Health Technology Briefing
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Semaglutide for treating overweight and obesity

Company/Developer	Novo Nordisk Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 33816	NICE TSID: 11784	UKPS ID: 665538

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Semaglutide is in clinical development for the treatment of overweight and obesity in adults. Obesity is a chronic disease and global public health challenge, and the prevalence of obesity is rising in the UK. Obesity increases the risk of developing a range of health conditions such as stroke, hypertension and type 2 diabetes. Obesity can also affect the person's quality of life and lead to psychological problems, such as depression and low self-esteem. Recommendations for treatment include lifestyle changes such as increased exercise, healthy diet and a net calorie deficit, along with help through counselling and medication. Currently existing drug treatments often involve injections as the primary route of administration. Concerns with injection, including pain and fear, have been noted as barriers to administering effective therapies for overweight and obesity, hence the need for more convenient therapy options.

Semaglutide is a medicinal product that acts in the same way as glucagon-like peptide-1 (GLP-1) which is a natural hormone in the body. Semaglutide regulates appetite by increasing a person's feelings of fullness, while reducing their food intake, hunger and cravings. The oral formulation of semaglutide provides a promising therapeutic option for people who have concerns with injection use. If licensed, semaglutide would provide an oral treatment option for adults with obesity or overweight in the presence of at least one weight-related complication.

Proposed Indication

Adults with a BMI of ≥30 kg/m^2 (obesity), or ≥27 kg/m^2 to <30 kg/m^2 (overweight) in the presence of at least one weight-related comorbidity.[1]

Technology

Description

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. 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. 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 clinical development for the treatment of adult patients with obesity or overweight in the presence of at least one weight-related complication. In the phase III clinical trial (OASIS 1; NCT05035095), participants will receive once daily semaglutide tablets in a dose escalating manner for 68 weeks: 3 mg (week 1-4), 7 mg (week 5-8), 14 mg (week 9-12), 25 mg (week 13-16) and 50 mg (week 17-68).[1]

Key Innovation

GLP-1 receptor agonists such as semaglutide are a class of antidiabetic medications that have shown promise in encouraging glycaemic control and promoting weight loss in patients with or without type 2 diabetes. Another significant benefit of semaglutide is that it can be used for long-term management of weight, leading to improvement in patients' weight loss-related outcomes and quality of life.[3]

Despite the abundant complementary benefits of GLP-1 receptor agonists, their subcutaneous administration limits their usage amongst patients. The co-formulation of oral semaglutide with an absorption enhancer has shown to increase its bioavailability and has made its oral absorption possible. With the introduction of an oral option to this drug class, such as oral semaglutide, there is potential to eliminate the limitation of subcutaneous administration providing a more convenient therapeutic option for patients.[4] If licensed, oral semaglutide would provide a novel treatment option for adult patients who are overweight or living with obesity.

Regulatory & Development Status

Semaglutide has Marketing Authorisation in the EU/UK for the following indications:[2,5,6]

- 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.
- as monotherapy or in combination, 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:[7]

- Type 2 Diabetes Mellitus

- Myocardial injury
- Atherosclerosis
- Chronic Kidney Disease
- Non-alcoholic fatty liver disease (NAFLD)

Patient Group

Disease Area and Clinical Need

The term 'obese' describes a person who is very overweight, with abnormal or excessive fat accumulation that presents a risk to health.[8] Obesity is generally caused by eating too much and moving too little. If you consume high amounts of energy, particularly fat and sugars, but do not burn off the energy through exercise and physical activity, much of the surplus energy will be stored by the body as fat.[9] There are many ways in which a person's health in relation to their weight can be classified, but the most widely used method is body mass index (BMI). BMI is a measure of whether a person is a healthy weight for their height. Obesity causes obvious physical changes and is a major risk factor for a number of serious and potentially life-threatening conditions, such as type 2 diabetes, coronary heart disease, some types of cancer (such as breast cancer and bowel cancer) and stroke. Obesity can also affect the person's quality of life and lead to psychological problems, such as depression and low self-esteem.[10]

