

NCPE Assessment

Summary

Semaglutide (Wegovy®)

HTA ID: 25024

13 October 2026

Applicant: Novo Nordisk

Semaglutide (Wegovy®) 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 e.g. dysglycaemia (prediabetes or type 2 diabetes mellitus), hypertension, dyslipidaemia, obstructive sleep apnoea or cardiovascular disease.

The National Centre for Pharmacoeconomics (NCPE) has issued a recommendation regarding the cost-effectiveness of semaglutide (Wegovy®) as an adjunct to a reduced-calorie diet and increased physical activity for management of overweight and obesity.

Following assessment of the Applicant's submission, the NCPE recommends that semaglutide (Wegovy®) be considered for reimbursement for the indication under assessment*. Budget impact estimates associated with semaglutide are substantial. Consideration will need to be given, regarding the affordability of semaglutide, when making a decision regarding reimbursement.

The Health Service Executive (HSE) asked the NCPE to carry out an evaluation of the Applicant's (Novo Nordisk) Health Technology Assessment of semaglutide (Wegovy®). The NCPE uses a decision framework to systematically assess whether a technology is cost-effective. This includes comparative clinical effectiveness and health related quality of life benefits, which the new treatment may provide and whether the cost requested by the pharmaceutical company is justified.

Following the recommendation from the NCPE, the HSE examines all the evidence which may be relevant for the decision; the final decision on reimbursement is made by the HSE. In the case of cancer drugs the NCPE recommendation is also considered by the National Cancer Control Programme (NCCP) Technology Review Group.

About the National Centre for Pharmacoeconomics

The NCPE are a team of clinicians, pharmacists, pharmacologists and statisticians who evaluate the benefit and costs of medical technologies and provide advice to the HSE. We also obtain valuable support from clinicians with expertise in the specific clinical area under consideration. Our aim is to provide impartial advice to help decision makers provide the most effective, safe and value for money treatments for patients. Our advice is for consideration by anyone who has a responsibility for commissioning or providing healthcare, public health or social care services.

Summary

In February 2026, Novo Nordisk submitted a dossier which investigated the comparative clinical effectiveness, cost-effectiveness and budget impact of semaglutide (Wegovy®). Semaglutide is licensed 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 $\geq 30 \text{ kg/m}^2$ (obesity), or $\geq 27 \text{ kg/m}^2$ to $< 30 \text{ kg/m}^2$ (overweight) in the presence of at least one weight-related comorbidity (WRC). These WRCs can include dysglycaemia (prediabetes or type 2 diabetes mellitus (T2DM)), hypertension, dyslipidaemia, obstructive sleep apnoea (OSA) or cardiovascular disease (CVD). Novo Nordisk is seeking reimbursement of semaglutide on the Community Drug Schemes.

Semaglutide is a glucagon-like peptide-1 (GLP-1) receptor agonist (RA). It stimulates the GLP-1 receptor, which regulates appetite and calorie intake. Semaglutide (Wegovy®) is formulated as a solution for subcutaneous injection contained in a reusable pre-filled pen; it is available in multiple strengths. One pre-filled pen provides four doses of the specified strength. Following dose titration, the recommended maintenance dose is 2.4mg once weekly. The maintenance dose may be increased to 7.2mg once weekly, if required, for patients with BMI $\geq 30 \text{ kg/m}^2$ at treatment initiation and who have received a minimum of four weeks on the 2.4mg once weekly maintenance dose.

Management of overweight and obesity requires a personalised approach to support individuals in their weight loss goals. Behavioural and lifestyle modifications, such as adopting a Diet and Exercise intervention, are the primary therapeutic modality. However, Diet and Exercise as an intervention is not standardised and varies considerably throughout Irish clinical practice. Pharmacotherapy is prescribed as an adjunctive treatment to Diet and Exercise. In Ireland, liraglutide (Saxenda®) is the only GLP-1 RA currently approved for reimbursement and is subject to a HSE Managed Access Protocol (MAP). Adults with initial BMI $\geq 35 \text{ kg/m}^2$, and who have prediabetes and are high-risk for CVD (hereafter referred to as the BMI ≥ 35 (liraglutide MAP) subpopulation), are eligible, under the HSE MAP, for consideration for liraglutide. Following dose titration, the recommended dose of liraglutide is 3mg once daily by subcutaneous injection. A Health Technology Assessment for

tirzepatide (Mounjaro®), for management of overweight and obesity, was completed, by the NCPE, in December 2025. Following dose titration, recommended once weekly doses of tirzepatide are 5mg, 10mg or 15mg. At the date of this summary publication, tirzepatide remains under consideration for reimbursement by the HSE.

