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Health Technology Briefing
April 2026

Cagrilintide-semaglutide for treating overweight and obesity

Company/Developer	Novo Nordisk Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 38254	NICE ID: Not Available	UKPS ID: 675046

Licensing and Market Availability Plans

Currently in phase II clinical development.

Summary

Cagrilintide-semaglutide is being developed as a treatment for overweight and obesity in adults. Overweight and obesity in adults are typically defined by a body mass index over 25 and 30, respectively. While this is commonly caused by excessive calorie intake, overweight and obesity are complex conditions with many causes, such as genetics. In the UK, about 25% of adults are living with obesity. For many people, lifestyle and behavioural changes alone may not help. There is a need for new treatment options that will allow obese or overweight patients to reach their individual treatment goals to improve their health.

Cagrilintide-semaglutide is a combination of two medicines, cagrilintide and semaglutide, and is injected into the fat under the skin (subcutaneously). Cagrilintide works like a hormone called amylin, while semaglutide mimics a hormone called glucagon-like peptide-1. These are both released after a meal and work by making a person feel full, reducing cravings and releasing insulin – another hormone that regulates blood sugar. Since cagrilintide-semaglutide mimics the action of multiple hormones, it might be particularly effective in weight management therapy. If licensed, cagrilintide-semaglutide will offer an additional treatment option for people with overweight and obesity.

This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.

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Proposed Indication

Treatment of overweight and obesity in adults.[1]

Technology

Description

Cagrilintide-semaglutide (CagriSema) is a combination of analogues of amylin and glucagon-like peptide-1 (GLP-1) being developed for weight management.[2] Cagrilintide is an amylin analogue being developed in combination with the GLP-1 agonist semaglutide to achieve sustained weight loss in persons with overweight and obesity. Amylin, released with insulin from beta cells in the pancreas, induces its satiating effect via both the homoeostatic and hedonic regions of the brain. Semaglutide, a GLP-1 receptor agonist, reduces appetite via GLP-1 receptors in the hypothalamus, reduces glucagon secretion and increases production of insulin, delaying gastric emptying. These separate, but related, mechanisms of action appear to have an additive effect on appetite reduction.[3]

In the phase III trials NCT07357766, NCT07011667, NCT06780449, NCT06388187, NCT06131437 (REDEFINE 1), NCT05567796 and NCT05394519 (REDEFINE 2), participants received subcutaneous cagrilintide-semaglutide once weekly.[1,4-10]

Key Innovation

Currently, lifestyle changes such as increasing exercise and reducing calorie intake are recommended prior to taking weight loss medications. However, for some patients lifestyle changes alone may be ineffective due to physiological, social and environmental factors.[11,12] There is a need for treatment options that will allow people with overweight and obesity to reach their individual treatment goals to improve their health.[13] Given the heterogeneity and complex pathogenesis of overweight and obesity, combination therapy with multiple pathophysiological targets is a logical approach to increasing weight loss response with pharmacotherapy.[3] Cagrilintide, both alone and in combination with semaglutide, has shown promising weight loss in clinical trials. In one study, average bodyweight reduction of 20.4% was observed with semaglutide and cagrilintide in comparison to 3.0% with placebo.[14]

If licensed, cagrilintide-semaglutide would offer an additional treatment option for patients with overweight and obesity.

Regulatory & Development Status

Cagrilintide-semaglutide does not currently have Marketing Authorisation in the EU/UK for any indication.

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Semaglutide currently has Marketing Authorisation in the EU/UK for the following indications:[15]

- as monotherapy for the treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise when metformin is considered inappropriate due to intolerance or contraindications
- in combination with other medicinal products for the treatment of diabetes

Cagrilintide-semaglutide is in phase II/III clinical development for[16]:

- Cardiovascular disease

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- Diabetic peripheral neuropathy
- Diabetes mellitus type 2

Patient Group

Disease Area and Clinical Need

Overweight and obesity are defined as abnormal or excessive fat accumulation that presents a risk to health. For most adults a body mass index (BMI) over 25 is considered overweight, and over 30 is obese, although for those with an Asian, Chinese, Middle Eastern, Black African or African-Caribbean family background a lower BMI score is used (23-27.4 is considered overweight and 27.5 or above is considered obese).[11,17] Obesity and overweight are caused when extra calories, particularly those from foods high in fat and sugar, are stored in the body as fat. In most cases obesity is a multifactorial disease due to obesogenic environments, psychosocial factors and genetic variants.[18] The role of genetic predisposition to obesity has been widely demonstrated, with the approximate heritability of obesity ranging from 40–70%.[19] Living with obesity can cause a number of further problems, including mental health problems such as depression, as well as health conditions including type 2 diabetes, cardiovascular disease, certain cancers, osteoarthritis and sleep apnoea.[11,19]

