NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Semaglutide for managing overweight and obesity and the reduction of associated cardiovascular risk (ID6441 including a review of TA875 and TA910)

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of semaglutide within its marketing authorisation, in addition to a reduced calorie diet and increased physical activity, for managing overweight and obesity and the reduction of associated cardiovascular risk.

Background

Overweight and obesity is a chronic condition characterised by increased body fat. People living with overweight or obesity are at an increased risk of developing cardiovascular disease, type 2 diabetes, atherosclerosis (the presence of fatty deposits in the arteries), hypertension and dyslipidaemia (abnormal levels of fats in the blood). Other conditions associated with obesity are non-alcoholic fatty liver disease, non-diabetic hyperglycaemia, subfertility, osteoarthritis, dyslipidaemia, obstructive sleep apnoea and idiopathic intracranial hypertension. The most common method for measuring obesity is body mass index (BMI) which is calculated as the ratio of weight to height squared. Overweight is typically defined by a BMI of 25 kg/m^2 to <30 kg/m^2 and obesity by a BMI of 30 kg/m^2 or more. Some ethnic groups may be at increased risk of some ill health conditions at lower BMI than people of European family origin.

Obesity affects approximately one in four adults in the UK.[1] In 2019/20 there were 10,780 hospital admissions directly attributable to obesity in England, an decrease of 3% on 2018/19 (11,117 admissions).[2] In 2019/20, there were over 1 million hospital admissions in England where obesity was a factor, an increase of 17% on 2018/19 (876,000).[2]

Cardiovascular disease refers to a range of conditions affecting the health and circulatory systems. CVD is typically associated with the build-up of fatty deposits (atherosclerosis) in the blood vessels which leads to them becoming blocked, increasing a person's risk of cardiovascular events including angina, heart attacks, heart failure, arrhythmias and certain strokes.[3] In the UK it is estimated that around 1 in 6 heart and circulatory deaths are associated with a high body mass index (BMI).[4]

NICE guideline 246 (NG246) 'Overweight and obesity management' states multicomponent interventions are the treatment of choice. Weight management programmes include behaviour change strategies to increase people's physical activity levels or decrease inactivity, improve eating behaviour and the quality of the

person's diet, and reduce energy intake. Pharmacological treatments are usually considered only after dietary, exercise and behavioural approaches have been started and evaluated. It recommends various pharmacological treatments as options, including orlistat for the management of obesity in people with a BMI of 30 kg/m^2 or more, and in people with a BMI of 28 kg/m^2 or more and significant comorbidities. The NICE guideline recommends a referral for bariatric surgery for people with: a BMI of ≥40 kg/m^2; a BMI of between 35 kg/m^2 and <40 kg/m^2 with a significant health condition that could be improved if they lost weight. It also recommends an expedited assessment for bariatric surgery for people with a BMI between 30 kg/m^2 and 35 kg/m^2 and with recent-onset of type 2 diabetes (surgery can be considered for people of Asian family origin who have recent-onset type 2 diabetes at a lower BMI than other populations).

NICE technology appraisal 664 recommends liraglutide as an option for managing overweight and obesity alongside a reduced-calorie diet and increased activity in adults if they have a BMI of at least 35 kg/m^2 (or at least 32.5 kg/m^2 for members of minority ethnic groups known to be at equivalent risk of the consequences of obesity at a lower BMI than the white population) and they have non-diabetic hyperglycaemia (defined as a haemoglobin A1c level of 42 mmol/mol to 47 mmol/mol [6.0% to 6.4%] or a fasting plasma glucose level of 5.5 mmol/litre to 6.9 mmol/litre) and they have a high risk of cardiovascular disease based on risk factors such as hypertension and dyslipidaemia and it is prescribed in secondary care by a specialist multidisciplinary tier 3 weight management service.

NICE technology appraisal 1026 recommends tirzepatide as an option for managing overweight and obesity, alongside a reduced-calorie diet and increased physical activity in adults if they have an initial BMI of at least 35 kg/m^2 (usually reduced by 2.5 kg/m^2 for people from South Asian, Chinese, other Asian, Middle Eastern, Black African or African-Caribbean ethnic backgrounds) and at least 1 weight-related comorbidity.

NICE Clinical Guideline 238 recommendations for the prevention of secondary cardiovascular events focuses on lowering levels of lipoproteins. It recommends offering atorvastatin for secondary prevention and, if further treatment is required, to consider other lipid-lowering treatments (such as alirocumab, evolocumab, ezetimibe and inclisiran). It recommends a low-density lipoprotein (LDL) cholesterol target of 2.0 mmol per litre or less, or non-high density lipoprotein (non-HDL) levels of 2.6 mmol per litre or less for the secondary prevention of cardiovascular disease.

NICE also recommends the following treatments for the secondary prevention of cardiovascular events:

- NICE technology appraisal 805 recommends icosapent ethyl with statin therapy for reducing the risk of cardiovascular events in people with raised triglycerides
- NICE technology appraisal 607 recommends rivaroxaban for preventing atherothrombotic events in people with coronary or peripheral artery disease

- NICE technology appraisal 420 recommends ticagrelor for preventing atherothrombotic events after myocardial infarction

NICE technology appraisal 875 recommends semaglutide as an option for managing overweight and obesity alongside a reduced-calorie diet and increased activity in adults if they have a BMI of at least 35 kg/m^2 (or at least 32.5 kg/m^2 for members of minority ethnic groups known to be at equivalent risk of the consequences of obesity at a lower BMI than the white population) or they have a BMI of at least 30 kg/m^2 (or at least 27.5 kg/m^2 for members of minority ethnic groups known to be at equivalent risk of the consequences of obesity at a lower BMI than the white population) and meet the criteria for referral to specialist weight management services, and they have at least 1 weight-related comorbidity. A review of this guidance is proposed in this draft scope because of a marketing authorisation indication for semaglutide has been granted for reducing the risk of major adverse cardiovascular events in adults with cardiovascular disease and overweight or obesity. NICE considers this new population to be a subgroup of the population considered in NICE technology appraisal 875.

