NIHR | Innovation Observatory

Newcastle University

Health Technology Briefing
May 2022

Semaglutide for treating overweight and obesity in adolescents ages 12 to 17 years old

Company/Developer	Novo Nordisk Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 27613	NICE ID: 10563	UKPS ID: -

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Semaglutide is in clinical development for the treatment of overweight and obese adolescents between the ages of 12 and 17. Obesity is a chronic disease and global public health challenge and the prevalence of childhood obesity rising in the UK. Obesity increases the risk of developing a range of health conditions in childhood and later life, including stroke, hypertension and type 2 diabetes. More than 70% of people who have obesity before puberty will also have obesity as adults, which may lead to significant health risks and underscores the need for effective treatments. Currently in paediatric patients, first-line treatment for obesity is typically lifestyle therapy (diet and exercise) which often yields poor responses.

Semaglutide is a medicinal product administered as an injection under the skin (subcutaneously). It reduces body weight and body fat mass through lowered energy intake. It binds to, and activates, the glucagon-like peptide-1 (GLP-1) receptor to increase insulin secretion, suppress glucagon secretion, and slow gastric emptying. It also reduces body weight and fat mass through lowered energy intake, involving an overall reduced appetite. If licensed, semaglutide would provide a novel treatment option with an acceptable benefit-risk profile for adolescents aged 12 to 17 years old with overweight or obesity.

Proposed Indication

Weight management in adolescents with overweight or obesity aged 12 to 17 years old with a BMI equal to or above 95th percentile OR equal to or above 85th percentile with 1 or more weight related comorbidity (hypertension, dyslipidaemia, obstructive sleep apnoea or type 2 diabetes).[1]

Technology

Description

Semaglutide binds to, and activates, the GLP-1receptor to increase insulin secretion, suppress glucagon secretion, and slow gastric emptying. GLP-1 is a physiological hormone that has multiple actions in glucose and appetite regulation, and in the cardiovascular system.[2] Semaglutide reduces blood glucose in a glucose dependent manner by stimulating insulin secretion and lowering glucagon secretion when blood glucose is high. It also 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 phase III clinical trials (NCT04102189) for weight management in adolescents aged 12 to 17 years old with a BMI equal to or above 95th percentile OR equal to or above 85th percentile with 1 or more weight related comorbidity (such as hypertension or type 2 diabetes). It is proposed to be given at the dose of 2.4mg once a week via subcutaneous injection for a dose escalation period of 16 weeks and a maintenance period of 52 weeks.[1]

Key Innovation

In paediatric patients, first-line treatment for obesity is typically lifestyle therapy, which often yields poor responses.[3] However, the use of available medications remains limited by modest efficacy, safety concerns, and cost.[4] Identifying effective treatment strategies for adolescent obesity is paramount but complicated by the multifactorial etiology of obesity given that appropriate treatment approaches for adolescent obesity must account for age, sex, pubertal status, severity of obesity, underlying etiology, obesity-related complications, psychosocial factors, and patient and family preferences. Pharmacologic interventions have been proposed for youths with obesity who respond suboptimally to multicomponent, intensive behavioral therapy, however, options are extremely limited.[5]

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.[6] If licensed, semaglutide would provide a novel treatment option with an acceptable benefit-risk profile for adolescents aged 12 to 17 years old with overweight or obesity.

Regulatory & Development Status

Semaglutide 2.4mg is licensed in the UK 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.[7]

Additionally, semaglutide currently has market authorization in the UK/EU at the 0.5 mg and 1 mg dose (Ozempic) and as a once-daily oral tablet (Rybelsus) as monotherapy for the treatment of adults with insufficiently controlled type 2 diabetes mellitus. It aims to improve glycaemic control as an adjunct to diet

and exercise, when metformin is considered inappropriate due to intolerance or contraindications or in addition to other medicinal products for the treatment of diabetes.[2]

Semaglutide is also currently in clinical trials for the following:[8]

- Type 2 Diabetes
- Myocardial Injury
- Atherosclerosis
- Chronic Kidney Disease
- Non-alcoholic fatty liver disease (NAFLD)
- Heart failure with preserved ejection fraction (HFpEF)
- Alzheimer's disease
- Non-alcoholic steatohepatitis (NASH)
- Atrial fibrillation (AF)
- Polycystic ovarian syndrome (PCOS)
- Cognitive dysfunction
- Lipohypertrophy

