

Reimbursement Review Sponsor Summary Template

Instructions for Sponsors

Background

Please read the instructions below and consult the recommended documentation before completing the template. If you have any questions regarding the application process, please [contact us](#) with the complete details of your question(s). Please note that the completed document will not be posted on the CDA-AMC website. CDA-AMC will use this document as one of the considerations when preparing the review report.

Before Completing the Template

Please review the following documents to ensure an understanding of the procedures and submission guidelines:

- [Procedures for Reimbursement Reviews](#)
- Pharmaceutical Review Updates for any applicable information.

Completing the Template

General Guidelines

Complete all sections of the template using 10-point Arial font type in text and 9-point Arial font in tables. Include figure and table numbers and provide a list of figures and a list of tables after the table of contents. Data should reflect the results reported in the clinical study report(s) whenever possible. Do not exceed the page limitations where noted.

Provide clear references to source documentation (including citations and corresponding table and figure numbers from data sources) used when completing the template. In-text citations to sponsor references must be referenced numerically in order of appearance using superscript numbers. The sponsor must provide an RIS file containing the references used in the report. A RIS file is a standardized bibliographic format that enables citation management programs to exchange documents.

When the template is complete, delete this cover page with the instructions CDA-AMC and the record of updates section, delete all red font instructions through the template. Please feel free to add company-specific elements such as a cover page, disclaimer, header, footer, etc. as required. Save and submit the completed template as a Word document.

Section 1

In this section the sponsor is required to summarize key background information regarding the drug under review and the condition for which the drug under review is indicated. Please ensure that statements are appropriately referenced.

Section 2

In this section the sponsor is required to summarize the results from a systemic literature review. The literature review must be conducted and reported in accordance with the instructions provided within this template.

Section 3

In this section the sponsor is required to summarize long-term extension studies. The sponsor should ensure that all source documentation, including the clinical study report (if available), are included in the application materials. If data

from long-term extension studies are not available at the time of filing the application, this should be noted within this section (i.e., do not delete the section if there are no data available).

Section 4

In this section of the template the sponsor must summarize all indirect comparisons that have been included in the application (i.e., to support comparative efficacy or safety and/or the assumptions in the pharmacoeconomic model). In addition to this summary, the sponsor must provide the complete technical reports for the indirect comparisons as described in the [Procedures for Reimbursement Reviews](#). Any sponsors who have not included one or more indirect comparisons in the application should explain within the template why an indirect comparison is not relevant for the review and/or why an indirect comparison was not feasible with the available information (i.e., do not delete the section if there are no data available).

Section 5 (for applications eligible for a complex review only)

This section allows the sponsor to summarize evidence from additional studies that address important gaps in the evidence presented in sections 2 and 3 of the template. Prior to completing Section 5, sponsors must clearly identify the gaps in the evidence that has been provided in each of the preceding sections. Examples of gaps in the evidence include the following:

- Studies designed to demonstrate safety and effectiveness in relevant patient populations that were not included in the clinical trials.
- Studies designed to address outcomes that require longer-term follow-up and were not investigated in the clinical trials and/or extension studies.
- Studies that address uncertainty regarding the dosage of the drug under review that is used in actual clinical practice.

CDA-AMC will consider the information provided by the sponsor in Section 5 and make a case-by-case determination of which additional evidence will be included in the clinical report. The inclusion of evidence from section 5 in the clinical report will be determined solely by CDA-AMC based on the following factors:

- the additional information may address a clear and relevant gap in the pivotal and RCT evidence
- the sponsor has provided the additional information in a format that allows CDA-AMC to complete a detailed review and appraisal of the data (e.g., in accordance with the CONSORT reporting guidelines or [Guidance for Reporting Real-World Evidence](#), as applicable).

When assessing eligibility of an application for a complex review under scenario 5, CDA-AMC will determine during the eligibility assessment whether additional evidence will be included in this section of the clinical report.

Section 6

In this section of the template the sponsor must summarize the key methods and results of the pharmacoeconomic submission. The information provided by the sponsor will be incorporated into the Supplemental Materials document that is prepared by CDA-AMC. The information is intended to be a summary and additional relevant details should be included in the economic evaluation technical report. **Note: All sponsors are encouraged to complete this section; however, it is only a requirement for applications that will target the December 2026 expert committee meetings or later.**

Submitting the Completed Template

Incorporate the completed sponsor submission into the package of required documents. Please consult the relevant procedural documentation for details on how to file the application with CDA-AMC.