In the UK, it is estimated that around 1 in 4 adults are living with obesity, and the disease can reduce life expectancy by an average of 3 to 10 years, depending on severity.[11] In England (2024-25), there were 13,126 finished consultant episodes (FCE) and 11,835 admissions for obesity (ICD-10 code E66) which resulted in 23,093 FCE bed days and 2,878 day cases.[20]

Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) recommends prevention and lifestyle weight management services adults who are becoming overweight or obese.[21] Drug treatment should only be considered once dietary and physical activity interventions have been started and evaluated.[22]

NICE recommends the following treatment options for managing overweight or obesity in adults:[23]

- Orlistat
- Liraglutide
- Semaglutide
- Tirzepatide

Clinical Trial Information

Trial	NCT06780449; Long-term Efficacy and Safety of Cagrilintide s.c. 2.4 mg in Combination With Semaglutide s.c. 2.4 mg (CagriSema 2.4 mg/2.4 mg) Once Weekly Versus Placebo in Participants With Obesity **Phase III:** Active, not recruiting **Locations:** 3 EU countries, UK, USA and Canada **Primary completion date:** August 2028
Trial Design	Randomised, parallel assignment, quadruple blind
Population	N=400 (estimated); patients with BMI ≥35; aged 18 and older
Intervention(s)	Subcutaneous cagrilintide-semaglutide

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Comparator(s)	Matched placebo
Outcome(s)	Primary outcome: Relative change in body weight [Time frame: from baseline (week 0) to week 104] See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

Trial	NCT06388187; Efficacy and Safety of Cagrilintide s.c. in Combination With Semaglutide s.c.(CagriSema s.c. 1.0 mg/1.0 mg and 1.7 mg/1.7 mg) Once-weekly in Participants With Overweight or Obesity **Phase III:** Active, not recruiting **Locations:** 2 EU countries, UK, USA and Canada **Primary completion date:** April 2026
Trial Design	Randomised, parallel assignment, quadruple blind
Population	N=300 (estimated); patients with BMI ≥30 or ≥27 with the presence of at least one weight-related comorbidity; aged 18 and older
Intervention(s)	Subcutaneous cagrilintide-semaglutide
Comparator(s)	Matched placebo
Outcome(s)	Primary outcomes: • Relative change in body weight [Time frame: from baseline (week 0) to end of treatment (week 68)] • Achievement of ≥ 5% weight reduction [Time frame: from baseline (week 0) to end of treatment (week 68)] See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

Trial	**REDEFINE 1;** NCT05567796; EudraCT 2020-005435-75; Efficacy and Safety of Cagrilintide s.c. 2.4 Milligram (mg) in Combination With Semaglutide Subcutaneous (s.c). 2.4 mg (CagriSema s.c. 2.4 mg/2.4 mg) Once-weekly in Participants With Overweight or Obesity **Phase III:** Active, not recruiting **Locations:** 10 EU countries, UK, USA, Canada and other countries **Primary Completion Date:** October 2024
Trial Design	Randomised, parallel assignment, quadruple blind
Population	N=3400 (estimated); patients with BMI ≥30 or ≥27 with the presence of at least one weight-related comorbidity; aged 18 and older

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Intervention(s)	Subcutaneous cagrilintide-semaglutide
Comparator(s)	• Active comparator: cagrilintide • Active comparator: semaglutide • Matched placebo
Outcome(s)	Primary outcomes: • Relative change in body weight [Time frame: from baseline (week 0) to end of treatment (week 68)] • Achievement of ≥5% weight reduction [Time frame: from baseline (week 0) to end of treatment (week 68)] See trial record for full list of other outcomes.
Results (efficacy)	The estimated mean percent change in body weight from baseline to week 68 was -20.4% with cagrilintide-semaglutide compared to -3.0% with placebo (estimated difference, -17.3 percentage points; 95% confidence interval: -18.1 to -16.6; P<0.001).[14]
Results (safety)	Gastrointestinal adverse events (affecting 79.6% in the cagrilintide-semaglutide group and 39.9% in the placebo group), including nausea, vomiting, diarrhoea, constipation, or abdominal pain, were mainly transient and mild-to-moderate in severity.[14]

Trial	NCT07011667; Efficacy and Safety of Cagrilintide s.c. in Combination With Semaglutide s.c. (CagriSema s.c.) Once Weekly for Weight Management and Long-term Weight Maintenance in Participants With Obesity **Phase III:** Active, not recruiting **Location:** USA **Primary completion date:** March 2027
Trial Design	Randomised, parallel assignment, quadruple blind
Population	N=609 (actual); patients with BMI ≥30; aged 18 and older
Intervention(s)	Subcutaneous cagrilintide-semaglutide
Comparator(s)	Matched placebo
Outcome(s)	Primary outcome: relative change in body weight [Time frame: from baseline (week 0) to week 80]. See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