The base case cost-effectiveness analysis compared semaglutide 2.4mg once weekly versus Diet and Exercise in the full licensed population. As the full licensed population for semaglutide represents a large, heterogeneous patient cohort, scenario analyses conducted in pre-specified subpopulations were also presented. The HSE identified six subpopulations of interest to the Applicant. These subpopulations were subdivided according to BMI categories ($\text{BMI} \geq 30\text{kg/m}^2$, $\text{BMI} \geq 35\text{kg/m}^2$, $\text{BMI} \geq 40\text{kg/m}^2$) and the presence or absence of WRCs. Additional scenario analyses presented by the Applicant included semaglutide 2.4mg once weekly versus liraglutide 3mg once daily in the $\text{BMI} \geq 35$ (liraglutide MAP) subpopulation; semaglutide 7.2mg once weekly versus Diet and Exercise in the $\text{BMI} \geq 30\text{kg/m}^2$ subpopulation; and semaglutide 2.4mg once weekly versus tirzepatide 5mg once weekly in the full licensed population.

1. Comparative effectiveness of semaglutide

Evidence from the STEP (Semaglutide Treatment Effect in People with Obesity) clinical trial programme informed the efficacy and safety of semaglutide in people with overweight and obesity. The STEP trials were phase III, double-blind, randomised controlled trials. Adults with a BMI of $\geq 30\text{ kg/m}^2$ or $\geq 27\text{ kg/m}^2$ in the presence of at least one WRC (hypertension, dyslipidaemia, OSA or CVD), and with at least one self-reported unsuccessful dietary effort to lose body weight, were recruited to the trials. The intervention was semaglutide. Placebo was the comparator in most of the STEP trials; liraglutide was included as a comparator in STEP 8. In all STEP trials, both the intervention and comparator were given as adjunctive treatment to Diet and Exercise. Co-primary endpoints were change from baseline in bodyweight and proportion of patients achieving at least 5% weight loss from baseline to end of treatment. Secondary endpoints included percentage of patients achieving pre-specified weight-loss thresholds; changes in cardiometabolic risk factors such as blood pressure, glycated haemoglobin, and lipid profiles; and change in health-related quality of life (HRQoL). Outcomes were measured at different time points ranging from 52 weeks (STEP 10 and STEP-HFpEF) to 104 weeks (STEP 5). The standard timepoint for measuring primary

outcomes for the majority of STEP trials was 68 weeks (STEP 1, 2, 3, 4, and 8).

Treatment with semaglutide consistently demonstrated statistically significant and clinically meaningful reductions in bodyweight compared with placebo. Semaglutide also demonstrated superior efficacy when compared with liraglutide. Statistically significant improvements in HRQoL were also observed for semaglutide compared to placebo.

Limitations of the clinical evidence included lack of comparative efficacy data beyond four years, and uncertainty regarding generalisability of the Diet and Exercise modality used in the clinical trials compared to Diet and Exercise regimens adopted by people in Irish clinical practice.

Direct comparative evidence was available, from the STEP trials, for the comparisons of semaglutide 2.4mg once weekly versus placebo, semaglutide 7.2mg once weekly versus placebo, and semaglutide 2.4mg once weekly versus liraglutide 3mg once daily. For the scenario comparing semaglutide 2.4mg once weekly versus tirzepatide 5mg once weekly in the full licensed population, an indirect treatment comparison was required to generate an estimate of comparative efficacy. The Applicant conducted a network meta-analysis (NMA). Data from three trials in the STEP programme were used to inform efficacy for semaglutide: STEP 1, STEP 8 and STEP UP. Data from SURMOUNT-1, which was a phase III, double-blind randomised controlled trial, informed efficacy for tirzepatide. All four studies were broadly comparable with respect to trial design, recruited population, comparators and outcomes. The accompanying Diet and Exercise modality included in each of the studies was also similar. However, some differences between studies were noted. These included differences between trials with respect to baseline BMI, in proportion of female representation, and in the time points at which outcomes were measured (Week 68 in STEP 1 and STEP 8 versus Week 72 in STEP UP and SURMOUNT-1). The primary outcome of the NMA was change in bodyweight; secondary outcomes included change in systolic blood pressure, total cholesterol and high-density lipoprotein cholesterol. Sensitivity analyses were conducted to assess the impact of differences between studies. Despite the inter-study heterogeneity, the Review Group considered the risk of potential bias to the NMA to be relatively small. Results from the NMA suggested that there was no statistically significant difference in change in weight from baseline between semaglutide 2.4mg once weekly and tirzepatide 5mg once

weekly. Tirzepatide was suggested to confer a statistically significant increase in high-density lipoprotein cholesterol compared to semaglutide. Differences across other outcomes (total cholesterol and systolic blood pressure) were not statistically significant.