Record of Updates to Template

Version	Date	Summary of revisions
5	January 29, 2026	• Addition of the summary of the sponsor's pharmacoeconomic submission. • Clarified how the proposed reimbursement conditions will be considered by the expert committee.
4	February 27, 2025	• Updated from CADTH to CDA-AMC • Added guidance throughout to include corresponding table and figure numbers from data sources when they are cited. • Added a new section for proposed reimbursement conditions • Updated section 5 instructions to reflect changes to complex review eligibility • Made minor revisions to Table 1 (submission type and mechanism of action of the drug under review added) • Clarified guidance for providing a reference list and copies of articles addressing the validity of outcome measures • Added guidance to summarize the clinical evidence underlying or justifying the use of a surrogate outcome as well as the evidence for the validation of the surrogate outcome. • Added guidance for reporting statistical testing details for noninferiority studies and for reporting how intercurrent events were handled. • Added guidance on describing the feasibility assessment for included indirect treatment comparisons • Clarified guidance for reporting assessment of homogeneity for indirect treatment comparisons • Clarified guidance for focussing on relevant comparators when reporting results of network meta-analyses • Added example tables for reporting results of network meta-analyses • Clarified guidance that absolute effects for efficacy results should be reported when possible
3	June 8, 2023	Updated instructions for reporting efficacy results in the systematic review section now specify types of data that should be reported, including absolute differences in effects. In the absence of this information, the CADTH review team may not be able to fully assess the clinical importance of the estimated effect for a given outcome.
2	April 20, 2023	Clarification to the template instructions that section 2 of the template must be completed by sponsors and that all indirect comparisons included in the application must be summarized in section 4.
1	March 31, 2022	Original version posted

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List of Figures

Figure 1: PRISMA flow (not reported in CSR).

Figure 1: Economic model structure (not reported in CSR).

No new figures were supplied; original figure locations are retained.

Abbreviations

Examples of commonly used abbreviations are provided below. Please add or remove from the list as needed.

AE	adverse event
CI	confidence interval
DB	double blind
EMA	European Medicines Agency
FAS	full analysis set
FDA	Food and Drug Administration
ITT	intention-to-treat population
PP	per-protocol
RCT	randomized controlled trial
RR	relative risk
SAE	serious adverse event
SD	standard deviation
WDAE	withdrawal due to adverse event

ANCOVA = analysis of covariance; BMI = body mass index; DEXA = dual-energy X-ray absorptiometry; GLP-1 = glucagon-like peptide-1; IWQOL-Lite-CT = Impact of Weight on Quality of Life-Lite for Clinical Trials; MMRM = mixed model for repeated measurements; SAS = safety analysis set. [CSR PDF pp. 25-28]

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Section 1. Introduction

Application Summary

Table 1: Submitted for Review

Item	Description
Drug (product)	Semaglutide 2.4 mg once weekly, subcutaneous solution for injection. Trial products: 1.0 and 3.0 mg/mL in a 3 mL PDS290 pre-filled pen-injector. [CSR PDF pp. 39-40; Table 9-1] The Wegovy brand and marketed Canadian presentations are not established in this CSR.
Sponsor	Novo Nordisk, Novo Allé, 2880 Bagsvaerd, Denmark. [CSR PDF p. 2]
Health Canada indication	Not reported in the supplied CSR: Canadian indication, approval status/pathway and NOC dates cannot be established from this trial report.
Health Canada approval status	Not reported in the supplied CSR: Canadian indication, approval status/pathway and NOC dates cannot be established from this trial report.
Health Canada review pathway	Not reported in the supplied CSR: Canadian indication, approval status/pathway and NOC dates cannot be established from this trial report.
NOC date	Not reported in the supplied CSR: Canadian indication, approval status/pathway and NOC dates cannot be established from this trial report.
Mechanism of action	Semaglutide is a long-acting, selective GLP-1 receptor agonist with 94% homology to human GLP-1. Weight reduction is mediated mainly by reduced energy intake through increased satiety/fullness and reduced hunger. [CSR PDF pp. 31-32]
Recommended dosage	Trial regimen: 0.25 mg once weekly for 4 weeks, then 0.5, 1.0 and 1.7 mg once weekly for 4 weeks each, then 2.4 mg once weekly for 52 weeks (68 weeks total). If 2.4 mg was not tolerated, 1.7 mg was permitted to avoid complete discontinuation, with an attempt to re-escalate recommended. [CSR PDF pp. 39-40; Tables 9-1 and 9-2] Product-monograph dosing and subgroup adjustments are not reported in the supplied CSR.
Submission type	Not reported in the supplied CSR. The CSR does not provide this Canadian regulatory, reimbursement or prescribing submission information.
Reimbursement request	Not reported in the supplied CSR. The CSR does not provide this Canadian regulatory, reimbursement or prescribing submission information.