Trial	NCT07357766; A Placebo-controlled Comparability Study to Compare Two Presentations of CagriSema in Participants With Overweight or Obesity

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	Phase III: Not yet recruiting **Locations:** 8 EU countries, USA and other countries **Primary completion date:** November 2027
Trial Design	Randomised, parallel assignment, quadruple blind
Population	N=1400 (estimated); patients with BMI ≥30 or ≥27 with the presence of at least one weight-related comorbidity; aged 18 and older
Intervention(s)	Subcutaneous cagrilintide-semaglutide
Comparator(s)	Matched placebo
Outcome(s)	Primary outcome: relative change in body weight [time frame: from baseline (week 0) to end of treatment (week 44)]. See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

Trial	**REDEFINE 2; NCT05394519; EudraCT 2021-005121-24;** Efficacy and Safety of Cagrilintide s.c. 2.4 mg in Combination With Semaglutide s.c. 2.4 mg (CagriSema s.c. 2.4 mg/2.4 mg) Once-weekly in Participants With Overweight or Obesity and Type 2 Diabetes **Phase III:** Completed **Locations:** 5 EU countries, UK, USA, Canada and other countries **Study completion date:** February 2025
Trial Design	Randomised, parallel assignment, quadruple blind
Population	N=1200 (actual); patients with BMI ≥27 and type 2 diabetes mellitus diagnosed at least 180 days before screening; aged 18 and older
Intervention(s)	Subcutaneous cagrilintide-semaglutide
Comparator(s)	Matched placebo
Outcome(s)	Primary outcomes: • Relative change in body weight [Time frame: from baseline (week 0) to end of treatment (week 68)] • Achievement of ≥5% weight reduction [Time frame: from baseline (week 0) to end of treatment (week 68)] See trial record for full list of other outcomes.
Results (efficacy)	The estimated mean change in body weight from baseline to week 68 was -13.7% in the cagrilintide-semaglutide group and -3.4% in the placebo group (estimated difference, -10.4 percentage points; 95% confidence interval: -11.2 to -9.5; P<0.001).[24]

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Results (safety)	Gastrointestinal adverse events were reported by 72.5% of the patients in the cagrilintide-semaglutide group and 34.4% in the placebo group, most of which were transient and mild or moderate in severity.[24]

Trial	NCT06131437; Efficacy and Safety of Cagrilintide 2.4 mg s.c. in Combination With Semaglutide 2.4 mg s.c. (CagriSema s.c. 2.4 mg/2.4 mg) Once-weekly Compared to Tirzepatide 15 mg s.c. Once-weekly in Participants With Obesity **Phase III:** Completed **Location:** USA **Study completion date:** January 2026
Trial Design	Randomised, parallel assignment, open label
Population	N=809 (actual); patients with BMI ≥30; aged 18 and older
Intervention(s)	Subcutaneous cagrilintide-semaglutide
Comparator(s)	Subcutaneous tirzepatide
Outcome(s)	Primary outcome: relative change in body weight [Time frame: from baseline (week 0) to end of treatment (week 84)]. See trial record for full list of other outcomes.
Results (efficacy)	Under the efficacy estimand (the effect if all people adhered to the study treatment), patients treated with cagrilintide-semaglutide achieved a 23.0% weight loss compared with 25.5% in those treated with tirzepatide. Similarly, when evaluating based on the treatment regimen estimand (treatment effect regardless of treatment adherence), the cagrilintide-semaglutide arm achieved a 20.2% weight reduction vs 23.6% in the tirzepatide arm.[25]
Results (safety)	-

Estimated Cost

The cost of cagrilintide-semaglutide is not yet known.

Relevant Guidance

NICE Guidance

- NICE technology appraisal. Tirzepatide for managing overweight and obesity (TA1026). December 2024
- NICE technology appraisal. Semaglutide for managing overweight and obesity (TA875). March 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.

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- NICE guideline in development. Orforglipron for managing overweight and obesity ID6516 (GID-TA11650). Expected date of issue to be confirmed.
- NICE clinical guideline. Overweight and obesity management (NG246). January 2025.
- NICE quality standard. Overweight and obesity management (QS212). August 2025.
- NICE HealthTech guidance. Endoscopic sleeve gastroplasty for obesity (HTG711). February 2024.

NHS England (Policy/Commissioning) Guidance

- NHS England. Enhanced service specification: Weight management 2024/25. March 2024.
- 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

- The European Association for the Study of Obesity. A new framework for the diagnosis, staging and management of obesity in adults. July 2024.[26]
- Obesity Management Task Force of the European Association for the Study of Obesity. European Guidelines for Obesity Management in Adults. December 2015.[27]

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