-esteem, and increased risk of heart disease, stroke, and type 2 diabetes. Weight can be affected by factors such as diet, physical activity, genetics, and general health conditions, however diet and exercise are the two main contributing factors. Being overweight may be reversible through lifestyle changes such as increased exercise, healthy diet, and a net calorie deficit, along with help through counselling and medication. If weight is not able to be controlled, surgery may be required. Therefore, there is an unmet need for pharmacological therapies that target weight control.

Tirzepatide is a new medicine, given as a subcutaneous (under the skin) injection. Tirzepatide is a type of protein called a peptide, that is created from a naturally occurring protein called glucose-dependent insulinotropic polypeptide (GIP). It can bind to GIP and another peptide, glucagon-like peptide-1 (GLP-1) to exert a positive effect, leading to decrease in food intake, increase in energy expenditure, and weight reduction. If licensed, tirzepatide will offer a new treatment option for people who are obese or are overweight with weight-related comorbidities.

Proposed Indication

For people who are obese or are overweight with weight-related comorbidities.¹

Technology

Description

Tirzepatide (LY3298176; Mounjaro) is a novel peptide molecule derived from the native glucose-dependent insulintropic polypeptide (GIP) sequence with agonist activities at both GIP and glucagon-like peptide-1 (GLP-1) receptors, representing a new class of medicine being studied for obesity treatment.¹⁻³ Tirzepatide has been shown to reduce body weight with additional improvements in metabolic markers including lipids and glucose. It has also demonstrated decreased food intake and increased energy expenditure, resulting in weight reduction.^{2,4}

Tirzepatide is in phase III clinical development (SURMOUNT-1, NCT04184622) for the treatment of adults who are overweight or obese. It is administered by once-weekly subcutaneous (SC) injection in 5mg, 10mg or 15mg doses.¹

Key Innovation

Administrations of 5mg, 10mg or 15mg of tirzepatide once-weekly provides substantial and sustained reductions in body weight. It is the first investigational medicine to deliver more than 20% weight loss on average in a phase III study.^{2,4} Tirzepatide could offer an alternative to bariatric surgery in some individuals.⁵

Regulatory & Development Status

Tirzepatide does not currently have Marketing Authorisation in the EU/UK for any indication.

In July 2022, the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion, recommending the granting of a marketing authorisation for tirzepatide, intended for the treatment of type 2 diabetes mellitus.³

Tirzepatide is also in phase II/III clinical development for:⁶

- Heart failure with preserved ejection fraction
- Type 2 diabetes
- Metabolism and nutrition disorder
- Non-alcoholic steatohepatitis (NASH)
- Sleep apnoea

Patient Group

Disease Area and Clinical Need

Body Mass Index (BMI) is used as a predictor of a healthy weight based on a person's height and weight, but other factors such as age and ethnic origin can influence whether someone is more likely to develop health conditions because of a high BMI. A BMI cannot measure body fat percentage and only determines how much weight a person is carrying based on their current height and weight measurements.^{7,8} People who are overweight are those that measure at a BMI of between 25 and 29.9kg/m², whilst the range for obesity is between 30 and 39.9kg/m² (with morbid obesity exceeding 40kg/m²). BMI is a starting point for estimating if a patient is more likely to be at an unhealthy weight, whether higher or lower than the BMI

range 18.5 and 24.9, however further measures are used to provide a more accurate assessment such as waist size.⁸

There are several factors that can lead to a person becoming overweight, including excess calories, poor nutrition, sedentary lifestyle, genetic conditions such as Prader-Willi syndrome and medical conditions such as Cushing's and hypothyroidism.⁹ Common symptoms of being overweight include breathlessness, increased sweating, tiredness, joint and back pain, and difficulty completing physical activity.¹⁰ Being overweight or obese can lead to increased risk of developing comorbidities such as:^{10,11}

- Cardiovascular disease such as stroke and heart disease
- Type 2 diabetes (T2D)
- Musculoskeletal disorders
- Cancers such as breast and bowel
- Depression

Obesity affects approximately one in four adults in the UK, with most adults in England (2018-19) being overweight or obese (67% of men and 60% women).¹⁰ In England, 2020-21, there were over 1.1 million people admitted to hospital with a diagnosis of obesity (ICD-10 E66), and 5,289 finished consultant episodes (FCE) directly attributed to obesity, resulting in 10,282 FCE bed days and 1,371 day cases.¹² Depending on severity it is estimated that obesity reduces life expectancy by an average of 3 to 10 years. It is estimated that obesity and being overweight contribute to at least 1 in every 13 deaths in Europe.¹⁰