Obesity is a common problem in the UK that is estimated to affect around one in every four adults.[10] In England, in 2018-2019, the majority of adults (67% of men and 60% of women) were overweight or obese.[11] In England (2020-21), there were 5,289 finished consultant episodes (FCE) and 4,487 admissions for obesity (ICD-10 code E66) which resulted in 10,282 FCE bed days and 1,371 day cases.[12]

Recommended Treatment Options

NICE recommends prevention and lifestyle weight management services for adults who are becoming overweight or obese.[13] 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.[14]

NICE recommends the following drug treatment options for managing a person who is overweight or obese:[15,16]

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

Clinical Trial Information

Trial	**OASIS 1,** NCT05035095, 2020-002953-11; Efficacy and Safety of Oral Semaglutide 50 mg Once Daily in Subjects With Overweight or Obesity **Phase III:** Active, not recruiting **Location(s):** Five EU countries, USA, Canada and other countries **Primary completion date:** March 2023
Trial Design	Randomised, parallel assignment, quadruple masking

Population	N = 660 (estimated); adults aged 18 years and older with BMI greater than or equal to 27.0 kg/m^2 with the presence of at least one of the following weight-related complications (treated or untreated): hypertension, dyslipidaemia, obstructive sleep apnoea or cardiovascular disease, or greater than or equal to 30.0 kg/m^2
Intervention(s)	Semaglutide tablets (oral) taken once daily in a dose escalating manner for 68 weeks: 3 mg (weeks 1-4), 7 mg (weeks 5-8), 14 mg (weeks 9-12), 25 mg (weeks 13-16) and 50 mg (weeks 17-68)
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 body weight reduction greater than or equal to 5% (Yes/No) [time frame: at end-of-treatment (week 68)] See trial record for full list of outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

Oral semaglutide is already marketed in the UK; a pack of 30 x 3mg, 30 x 7mg, and 30 x 14mg each cost £78.48.[17]

Relevant Guidance

NICE Guidance

- 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 interventional procedures guidance. Implantation of a duodenal–jejunal bypass sleeve for managing obesity (IPG471). November 2013.
- NICE public health guidance. Weight management: lifestyle services for overweight or obese adults (PH53). May 2014.

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

- UK Department of Health and Social Care. Tackling obesity: empowering adults and children to live healthier lives. July 2020.[18]
- Yumuk V et al. European Guidelines for Obesity Management in Adults. December 2015.[19]
- Scottish Intercollegiate Guidelines Network. Management of Obesity – A national clinical guideline. 2010.[20]

Additional Information

References

1 Clinicaltrials.gov. *Research Study to Investigate How Well Semaglutide Tablets Taken Once Daily Work in People Who Are Overweight or Living With Obesity (OASIS 1) (OASIS 1)*. *Trial ID: NCT05035095*. 2021. Status: Active, not recruiting. Available from: https://clinicaltrials.gov/ct2/show/NCT05035095 [Accessed August 5th 2022].

2 Electronic Medicines Compendium (EMC). *Ozempic 0.25 mg solution for injection in pre-filled pen*. 2021. Available from: https://www.medicines.org.uk/emc/product/9748/smpc#PHARMACOLOGICAL_PROPS [Accessed August 5th 2022].

3 Singh G, Krauthamer M, Bjalme-Evans M. Wegovy (semaglutide): a new weight loss drug for chronic weight management. *Journal of Investigative Medicine*. 2022;70(1):5. Available from: https://doi.org/10.1136/jim-2021-001952.

4 Kim HS, Jung CH. Oral Semaglutide, the First Ingestible Glucagon-Like Peptide-1 Receptor Agonist: Could It Be a Magic Bullet for Type 2 Diabetes? *Int J Mol Sci*. 2021;22(18). Available from: https://doi.org/10.3390/ijms22189936.