NICE technology appraisal 910 assessing semaglutide for managing overweight and obesity in young people aged 12 to 17 years was terminated because the company did not provide an evidence submission. A review of this guidance is also proposed in this draft scope as part of the review of NICE technology appraisal 875 outlined above.

The technology

Semaglutide (Wegovy, Novo Nordisk) has a marketing authorisation 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/m^2 (obesity), or
    - ≥ 27 kg/m^2 to <30 kg/m^2 (overweight) in the presence of at least one weight-related comorbidity
- an adjunct to a reduced-calorie diet and increased physical activity for weight management in adolescents ages 12 years and above with
    - obesity (BMI ≥ 95th percentile as defined on sex- and age-specific BMI growth charts) and
    - body weight above 60 kg
- an adjunct to a reduced-calorie diet and increased physical activity to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-

fatal myocardial infarction, or non-fatal stroke) in adults with established cardiovascular disease and either obesity or overweight (BMI ≥ 27 kg/m^2).

Intervention(s)	Semaglutide
Population(s)	Adults who have a BMI of: • ≥30 kg/m^2 (obese) or • ≥27 kg/m^2 to <30 kg/m^2 (overweight) in the presence of at least one weight-related comorbidity Young people aged 12 to 17 years who on a recognised child growth reference adjusted for age and sex, have: • a BMI equal to or above the 95th centile and • body weight above 60kg
Subgroups	If the evidence allows the following subgroups will be considered: • Adults with a diagnosis of cardiovascular disease • People with type 2 diabetes • People with non-diabetic hyperglycaemia • People with BMI > 35 • People with heart failure • People with chronic kidney disease
Comparators	Standard management without semaglutide (including a reduced calorie diet and increased physical activity, and standard cardiovascular risk reduction), with or without: • liraglutide (for the population for whom liraglutide is recommended in technology appraisal 664) • tirzepatide (for the population for whom tirzepatide is recommended in technology appraisal 1026) • orlistat (prescription dose)

Outcomes	The outcome measures to be considered include: • BMI • weight loss • waist circumference • incidence of type 2 diabetes • glycaemic status • cardiovascular events • mortality • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability and cost of biosimilar and generic products should be taken into account.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations	**Related technology appraisals:** Naltrexone–bupropion for managing overweight and obesity (2017). NICE technology appraisal 494. Liraglutide for managing overweight and obesity (2020). NICE technology appraisal 664.

	Semaglutide for managing overweight and obesity (2023). NICE technology appraisal 875. Tirzepatide for managing overweight and obesity (2024). NICE technology appraisal guidance 1026. **Related NICE guidelines:** Overweight and obesity management (2025) NICE guideline 246. **Related interventional procedures:** Endoscopic sleeve gastroplasty for obesity (2024). NICE interventional procedures guidance 783. Single-anastomosis duodeno-ileal bypass with sleeve gastrectomy for treating morbid obesity (2016). NICE interventional procedures guidance 569. Implantation of a duodenal–jejunal bypass sleeve for managing obesity (2013). NICE interventional procedures guidance 471. Laparoscopic gastric plication for the treatment of severe obesity (2012). NICE interventional procedures guidance 432. **Related quality standards:** Obesity: clinical assessment and management (2016) NICE quality standard 127. Obesity in adults: prevention and lifestyle weight management programmes (2016) NICE quality standard 111. Obesity in children and young people: prevention and lifestyle weight management programmes (2015) NICE quality standard 94.
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan NHS England (2023) Manual for prescribed specialist services (2023/2024) Section 139A

Questions for consultation

Where do you consider semaglutide will fit into the existing care pathway for overweight and obesity?

Should this appraisal include the use of semaglutide in people with type 2 diabetes and overweight and obesity?

Are the subgroups suggested appropriate? Which are the most important to consider?

Please select from the following, will semaglutide be:

A. Prescribed in primary care with routine follow-up in primary care
B. Prescribed in secondary care with routine follow-up in primary care
C. Prescribed in secondary care with routine follow-up in secondary care
D. Other (please give details):

For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.

Would semaglutide be a candidate for managed access?

Do you consider that the use of semaglutide can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

Please indicate if any of the treatments in the scope are used in NHS practice differently than advised in their Summary of Product Characteristics. For example, if the dose or dosing schedule for a treatment is different in clinical practice. If so, please indicate the reasons for different usage of the treatment(s) in NHS practice. If stakeholders consider this a relevant issue, please provide references for data on the efficacy of any treatments in the pathway used differently than advised in the Summary of Product Characteristics.

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which semaglutide is licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

References

1. NHS. Obesity (2023). Available from: https://www.nhs.uk/conditions/obesity/.

2. NHS Digital. Statistics on Obesity, Physical Activity and Diet, England (2021). Available from: https://digital.nhs.uk/data-and-information/publications/statistical/statistics-on-obesity-physical-activity-and-diet/england-2021.

3. British Heart Foundation. Cardiovascular heart disease (2019). Available from: https://www.bhf.org.uk/informationsupport/conditions/cardiovascular-heart-disease.

4. NHS England. Health Survey for England, 2021 part 1 (2022). Available from: https://digital.nhs.uk/data-and-information/publications/statistical/health-survey-for-england/2021/overweight-and-obesity-in-adults