2. Safety of semaglutide

Safety and tolerability of semaglutide versus placebo, in people with overweight and obesity, was primarily informed by data from four trials in the STEP programme (STEP 1, STEP 2, STEP 3 and STEP 4). Approximately 88.5% of participants assigned to semaglutide experienced an adverse event (AE) compared to 83.6% assigned to placebo. Comparative safety of semaglutide versus liraglutide, and semaglutide versus tirzepatide, was informed by STEP 8 and SURMOUNT-5, respectively. Proportions of participants experiencing AEs in STEP 8 were 95.2% assigned to semaglutide, 96.1% assigned to liraglutide, and 95.3% assigned to placebo. SURMOUNT-5 compared tirzepatide 10mg or 15mg once weekly to semaglutide 1.7mg or 2.4mg once weekly. The proportions of participants assigned to semaglutide and tirzepatide who experienced an AE were 79% and 76.7%, respectively. However, the incidence of serious AEs was higher in the tirzepatide arm (4.8%) compared to the semaglutide arm (3.5%). In all studies, gastrointestinal AEs were most frequently reported, and were a leading cause of treatment discontinuation. They included nausea, diarrhoea and vomiting.

Semaglutide should be used with caution in patients with history of pancreatitis, gastroparesis, and diabetic retinopathy. Data from epidemiological studies indicates an increased risk for non-arteritic anterior ischaemic optic neuropathy (NAION) during treatment with semaglutide. A sudden loss of vision should lead to ophthalmological examination and treatment with semaglutide should be discontinued if NAION is confirmed.

3. Cost effectiveness of semaglutide

Methods

Cost-effectiveness was assessed, from the perspective of the HSE, using a Markov cohort state-transition model developed in Microsoft Excel®. It comprised 23 mutually exclusive health states. Each health state denoted a single WRC, or a combination of WRCs. Transitions between health states represented the incidence of a new WRC. These transitions were modelled using risk equations derived from external data. Surrogate

outcomes, including weight (and corresponding BMI), systolic blood pressure, glycated haemoglobin, high-density lipoprotein cholesterol and total cholesterol, were modelled based on outcomes from the STEP trials. These surrogate outcomes were used as inputs to these risk equations. WRCs modelled as health states included T2DM, cardiovascular events (acute coronary syndrome, stroke) and cancer (colon cancer in all patients; breast cancer and endometrial cancer in female patients who were post-menopause only). Additionally, four WRCs representing acute clinical events (OSA, knee replacement, bariatric surgery and hospitalisation for heart failure) were included. Change in weight (and corresponding change in BMI) was the main driver of clinical effectiveness. Two different model cycle lengths were utilised. The first year (Year Zero) in the model comprised four model cycles; each was three months duration. From Year One onwards, model cycle length was one year. A half-cycle correction was applied. The baseline starting age was 46 years; this was informed by the STEP 1 trial. The modelled time horizon was 40 years. The modelled intervention was semaglutide 2.4mg once-weekly, A scenario was included where the modelled intervention was semaglutide 7.2mg once weekly. Modelled comparators were Diet and Exercise, liraglutide 3mg once daily, and tirzepatide 5mg once weekly.

Various data sources informed the different risk equations used to predict the incidence of individual WRCs associated with different BMI ranges. The Review Group considered most of the data sources utilised by the Applicant to be acceptable. However, alternative data sources to inform the risk equations predicting incidence of knee replacement, OSA and endometrial cancer were considered to be more appropriate. Compared to studies utilised by the Applicant, these alternative sources provided data which was considered to be more generalisable to the Irish setting. They included studies which were conducted more recently, which were UK-based rather than international, and which had similar or larger sample sizes.