Rationale for Filing the Resubmission or Reassessment

Not reported in the supplied CSR. The CSR does not provide this Canadian regulatory, reimbursement or prescribing submission information.

Drug under Review

Indication and Reimbursement Request

Not reported in the supplied CSR. The CSR does not provide this Canadian regulatory, reimbursement or prescribing submission information.

Dosing and Administration

Trial regimen: 0.25 mg once weekly for 4 weeks, then 0.5, 1.0 and 1.7 mg once weekly for 4 weeks each, then 2.4 mg once weekly for 52 weeks (68 weeks total). If 2.4 mg was not tolerated, 1.7 mg was permitted to avoid complete

discontinuation, with an attempt to re-escalate recommended. [CSR PDF pp. 39-40; Tables 9-1 and 9-2] Product-monograph dosing and subgroup adjustments are not reported in the supplied CSR.

Mechanism of action

Semaglutide is a long-acting, selective GLP-1 receptor agonist with 94% homology to human GLP-1. Weight reduction is mediated mainly by reduced energy intake through increased satiety/fullness and reduced hunger. [CSR PDF pp. 31-32]

Prescribing

Not reported in the supplied CSR. The CSR does not provide this Canadian regulatory, reimbursement or prescribing submission information.

Disease Background

Overview of the Condition

Obesity is described as a disease with substantial medical, societal and economic impact, reduced health-related quality of life, and increased morbidity and mortality. Associated complications include type 2 diabetes, hypertension, dyslipidaemia, sleep apnoea, cardiovascular disease, osteoarthritis, urinary incontinence, non-alcoholic steatohepatitis and some cancers. Risk increases with BMI; 5%-10% weight loss can improve comorbidities, physical symptoms and quality of life. Lifestyle-induced weight loss is opposed by increased appetite and reduced energy expenditure, contributing to regain. [CSR PDF p. 31] Canadian incidence/prevalence, formal staging and quantified survival estimates are not reported.

Estimated Disease Prevalence

Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.

Table Number: Sample table for presenting the estimated prevalence in each region

Region	Estimated Prevalence		
	Lower Estimate	Best Estimate	Upper Estimate
Pan-Canadian (excluding Quebec)	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.
Alberta	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.

British Columbia	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.
Manitoba	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.
New Brunswick	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.
Newfoundland and Labrador	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.
Northwest Territories	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.
Nova Scotia	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.
Nunavut	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.
Ontario	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.
Prince Edward Island	Not reported in the	Not reported in the	Not reported in the

	supplied CSR: Canadian regional prevalence estimates are not provided.	supplied CSR: Canadian regional prevalence estimates are not provided.	supplied CSR: Canadian regional prevalence estimates are not provided.
Saskatchewan	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.
Yukon	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.
Non-Insured Health Benefits	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.	Not reported in the supplied CSR: Canadian regional prevalence estimates are not provided.

Diagnosis of the Condition

Diagnostic Testing Requirements

Adults ≥ 18 years with BMI ≥ 30 kg/m², or ≥ 27 kg/m² with ≥ 1 treated or untreated weight-related comorbidity (hypertension, dyslipidaemia, obstructive sleep apnoea or cardiovascular disease), and ≥ 1 self-reported unsuccessful dietary weight-loss effort. [CSR PDF p. 37] Trial screening assessed eligibility, HbA1c, mental health using PHQ-9/C-SSRS, and weight/height for BMI; baseline assessments preceded the first dose. [CSR PDF pp. 37-38,43-46] Canadian diagnostic availability, professional restrictions and product-monograph testing requirements are not reported.

Availability of Diagnostic Testing

Not reported in the supplied CSR. Canadian test access and access initiatives are not described.

Health Care Resources

Pre-Treatment Phase

Trial preparation included screening/eligibility assessment, informed consent, food diary instruction, a barriers-and-motivation interview, fasting baseline assessments, diet/activity counselling and pen-handling training. [CSR PDF pp. 43-44] Required Canadian pre-treatment drugs, procedures and recovery resource use are not reported.