Patient Group

Disease Area and Clinical Need

Obesity is a chronic disease and global public health challenge. The prevalence of childhood obesity is rising in the UK and new figures show a record increase in childhood obesity since the COVID-19 pandemic.[9] Obesity is a common problem in the UK that is estimated to affect around 1 in every 4 adults and around 1 in every 5 children aged 10 to 11.[10] Overweight and obesity in childhood are known to have significant impact on both physical and psychological health. Children with obesity are likely to continue having obesity into adulthood and more likely to develop non-communicable diseases such as diabetes and cardiovascular disease at a younger age.[11]

In England, in 2018-2019, the majority of adults (67% of men and 60% of women) were overweight or obese.[12] Furthermore, about 15% of children aged 4-5 years and 20% of year 6 children (aged 10-11 years) were classified as obese (2020-21).[13] 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.[14] Hospital admissions for obesity and related conditions in children has quadrupled in the last decade.[15]

Recommended Treatment Options

NICE currently recommends lifestyle weight management services for children and young people under 18 who are overweight or obese.[16] It also outlines guidelines promoting physical activity for children and young people aged under 18 at home, preschool, school and in the community.[17]

Clinical Trial Information

Trial	**STEP TEENS, NCT04102189, EudraCT2018-002431-18;** Effect and Safety of Semaglutide 2.4 mg Once Weekly on Weight Management in Adolescents With Overweight or Obesity **Phase III:** Active, not recruiting

	Location(s): 4 EU countries, UK, US, and other countries **Primary completion date:** February 2022
Trial Design	Randomized, parallel assignment, double masking
Population	N=163; 12 to 17 years old; BMI equal to or above 95th percentile OR equal to or above 85th percentile (on gender and age-specific growth charts (CDC.gov)) with 1 or more weight related comorbidity (treated or untreated): hypertension, dyslipidaemia, obstructive sleep apnoea or type 2 diabetes; history of at least one self-reported unsuccessful dietary effort to lose weight
Intervention(s)	Semaglutide (SC injection) 2.4mg or maximum tolerated dose as an adjunct to diet and exercise
Comparator(s)	Semaglutide placebo (SC injection) as an adjunct to diet and exercise
Outcome(s)	Primary outcome: Change in Body Mass Index (BMI) [Time Frame: From baseline (week 0) to week 68] See trial record for full list of outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of semaglutide 0.25mg/0.19ml solution, 0.5mg/0.37ml solution and 1mg/0.74ml solution 1.5ml pre-filled pens for injection are £73.25.[18]

Relevant Guidance

NICE Guidance

- 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 children and young people: prevention and lifestyle weight management programmes (QS94). July 2015.
- NICE public health guidance. Weight management: lifestyle services for overweight or obese children and young people (PH47). October 2013.
- NICE public guidance. Physical activity for children and young people (PH17). January 2009.

NHS England (Policy/Commissioning) Guidance

- NHS England. Clinical Commissioning Policy: Obesity surgery for children with severe complex obesity. 16053/P. April 2017.
- 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 Society of Endocrinology and the Pediatric Endocrine Society. Pediatric Obesity Assessment, Treatment, and Prevention: An Endocrine Society Clinical Practice Guideline. 2017.[19]
- Scottish Intercollegiate Guidelines Network. Management of Obesity – A national clinical guideline. 2010.[20]

Additional Information

Novo Nordisk 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

1 ClinicalTrials.gov. *A Research Study on How Well Semaglutide Works in Adolescents With Overweight or Obesity*. *Trial ID: NCT04102189*. 2019. Status: Active, not recruiting. Available from: https://clinicaltrials.gov/ct2/show/NCT04102189 [Accessed 31st March 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 31st March 2022].

3 Kelly AS, Auerbach P, Barrientos-Perez M, Gies I, Hale PM, Marcus C, et al. A Randomized, Controlled Trial of Liraglutide for Adolescents with Obesity. *New England Journal of Medicine*. 2020;382(22):2117-28. Available from: https://doi.org/10.1056/NEJMoa1916038.