5 European Medicines Agency (EMA). *Wegovy*. 2022. Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/wegovy [Accessed August 5th 2022].

6 Electronic Medicines Compendium (EMC). *Rybelsus*. 2020. Available from: https://www.medicines.org.uk/emc/product/11507/smpc [Accessed August 5th 2022].

7 Clinicaltrials.gov. *Search: semaglutide | Recruiting, Not yet recruiting, Active, not recruiting, Completed, Enrolling by invitation Studies | Phase 2, 3*. 2022. Available from: https://clinicaltrials.gov/ct2/results?cond=&term=semaglutide&type=&rslt=&recrs=b&recrs=a&recrs=f&recrs=d&recrs=e&age_v=&gndr=&intr=&titles=&outc=&spons=&lead=&id=&cntry=&state=&city=&dist=&locn=&phase=1&phase=2&rsub=&strd_s=&strd_e=&prcd_s=&prcd_e=&sfpd_s=&sfpd_e=&rfpd_s=&rfpd_e=&lupd_s=&lupd_e=&sort= [Accessed August 5th 2022].

8 World Health Organization (WHO). *Obesity*. Available from: https://www.who.int/health-topics/obesity#tab=tab_1 [Accessed August 5th 2022].

9 NHS UK. *Causes - Obesity*. 2019. Available from: https://www.nhs.uk/conditions/obesity/causes/ [Accessed August 22nd 2022].

10 NHS Inform. *Obesity*. 2021. Available from: https://www.nhsinform.scot/illnesses-and-conditions/nutritional/obesity [Accessed August 5th 2022].
11 NHS Digital. *Statistics on Obesity, Physical Activity and Diet, England, 2020*. 2020. Available from: https://digital.nhs.uk/data-and-information/publications/statistical/statistics-on-obesity-physical-activity-and-diet/england-2020 [Accessed August 5th 2022].
12 NHS Digital. *Hospital Admitted Patient Care Activity 2020-21*. 2021. Available from: https://digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-patient-care-activity/2020-21 [Accessed August 5th 2022].
13 National Institute for Health and Care Excellence (NICE). *Obesity in adults: prevention and lifestyle weight management programmes*. 2016. Available from: https://www.nice.org.uk/guidance/qs111 [Accessed August 5th 2022].
14 National Institute for Health and Care Excellence (NICE). *Obesity: Scenario: Management*. 2022. Available from: https://cks.nice.org.uk/topics/obesity/management/management/#drug-treatment [Accessed August 5th 2022].
15 National Institute for Health and Care Excellence (NICE). *Naltrexone–bupropion for managing overweight and obesity*. 2017. Available from: https://www.nice.org.uk/guidance/TA494/chapter/1-Recommendations [Accessed August 5th 2022].
16 National Institute for Health and Care Excellence (NICE). *Semaglutide for managing overweight and obesity*. 2022. Available from: https://www.nice.org.uk/guidance/gid-ta10765/documents/final-appraisal-determination-document [Accessed August 5th 2022].
17 National Institute for Health and Care Excellence (NICE). *Semaglutide - Medicinal forms*. Available from: https://bnf.nice.org.uk/drugs/semaglutide/medicinal-forms/ [Accessed August 5th 2022].
18 Department of Health and Social Care (DHSC). *Tackling obesity: empowering adults and children to live healthier lives*. Available from: https://www.gov.uk/government/publications/tackling-obesity-government-strategy/tackling-obesity-empowering-adults-and-children-to-live-healthier-lives [Accessed August 5th 2022].
19 Yumuk V, Tsigos C, Fried M, Schindler K, Busetto L, Micic D, et al. European Guidelines for Obesity Management in Adults. *Obesity Facts*. 2015;8(6):402-24. Available from: https://doi.org/10.1159/000442721.
20 Scottish Intercollegiate Guidelines Network (SIGN). *Management of Obesity*. 2010. Available from: https://www.sign.ac.uk/assets/sign115.pdf [Accessed August 5th 2022].

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