Treatment Phase

Trial regimen: 0.25 mg once weekly for 4 weeks, then 0.5, 1.0 and 1.7 mg once weekly for 4 weeks each, then 2.4 mg once weekly for 52 weeks (68 weeks total). If 2.4 mg was not tolerated, 1.7 mg was permitted to avoid complete discontinuation, with an attempt to re-escalate recommended. [CSR PDF pp. 39-40; Tables 9-1 and 9-2] Matched

placebo injection once weekly using the same pen and escalating volumes for 68 weeks; both groups received diet counselling targeting a 500 kcal/day deficit and ≥ 150 minutes/week physical activity, with counselling every 4 weeks. [CSR PDF pp. 39-42] Subjects received pen-handling training at randomisation and on-site visits; injections could be given in thigh, abdomen or upper arm, irrespective of meals. [CSR PDF pp. 40,44] Canadian administration resource costs and mandatory concomitant-drug regimens are not reported.

Post-Treatment Phase

A safety follow-up visit was scheduled 7 weeks after treatment ended, including fasting attendance, to account for semaglutide's long half-life. [CSR PDF pp. 35,44] Post-treatment Canadian drugs, hospitalization and recovery resource requirements are not reported.

Place in Therapy and Comparators

Current Treatment Paradigm

CSR background describes reduced-calorie diet and increased activity as first-line treatment, bariatric surgery as an option for some people with severe obesity, and pharmacotherapy as a potential alternative to achieve and sustain weight loss and improve comorbidities. [CSR PDF pp. 31,36] Current Canadian guidelines, formulary access and a complete Canadian comparator list are not reported.

Unmet Therapeutic Needs

The CSR identifies difficulty achieving and maintaining weight loss with lifestyle intervention, procedural/follow-up burdens of surgery and the need for safer, effective, convenient medicines supporting weight maintenance and comorbidity management. [CSR PDF p. 31]

Impact of Drug on Treatment Paradigm

Proposed Place in Therapy

The trial rationale positions semaglutide 2.4 mg as an adjunct to reduced-calorie diet and increased physical activity in adults with overweight/obesity after an unsuccessful dietary effort. [CSR PDF pp. 32,36-37] A Canadian reimbursement sequence is not reported.

Potential Impact on Currently Reimbursed Treatments

Not reported in the supplied CSR. No Canadian reimbursement-impact analysis or treatment-sequencing diagram is provided.

Provisional Algorithm Diagram (oncology drugs)

Not reported in the supplied CSR. No Canadian reimbursement-impact analysis or treatment-sequencing diagram is provided.

Not reported in the supplied CSR. No Canadian reimbursement-impact analysis or treatment-sequencing diagram is provided.

Comparators

Matched placebo injection once weekly using the same pen and escalating volumes for 68 weeks; both groups received diet counselling targeting a 500 kcal/day deficit and ≥ 150 minutes/week physical activity, with counselling every 4 weeks. [CSR PDF pp. 39-42] Canadian economic-model comparators are not reported.

Table Number: Key characteristics of Drug 1, Drug 2, etc.

Drug	Indication(s)	Route and Dose	Role in Application	
			Included in indirect comparison	Included in PE
Semaglutide [CSR PDF p. 40]	Adults ≥ 18 years with BMI ≥ 30 kg/m ² , or ≥ 27 kg/m ² with ≥ 1 treated or untreated weight-related comorbidity (hypertension, dyslipidaemia, obstructive sleep apnoea or cardiovascular disease), and ≥ 1 self-reported unsuccessful dietary weight-loss effort. [CSR PDF p. 37] Canadian approved indication is not reported.	Trial regimen: 0.25 mg once weekly for 4 weeks, then 0.5, 1.0 and 1.7 mg once weekly for 4 weeks each, then 2.4 mg once weekly for 52 weeks (68 weeks total). If 2.4 mg was not tolerated, 1.7 mg was permitted to avoid complete discontinuation, with an attempt to re-escalate recommended. [CSR PDF pp. 39-40; Tables 9-1 and 9-2]	NA	NA
Placebo plus lifestyle intervention [CSR PDF pp. 39-41]	Not applicable: trial placebo comparator. Used as control with lifestyle intervention. [CSR PDF pp. 37,41]	Matched placebo injection once weekly using the same pen and escalating volumes for 68 weeks; both groups received diet counselling targeting a 500 kcal/day deficit and ≥ 150 minutes/week physical activity, with counselling every 4 weeks. [CSR PDF pp. 39-42]	Not reported in the supplied CSR. Systematic-review/economic-evaluation inclusion is not documented.	Not reported in the supplied CSR. Systematic-review/economic-evaluation inclusion is not documented.
No second study in CSR. [CSR PDF p. 1]	No second study in CSR. [CSR PDF p. 1]	No second study in CSR. [CSR PDF p. 1]	Not reported in the supplied CSR. Systematic-review/economic-evaluation inclusion is not documented.	Not reported in the supplied CSR. Systematic-review/economic-evaluation inclusion is not documented.
Not reported in the supplied CSR. No further Canadian comparator information is provided.	Not reported in the supplied CSR. No further Canadian comparator information is provided.	Not reported in the supplied CSR. No further Canadian comparator information is provided.	Not reported in the supplied CSR. No further Canadian comparator information is provided.	Not reported in the supplied CSR. No further Canadian comparator information is provided.