Recommended Treatment Options

Lifestyle interventions, such as a reduced-calorie diet, regular physical activity and weight-loss advice, in conjunction with weight-loss surgery (in cases with severe to morbid obesity) are used for treatment.^{13,14} The National Institute of Health and Care Excellence (NICE) recommends liraglutide for overweight or obese adults.¹⁵

Clinical Trial Information

Trial	SURMOUNT-1; NCT04184622 ; Efficacy and Safety of Tirzepatide Once Weekly in Participants Without Type 2 Diabetes Who Have Obesity or Are Overweight With Weight- Related Comorbidities: A Randomized, Double-Blind, Placebo-Controlled Trial Phase III – Active, not recruiting Location(s) : USA, Argentina, Brazil, and other countries Primary completion date : April 2022
Trial Design	Randomised, double-masked (participant, investigator), parallel assignment.
Population	N= 2539 (actual); aged 18 years and older; Body Mass Index (BMI) $\geq 30\text{kg/m}^2$ or $\geq 27\text{kg/m}^2$ with at least one of the following comorbidities: hypertension, dyslipidaemia, obstructive sleep apnoea, cardiovascular disease; history of at least one unsuccessful dietary effort to lose body weight
Intervention(s)	Experimental arms: 5mg, 10mg or 15mg tirzepatide administered subcutaneously (SC) once a week.
Comparator(s)	Matched placebo.
Outcome(s)	Primary outcomes:

	<ul style="list-style-type: none"> • Percent Change from Baseline in Body Weight [Time Frame: Baseline, Week 72] • Percentage of Participants who Achieve $\geq 5\%$ Body Weight Reduction [Time Frame: Week 72] <p>See trial record for full list of other outcomes.</p>
<p>Results (efficacy)</p>	<p>The percentage of participants who had weight reduction of 5% or more was 85% (95% CI, 82 to 89), 89% (95% CI, 86 to 92), and 91% (95% CI, 88 to 94) with 5 mg, 10 mg, and 15 mg of tirzepatide, respectively, and 35% (95% CI, 30 to 39) with placebo; 50% (95% CI, 46 to 54) and 57% (95% CI, 53 to 61) of participants in the 10-mg and 15-mg groups had a reduction in body weight of 20% or more, as compared with 3% (95% CI, 1 to 5) in the placebo group ($P < 0.001$ for all comparisons with placebo). Improvements in all prespecified cardiometabolic measures were observed with tirzepatide.⁴</p>
<p>Results (safety)</p>	<p>The most common adverse events with tirzepatide were gastrointestinal, and most were mild to moderate in severity, occurring primarily during dose escalation. Adverse events caused treatment discontinuation in 4.3%, 7.1%, 6.2%, and 2.6% of participants receiving 5-mg, 10-mg, and 15-mg tirzepatide doses and placebo, respectively.⁴</p>

Estimated Cost

The cost of tirzepatide was confidential at the time of producing this briefing.

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Semaglutide for managing overweight and obesity (ID3850). Expected publication date: To Be Confirmed.
- NICE technology appraisal. Liraglutide for managing overweight and obesity (TA664). December 2020.
- NICE technology appraisal. Naltrexone–bupropion for managing overweight and obesity (TA494). December 2017.
- NICE guideline. Obstructive sleep apnoea/hypopnoea syndrome and obesity hypoventilation syndrome in over 16s (NG202). August 2021.
- NICE clinical guideline. Obesity prevention (CG43). December 2006. Last updated March 2015.
- NICE clinical guideline. Obesity: identification, assessment and management (CG189). November 2014.
- NICE public health guideline. Obesity: working with local communities (PH42). November 2012. Last updated June 2017.
- NICE guideline. Preventing excess weight gain (NG7). March 2015.
- NICE public health guideline. Weight management: lifestyle services for overweight or obese adults (PH53). May 2014.
- NICE interventional procedures guidance. Laparoscopic gastric plication for the treatment of severe obesity (IPG432). November 2012.

NHS England (Policy/Commissioning) Guidance

- NHS England. Enhanced service specification: Weight management 2021/22. June 2021.
- NHS England. NHS Standard Contract for Severe and Complex Obesity – All Ages (A05/S/a). October 2013.

Other Guidance

- UK Department of Health and Social Care. Tackling obesity: empowering adults and children to live healthier lives. July 2020.¹⁶
- Public Health England. Weight management: guidance for commissioners and providers. June 2017.¹⁷
- European Association for the Study of Obesity. European Guidelines for Obesity Management in Adults. December 2015.¹⁸

Additional Information

References

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