General population mortality was informed by Irish-specific data. Death could occur from any health state. Additional mortality, due to overweight and obesity, was included in two ways: an increased mortality risk due incident WRCs and separately, an increased mortality risk with each unit of BMI increase. Disease-specific mortality was included for the following WRCs: T2DM, cancer, acute coronary syndrome and stroke. The correlation between increase in mortality risk per BMI unit increase, was estimated based on a digitised figure by

Bhaskaran et al., 2018. However, the Review Group identified a table in the same publication, containing exact values, which was considered to provide more accurate estimates. A limitation of the Applicant's approach to modelling mortality was the potential for double-counting, since mortality due to WRCs already implies a correlation between increased BMI and mortality. This may have overestimated mortality risk, in particular for patients with higher BMI. Whilst the Applicant performed adjustments to account for this, the Review Group considered that the risk could not be completely mitigated. However, removal of the assumption of increase in mortality risk per BMI unit increase would have underestimated mortality. Therefore, no changes were made to the NCPE adjusted base case.

The overall modelling approach adopted by the Applicant was generally considered to be appropriate; however, some limitations were identified. Overweight and obesity is a complex condition; the disease trajectory is highly heterogeneous between patients. Markov cohort models simulate disease progression of the average patient; they cannot capture the unique disease trajectory for each individual. In the absence of long-term efficacy data, the approach to modelling incidence of WRCs through risk equations was considered appropriate. However, the accuracy of these risk equations in predicting long-term WRC outcomes remains substantially uncertain. Finally, there is an association between age and cancer incidence. However, in the model, the dependence between cancer and age was limited. This may have resulted in predicted cancer incidence per age group to be less accurate.

A systematic literature review was conducted to identify HRQoL evidence to inform utility values in the model. A baseline utility value, derived from a UK-based study which examined the relationship between BMI and HRQoL, was assigned to individuals with no WRCs. Utility decrements, based on health state occupancy or experience of an acute clinical event or AE, were subsequently applied. Utility values were also adjusted for age. Limitations identified with utility modelling included potential for double counting and uncertainty that disutility due to all WRCs was accounted for. However, the Review Group considered the impact of these limitations on cost-effectiveness results was small.

Costs included in the model were drug acquisition costs for the intervention and

comparators, concomitant medication costs, healthcare resource use costs, and AE costs.

Results

Several changes were made to inform the NCPE adjusted base case. Alternative data sources were used to inform incidence of knee replacement, prevalence of OSA, and incidence of endometrial cancer in women who are post-menopause. The exact hazard ratio values for different BMI ranges, which were applied to general population mortality, were taken from Bhaskaran et al., 2018, in preference to using the values derived from the digitised figure.

Results of the Applicant and NCPE adjusted base case deterministic cost-effectiveness analyses, for the comparison of semaglutide 2.4mg once weekly versus Diet and Exercise in the full licensed population, are presented in Tables 1 and 2, respectively.

Table 1: Applicant base case incremental cost-effectiveness results (full licensed population) ^{a, b, c}

Treatments	Total costs (€)	Total QALYs	Incremental costs (€)	Incremental QALYs	ICER (€/QALY)
Full licensed population					
Diet and Exercise	43,831	14.48	-	-	-
Semaglutide 2.4mg	67,316	15.31	23,485	0.84	28,125

ICER: incremental cost-effectiveness ratio; mg milligram; QALY: quality adjusted life year

^a Corresponding probabilistic ICER using 1,000 iterations = €27,340/QALY for the Full licenced population for semaglutide 2.4 mg once weekly versus Diet and Exercise.

^b Costs and outcomes were discounted at 4%.

^c Figures in the table are rounded; calculations may not be directly replicable.

Table 2: NCPE adjusted base case incremental cost-effectiveness results (full licensed population) ^{a, b, c}

Treatments	Total costs (€)	Total QALYs	Incremental costs (€)	Incremental QALYs	ICER (€/QALY)
Full licensed population					
Diet and Exercise	46,564	14.69	-	-	-
Semaglutide 2.4mg	70,850	15.34	24,286	0.65	37,434

ICER: incremental cost-effectiveness ratio; mg milligram; NCPE: National Centre for Pharmacoeconomics; QALY: quality adjusted life year

^a Corresponding probabilistic ICER using 1,000 iterations was €36,891/QALY for the full licenced population for semaglutide 2.4 mg once weekly versus Diet and Exercise.

^b Costs and outcomes were discounted at 4%.

^c Figures in the table are rounded; calculations may not be directly replicable.