Source: Trial products and regimens: Tables 9-1 and 9-2; counselling: section 9.4.1.2. No Canadian product monograph is supplied. [CSR PDF pp. 39-41]

Proposed Reimbursement Conditions

Not reported in the supplied CSR: proposed reimbursement conditions and their sponsor rationale are not provided.

Table Number: Proposed Reimbursement Conditions for the Drug Under Review

Proposed reimbursement condition	Reason
Initiation	
Not reported in the supplied CSR: proposed reimbursement conditions and their sponsor rationale are not provided.	Not reported in the supplied CSR: proposed reimbursement conditions and their sponsor rationale are not provided.
Not reported in the supplied CSR: proposed reimbursement conditions and their sponsor rationale are not provided.	Not reported in the supplied CSR: proposed reimbursement conditions and their sponsor rationale are not provided.
Not reported in the supplied CSR.	Not reported in the supplied CSR.
Renewal	
Not reported in the supplied CSR: proposed reimbursement conditions and their sponsor rationale are not provided.	Not reported in the supplied CSR: proposed reimbursement conditions and their sponsor rationale are not provided.
Not reported in the supplied CSR: proposed reimbursement conditions and their sponsor rationale are not provided.	Not reported in the supplied CSR: proposed reimbursement conditions and their sponsor rationale are not provided.
Not reported in the supplied CSR.	Not reported in the supplied CSR.
Discontinuation	
Not reported in the supplied CSR: proposed reimbursement conditions and their sponsor rationale are not provided.	Not reported in the supplied CSR: proposed reimbursement conditions and their sponsor rationale are not provided.
Not reported in the supplied CSR.	Not reported in the supplied CSR.
Prescribing	
Not reported in the supplied CSR: proposed reimbursement conditions and their sponsor rationale are not provided.	Not reported in the supplied CSR: proposed reimbursement conditions and their sponsor rationale are not provided.
Not reported in the supplied CSR.	Not reported in the supplied CSR.

No reimbursement-condition abbreviations required; conditions are not reported in the CSR.

Section 2. Systematic Review

Objectives and Methods

Trial objective: compare semaglutide 2.4 mg weekly versus placebo, adjunctive to diet/activity, for weight loss, efficacy and safety in adults with overweight or obesity. [CSR PDF p. 33] A systematic-review objective/protocol is not supplied.

Review Protocol

Population

Adults ≥ 18 years with BMI ≥ 30 kg/m², or ≥ 27 kg/m² with ≥ 1 treated or untreated weight-related comorbidity (hypertension, dyslipidaemia, obstructive sleep apnoea or cardiovascular disease), and ≥ 1 self-reported unsuccessful dietary weight-loss effort. [CSR PDF p. 37] Canadian label-defined review population and reimbursement subgroups are not reported.

