

Health Technology Briefing

October 2023

Semaglutide for treating overweight or obesity with cardiovascular disease

Company/Developer

Novo Nordisk Ltd

New Active Substance

Significant Licence Extension (SLE)

NIHRIO ID: 26956

NICE ID: Not available

UKPS ID: 671841

Licensing and Market Availability Plans

Currently in phase III clinical trial

Summary

Semaglutide is in clinical development for the treatment of overweight or obesity in patients with cardiovascular disease (CVD). Obesity is a long-term (chronic) health condition that progresses over time and is commonly defined by excess body fat (adipose tissue) that may impair health. Obesity is associated with a higher risk of developing serious diseases, including CVD, type 2 diabetes, and cancer. Complex mix of factors like genetic, environmental, and psychological factors can increase a person's risk of obesity. Symptoms of overweight or obesity range from excess abdominal fat, shortness of breath, fatigue, and joint pain. People living with obesity are often faced with several different mental health conditions resulting in a higher risk of depression, poor self-esteem, and issues with body image. Currently, there are very limited effective and durable interventions available to reduce body weight and specifically target the increased cardiovascular risk associated with obesity.

Some formulation of semaglutide can be administered as an injection under the skin and works by reducing body weight and body fat mass through lowered energy intake. Semaglutide binds to and activates the glucagon-like peptide-1 (GLP-1) receptor to increase insulin secretion, lower the amount of glucagon released, delay gastric emptying, and reduce appetite. Semaglutide is used for weight loss in specific patients, and to lower blood sugar levels and reduce the risk of major cardiovascular events such as heart attack. If a license extension is approved, semaglutide will offer an additional treatment option in patients who have overweight or obesity with cardiovascular disease.

Proposed Indication

Treatment of adult patients with overweight or obesity and with prior cardiovascular disease.¹

Technology

Description

Semaglutide (Wegovy) is a Glucagon-like peptide-1 (GLP-1) analogue with 94% sequence homology to human GLP-1. Semaglutide acts as a GLP-1 receptor agonist that selectively binds to and activates the GLP-1 receptor, the target for native GLP-1. GLP-1 is a physiological hormone that has multiple actions in glucose and appetite regulation, and in the cardiovascular system. The glucose and appetite effects are specifically mediated via GLP-1 receptors in the pancreas and the brain. Semaglutide reduces blood glucose in a glucose dependent manner by stimulating insulin secretion and lowering glucagon secretion when blood glucose is high. The mechanism of blood glucose lowering also involves a minor delay in gastric emptying in the early postprandial phase. During hypoglycaemia, semaglutide diminishes insulin secretion and does not impair glucagon secretion. Semaglutide reduces body weight and body fat mass through lowered energy intake, involving an overall reduced appetite. In addition, semaglutide reduces the preference for high fat foods.²

Semaglutide is in a phase III clinical trial (SELECT, NCT03574597) for treatment of adult patients 45 years and above where participants will be injected with semaglutide into a skin fold, in the stomach, thigh or upper arm once a week at the same day of the week (to the extent possible) throughout the trial. Subjects will start semaglutide treatment at 0.24 mg; dose will gradually be increased every 4 weeks up to 2.4 mg.¹

Key Innovation

Cardiovascular disease (CVD) is a major cause of morbidity and mortality. Although it has been widely appreciated that obesity is a major risk factor for CVD, treatments that produce effective, durable weight loss and the impact of weight reduction in reducing cardiovascular risk have been elusive.³ Treatment approaches are changing, however, with renewed interest in using medications for weight management based on improved understanding of food intake and energy balance regulation. GLP-1 is a gut hormone released in response to food intake that acts as a satiety signal, stimulates insulin production in a glucose-dependent manner, inhibits glucagon secretion, and slows gastric emptying. GLP-1 receptor agonists reduce weight, improve glycemia, decrease cardiovascular events in those with diabetes, and may have additional cardioprotective effects.³

If a license extension is approved, semaglutide will provide an additional treatment option for adult patients with overweight or obesity and with prior cardiovascular disease.

Regulatory & Development Status

Semaglutide has Marketing Authorisation in the EU/UK as follows:^{2,4,5}

- Semaglutide (Wegovy) is indicated as an adjunct to a reduced-calorie diet and increased physical activity for weight management, including weight loss and weight maintenance, in adults with an initial Body Mass Index (BMI) of: ≥ 30 kg/m² (obesity), or ≥ 27 kg/m² to < 30 kg/m² (overweight) in the presence of at least one weight-related comorbidity.
- Semaglutide (Wegovy) is indicated as an adjunct to a reduced-calorie diet and increased physical activity for weight management in adolescents ages 12 years and above with obesity* and body weight above 60 kg.

- Semaglutide (Ozempic and Rybelsus) are indicated as monotherapy or in combination treatments, for the treatment of adults with insufficiently controlled type 2 diabetes mellitus to improve glycaemic control as an adjunct to diet and exercise.