The corresponding incremental cost-effectiveness ratios (ICERs) for the comparisons of semaglutide 2.4mg once weekly versus Diet and Exercise in each of the six HSE-specified subpopulations, using NCPE adjusted base case assumptions, ranged between €27,043 per quality adjusted life year (QALY) and €41,687 per QALY. The clinical efficacy data for the BMI ≥ 35 (liraglutide MAP) subpopulation differed from the full licensed population and other

subpopulations, given that it was informed by the STEP 8 clinical trial. The ICER for the comparison of semaglutide 2.4mg once weekly versus liraglutide 3mg once daily in the BMI ≥ 35 (liraglutide MAP) subpopulation, using NCPE adjusted base case assumptions, was €17,548 per QALY. This ICER was considerably lower compared to all cost-effectiveness results for comparisons of semaglutide 2.4mg once weekly versus Diet and Exercise in the full licensed population and in all HSE-specified populations. Liraglutide is similarly priced to semaglutide. Therefore, the incremental costs between semaglutide and liraglutide were substantially lower than the incremental costs between semaglutide and Diet and Exercise. However, the relative difference in incremental QALYs was less pronounced. This was the key driver in the lower ICER observed for semaglutide versus liraglutide.

A scenario was conducted for the comparison of semaglutide 7.2mg once weekly versus Diet and Exercise in the $\geq$ BMI 30 kg/m² subpopulation. Cost effectiveness results using Applicant and NCPE adjusted assumptions were €25,488 per QALY and €35,423 per QALY, respectively.

A comparison of semaglutide 2.4mg once weekly versus tirzepatide 5mg once weekly in the full licensed population was also conducted. Under both Applicant and NCPE adjusted base case assumptions, semaglutide 2.4mg once weekly was suggested to be less costly and less effective than tirzepatide 5mg once weekly. An analysis of net monetary benefit, using a willingness to pay threshold of €45,000 per QALY, indicated that semaglutide 2.4mg once weekly may be cost-effective when compared to tirzepatide 5mg once weekly.

Sensitivity analysis

Analyses suggested that the probability of cost-effectiveness of semaglutide versus Diet and Exercise, in both the Applicant and NCPE adjusted base cases, was 100% at the €45,000 per QALY threshold and 0% at the €20,000 per QALY threshold. However, the Review Group had concerns that this result did not capture uncertainty associated with the risk equations utilised in the model. Furthermore, because the cohort model structure models an average patient, it may not have fully reflected the substantial heterogeneity in baseline BMI in the patient population.

4. Budget impact of semaglutide

The prices to wholesaler per pre-filled pen of semaglutide 0.5mg, 1.7mg, 2.4mg and 7.2mg

are €127.03, €146.58, €169.13, and €255.57, respectively. The estimated annual treatment cost per patient of semaglutide 2.4mg once weekly and semaglutide 7.2mg once weekly are €2,918 and €4,370, respectively, inclusive of Value Added Tax, 9% Framework Agreement rebate, and pharmacy dispensing fees.

The Applicant submitted a budget impact model (BIM), estimating the gross and net drug budget impact associated with semaglutide reimbursement over the next five years. This assumed that 97% of patients are treated with semaglutide 2.4mg and the remainder receive semaglutide 7.2mg. There was considerable uncertainty associated with budget impact estimates. The Review Group addressed some limitations in the Applicant's BIM by adjusting the prevalence of obesity, which was considered to underestimate the subpopulation with a BMI of ≥ 35 kg/m². In the full licensed population, the five-year net drug-budget impact estimate was approximately €4.4 billion (including VAT). Using NCPE adjusted assumptions, the five-year estimated net drug budget impact within the six HSE-specified subpopulations ranged from €263 million (including VAT) in the subpopulation with a BMI of ≥ 40 kg/m² with at least one WRC to €3.2 billion (including VAT) in the subpopulation with a BMI of ≥ 30 kg/m² regardless of WRC status.

5. Patient Organisation Submission

A patient organisation submission was received from the Irish Coalition for People Living with Obesity (IPCO). This submission will form part of the information that the HSE considers when making their drug funding decision.

6. Conclusion

The NCPE recommends that semaglutide (Wegovy®) be considered for reimbursement for the indication under assessment*. Budget impact estimates associated with semaglutide are substantial. Consideration will need to be given, regarding the affordability of semaglutide, when making a decision regarding reimbursement.

*Next steps: The NCPE Assessment Report, NCPE recommendation, and Patient Organisation submission will be considered by the HSE when making their decision on reimbursement, while also having regard to the criteria specified in the Health (Pricing and Supply of Medical Goods) Act 2013.

Further information on this process may be found [here](#).