Intervention

Semaglutide 2.4 mg once weekly, subcutaneous solution for injection. Trial products: 1.0 and 3.0 mg/mL in a 3 mL PDS290 pre-filled pen-injector. [CSR PDF pp. 39-40; Table 9-1] The Wegovy brand and marketed Canadian presentations are not established in this CSR. Trial regimen: 0.25 mg once weekly for 4 weeks, then 0.5, 1.0 and 1.7 mg once weekly for 4 weeks each, then 2.4 mg once weekly for 52 weeks (68 weeks total). If 2.4 mg was not tolerated, 1.7 mg was permitted to avoid complete discontinuation, with an attempt to re-escalate recommended. [CSR PDF pp. 39-40; Tables 9-1 and 9-2]

Comparator(s)

Matched placebo injection once weekly using the same pen and escalating volumes for 68 weeks; both groups received diet counselling targeting a 500 kcal/day deficit and ≥ 150 minutes/week physical activity, with counselling every 4 weeks. [CSR PDF pp. 39-42] A Canadian systematic-review/economic-model comparator list is not reported.

Outcomes

Change in body weight (%) from week 0 to week 68, and achieving $\geq 5\%$ baseline body-weight reduction at week 68. [CSR PDF p. 59; Table 9-8] Confirmatory: $\geq 10\%$ and $\geq 15\%$ weight loss at week 68; baseline-to-week-68 change in waist circumference, systolic blood pressure, SF-36 physical functioning and IWQOL-Lite-CT physical function. Supportive: $\geq 20\%$ loss; weight (kg), BMI, diastolic pressure, lipids, CRP, PAI-1, other SF-36/IWQOL scores and physical-function responders, HbA1c, fasting glucose/insulin, leptin and soluble leptin receptor, and DEXA body composition/weight. Safety: TEAEs/SAEs through week 75 and pulse, amylase, lipase, calcitonin change to week 68. [CSR PDF pp. 59-61; Table 9-8] Baseline-to-week-68 glycaemic category, antihypertensive/lipid-lowering medication change, SPS-6 total, fatty liver index category, ICIQ-UI-SF in women; permanent product discontinuation and time to discontinuation through week 68; food diary days and physical activity minutes/week through week 68. [CSR PDF p. 61; Table 9-8]

Study design

One phase 3a, randomised, double-blind, parallel-group, placebo-controlled trial: STEP 1 (NN9536-4373). [CSR PDF pp. 2,35] A systematic-review study-design eligibility protocol is not supplied.

Table 2: Inclusion criteria for the systematic review

Criteria	Description
Population	Adults ≥ 18 years with BMI ≥ 30 kg/m², or ≥ 27 kg/m² with ≥ 1 treated or untreated weight-related comorbidity (hypertension, dyslipidaemia, obstructive sleep apnoea or cardiovascular disease), and ≥ 1 self-reported unsuccessful dietary weight-loss effort. [CSR PDF p. 37] Subgroups: DEXA body-composition subpopulation: acceptable baseline scan and BMI ≤ 40 kg/m²; 140 participants (95 semaglutide; 45 placebo). [CSR PDF pp. 38,72] No systematic-review subgroup list or efficacy treatment-by-subgroup analysis is reported in the supplied CSR.
Intervention	Trial regimen: 0.25 mg once weekly for 4 weeks, then 0.5, 1.0 and 1.7 mg once weekly for 4 weeks each, then 2.4 mg once weekly for 52 weeks (68 weeks total). If 2.4 mg was not tolerated, 1.7 mg was permitted to avoid complete discontinuation, with an attempt to re-escalate recommended. [CSR PDF pp. 39-40; Tables 9-1 and 9-2]
Comparator	Matched placebo injection once weekly using the same pen and escalating volumes for 68 weeks; both groups received diet counselling targeting a 500 kcal/day deficit and ≥ 150 minutes/week physical activity, with counselling every 4 weeks. [CSR PDF pp. 39-42]
Outcomes	Efficacy outcomes: Change in body weight (%) from week 0 to week 68, and achieving $\geq 5\%$ baseline body-weight reduction at week 68. [CSR PDF p. 59; Table 9-8] Confirmatory: $\geq 10\%$ and $\geq 15\%$ weight loss at week 68; baseline-to-week-68 change in waist circumference, systolic blood pressure, SF-36 physical functioning and IWQOL-Lite-CT physical function. Supportive: $\geq 20\%$ loss; weight (kg), BMI, diastolic pressure, lipids, CRP, PAI-1, other SF-36/IWQOL scores and physical-function responders, HbA1c, fasting glucose/insulin, leptin and soluble leptin receptor, and DEXA body composition/weight. Safety: TEAEs/SAEs through week 75 and pulse, amylase, lipase, calcitonin change to week 68. [CSR PDF pp. 59-61; Table 9-8] Baseline-to-week-68 glycaemic category, antihypertensive/lipid-lowering medication change, SPS-6 total, fatty liver index category, ICIQ-UI-SF in women; permanent product discontinuation and time to discontinuation through week 68; food diary days and physical activity minutes/week through week 68. [CSR PDF p. 61; Table 9-8] Harms outcomes: TEAEs, SAEs, permanent discontinuation/temporary interruption due to AEs, deaths, and safety focus areas including gastrointestinal, gallbladder, pancreatitis, cardiovascular, neoplastic, hepatic, renal, hypoglycaemic, immunogenic and psychiatric events. [CSR PDF pp. 61,128-129]
Study Designs	One phase 3a, randomised, double-blind, parallel-group, placebo-controlled trial: STEP 1 (NN9536-4373). [CSR PDF pp. 2,35] A systematic-review study-design eligibility protocol is not supplied.