4 Wilding JPH, Batterham RL, Calanna S, Davies M, Van Gaal LF, Lingvay I, et al. Once-Weekly Semaglutide in Adults with Overweight or Obesity. *New England Journal of Medicine*. 2021;384(11):989-1002. Available from: https://doi.org/10.1056/NEJMoa2032183.

5 Cardel MI, Atkinson MA, Taveras EM, Holm J-C, Kelly AS. Obesity Treatment Among Adolescents: A Review of Current Evidence and Future Directions. *JAMA pediatrics*. 2020;174(6):609-17. https://pubmed.ncbi.nlm.nih.gov/32202626.

6 Singh G, Krauthamer M, Bjalme-Evans M. Wegovy (semaglutide): a new weight loss drug for chronic weight management. *Journal of investigative medicine : the official publication of the American Federation for Clinical Research*. 2022;70(1):5-13. Available from: https://doi.org/10.1136/jim-2021-001952.

7 European Medicines Agency (EMA). *Wegovy* 2022. Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/wegovy [Accessed 31st March 2022].

8 ClinicalTrials.gov. *Search: Recruiting, Not yet recruiting, Active, not recruiting, Completed, Enrolling by invitation Studies | Semaglutide | Phase 2, 3*. Available from: https://clinicaltrials.gov/ct2/results?cond=&term=&type=&rslt=&recrs=b&recrs=a&recrs=f&recrs=d&recrs=e&age_v=&gndr=&intr=Semaglutide+&titles=&outc=&spons=&lead=&id=&cntry=&state=&city=&dist=&locn=&phase=1&phase=2&rsub=&strd_s=&strd_e=&prcd_s=&prc

d_e=&sfpd_s=&sfpd_e=&rfpd_s=&rfpd_e=&lupd_s=&lupd_e=&sort= [Accessed 31st March 2022].

9 Diabetes UK. *New figures show record increase in childhood obesity since pandemic*. Available from: https://www.diabetes.org.uk/about_us/news/new-figures-show-record-increase-childhood-obesity-pandemic [Accessed 11th May 2022].

10 NHS UK. *Overview - Obesity*. 2019. Available from: https://www.nhs.uk/conditions/obesity/ [Accessed 31st March 2022].

11 Sahoo K, Sahoo B, Choudhury AK, Sofi NY, Kumar R, Bhadoria AS. Childhood obesity: causes and consequences. *Journal of family medicine and primary care*. 2015;4(2):187-92. Available from: https://doi.org/10.4103/2249-4863.154628.

12 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 31st March 2022].

13 Parliament UK. *Obesity statistics*. 2022. Available from: https://researchbriefings.files.parliament.uk/documents/SN03336/SN03336.pdf [Accessed 11th May 2022].

14 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 31st March 2022].

15 Jones Nielsen JD, Laverty AA, Millett C, Mainous AG, 3rd, Majeed A, Saxena S. Rising obesity-related hospital admissions among children and young people in England: national time trends study. *PloS one*. 2013;8(6):e65764-e. Available from: https://doi.org/10.1371/journal.pone.0065764.

16 National Institute for Health and Care Excellence (NICE). *Weight management: lifestyle services for overweight or obese children and young people*. 2013. Available from: https://www.nice.org.uk/guidance/ph47 [Accessed 31st March 2022].

17 National Institute for Health and Care Excellence (NICE). *Physical activity for children and young people*. 2018. Available from: https://www.nice.org.uk/guidance/ph17 [Accessed 31st March 2022].

18 National Institute for Health and Care Excellence (NICE). *SEMAGLUTIDE*. Available from: https://bnf.nice.org.uk/medicinal-forms/semaglutide.html [Accessed 31st March 2022].

19 Styne DM, Arslanian SA, Connor EL, Farooqi IS, Murad MH, Silverstein JH, et al. Pediatric Obesity-Assessment, Treatment, and Prevention: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2017;102(3):709-57. Available from: https://doi.org/10.1210/jc.2016-2573.

20 Scottish Intercollegiate Guidelines Network (SIGN). *Management of Obesity - A national clinical guideline* 2010. Available from: https://www.sign.ac.uk/assets/sign115.pdf [Accessed 19th April 2022].

NB: This briefing presents independent research funded by the National Institute for Health and Care Research (NIHR). The views expressed are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health.