Semaglutide is currently in phase II and III clinical trials for several indications, some of which include.⁶

- Type 2 diabetes mellitus
- Peripheral Arterial Disease
- Chronic Kidney Disease
- Alzheimer's disease
- Heart Failure with Preserved Ejection Fraction (HFpEF)
- Non-alcoholic Steatohepatitis

Patient Group

Disease Area and Clinical Need

The term 'obese' describes a person who is very overweight, with a lot of body fat.⁷ A BMI of 30 and above indicates obesity, while a BMI of 25-29.9 indicates overweight.⁷ Obesity is also considered to be an independent risk factor for CVD.⁸ CVD is a general term for conditions affecting the heart or blood vessels. It is usually associated with a build-up of fatty deposits inside the arteries (atherosclerosis) and an increased risk of blood clots.⁹ Obesity is a serious health concern that increases the risk of many other health conditions like type 2 diabetes, coronary heart disease and some types of cancer. Obesity is a complex issue with many causes including genetics. There are also some underlying health conditions that can occasionally contribute to weight gain, such as an underactive thyroid gland (hypothyroidism). Some medicines can also make people more likely to put on weight, including steroids and some medicines for high blood pressure. Living with overweight and obesity can also affect quality of life and contribute to mental health problems, such as depression, and can also affect self-esteem.¹⁰

Obesity is a common problem in the UK that is estimated to affect around one in every four adults.⁷ The Health Survey for England, 2021 estimates that 25.9% of adults in England are obese and a further 37.9% are overweight but not obese.¹¹ Heart and circulatory deaths attributed to excess weight and obesity total around 31,000 every year in the UK. This is equivalent to around 85 deaths each day from heart and circulatory diseases which are attributable to a BMI of 25 or more.¹² In England (2021-22), there were 8,976 finished consultant episodes (FCEs) and 7,876 admissions for obesity (ICD-10 code E66) which resulted in 18,589 FCE bed days and 1,770 day cases.¹³

Recommended Treatment Options

NICE recommends prevention and lifestyle weight management services for adults who are becoming overweight or obese.¹⁴ Drug treatment should only be considered once dietary and physical activity interventions have been started and evaluated, or as part of an integrated approach to weight management.¹⁵

NICE recommends the following treatment options for managing a person who is overweight or obese.¹⁵⁻¹⁸

- Liraglutide 3mg as an adjunct to a reduced-calorie diet and increased physical activity.
- Semaglutide 2.4mg once-weekly subcutaneous injection as an adjunct to a reduced-calorie diet and increased physical activity.
- Orlistat in conjunction with a mildly hypocaloric diet

Clinical Trial Information

Trial	SELECT ; NCT03574597 ; 2017-003380-35 ; Semaglutide Effects on Cardiovascular Outcomes in People With Overweight or Obesity. Phase III - Completed Location(s) : 20 EU countries, UK, Canada, USA, and other countries Primary completion date : June 2023
Trial Design	Randomised, parallel assignment, quadruple masking
Population	N=17,609 (actual); adult patients with overweight or obesity and established CVD; aged 45 years and older.
Intervention(s)	Semaglutide subcutaneous
Comparator(s)	Matched placebo subcutaneous
Outcome(s)	Primary outcome measures: <ul style="list-style-type: none"> Time to first occurrence of a composite endpoint consisting of: cardiovascular (CV) death, non-fatal myocardial infarction, or non-fatal stroke [Time Frame: 0-59 months]
Results (efficacy)	The trial achieved its primary objective by demonstrating a statistically significant and superior reduction in major adverse cardiovascular events (MACE) of 20% for people treated with semaglutide 2.4 mg compared to placebo. ¹⁹
Results (safety)	In the trial, semaglutide 2.4 mg appeared to have a safe and well-tolerated profile in line with previous semaglutide 2.4 mg trials. ¹⁹

Estimated Cost

Semaglutide is already marketed in the UK for the treatment of type 2 diabetes mellitus; the 0.25mg/0.19ml, 0.5mg/0.37ml, and 1mg/0.74ml solution for injection (Ozempic) costs £73.25. 3mg, 7mg and 14mg tablets (Rybelsus) cost £78.48.²⁰ The price of Wegovy (another Semaglutide branded product available in the UK) is not currently known.

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Oral semaglutide for managing overweight and obesity. (ID6188). Expected publication date TBC.
- NICE technology appraisal in development. Tirzepatide for managing overweight and obesity. (ID6179). Expected date: March 2024.
- NICE technology appraisal. Semaglutide for managing overweight and obesity (TA875). September 2023.
- 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 clinical guideline. Obesity prevention (CG43). March 2015.
- NICE clinical guideline. Obesity: identification, assessment, and management (CG189). November 2014.
- NICE quality standard. Obesity: clinical assessment and management (QS127). August 2016.
- NICE quality standard. Obesity in adults: prevention and lifestyle weight management programmes (QS111). January 2016.
- NICE public health guidance. Weight management: lifestyle services for overweight or obese adults (PH53). May 2014.
- NICE public health guidance. Obesity: working with local communities. (PH42). June 2017

NHS England (Policy/Commissioning) Guidance

- NHS England. NHS Standard Contract for Severe and Complex Obesity – All Ages (A05/S/a). October 2013.
- NHS England. Clinical Commissioning Policy: Complex and Specialised Obesity Surgery. NHSCB/A05/P/a. April 2013

Other Guidance

- Yumuk V et al. European Guidelines for Obesity Management in Adults. December 2015.²¹
- Scottish Intercollegiate Guidelines Network. Management of Obesity – A national clinical guideline. 2010.²²

Additional Information

References

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