AE = adverse event; AESI = adverse event of special interest; SAE = serious adverse event; WDAE = withdrawal due to adverse event. Safety categories are defined in sections 9.5.4 and 12. [CSR PDF pp. 48-54,128-129]

Literature Search and Study Selection

Literature Search Methodology

Not reported in the supplied CSR: no systematic literature search or review-selection process is provided.

Not reported in the supplied CSR: no systematic literature search or review-selection process is provided. Not reported in the supplied CSR: no systematic literature search or review-selection process is provided.

Not reported in the supplied CSR: no systematic literature search or review-selection process is provided.

Study Selection

Figure 1: PRISMA Flow Diagram

Not reported in the supplied CSR: no systematic literature search or review-selection process is provided.
Not reported in the supplied CSR: no systematic literature search or review-selection process is provided.

Included Studies

Table 3: Details of Included Studies

	STEP 1 (NN9536-4373; NCT03548935) [CSR PDF p. 2]	No second study in CSR. [CSR PDF p. 1]
Designs & Populations		
Study Design	Phase 3a, multicentre, multinational, randomised (2:1), double-blind, placebo-controlled, two-arm trial. [CSR PDF pp. 2,35,42]	No second study in CSR. [CSR PDF p. 1]
Locations	129 sites in 16 countries: Argentina, Belgium, Bulgaria, Canada (7 sites), Denmark, Finland, France, Germany, India, Japan, Mexico, Poland, Russian Federation, Taiwan, UK and US. [CSR PDF p. 2]	No second study in CSR. [CSR PDF p. 1]
Patient Enrolment Dates:	Start date: Initiated 4 June 2018. [CSR PDF p. 2] End date: Completed 19 April 2020; primary completion 30 March 2020. [CSR PDF p. 2]	Start date: No second study in CSR. [CSR PDF p. 1] End date: No second study in CSR. [CSR PDF p. 1]
Randomized (N)	N=1961: semaglutide 1306; placebo 655. [CSR PDF p. 65; Table 10-1]	No second study in CSR. [CSR PDF p. 1]
Inclusion Criteria	Adults ≥ 18 years with BMI ≥ 30 kg/m ² , or ≥ 27 kg/m ² with ≥ 1 treated or untreated weight-related comorbidity (hypertension, dyslipidaemia, obstructive sleep apnoea or cardiovascular disease), and ≥ 1 self-reported unsuccessful dietary weight-loss effort. [CSR PDF p. 37]	No second study in CSR. [CSR PDF p. 1]
Exclusion Criteria	Key exclusions: HbA1c $\geq 6.5\%$; weight change > 5 kg within 90 days; history of type 1/type 2 diabetes; uncontrolled thyroid disease; severe psychiatric disorders/major depression and suicidality criteria; pregnancy/breast-feeding or inadequate contraception. Prior glucose-lowering drugs (90 days), GLP-1 RA (180 days), obesity medication (90 days), and prior/planned bariatric surgery/device were restricted. Randomisation additionally required food diary adherence, PHQ-9 < 15 and no specified suicidal behaviour/ideation. [CSR PDF pp. 37-38,43,209-210]	No second study in CSR. [CSR PDF p. 1]
Drugs		
Intervention	Trial regimen: 0.25 mg once weekly for 4	No second study in CSR. [CSR PDF p. 1]

	STEP 1 (NN9536-4373; NCT03548935) [CSR PDF p. 2]	No second study in CSR. [CSR PDF p. 1]
	weeks, then 0.5, 1.0 and 1.7 mg once weekly for 4 weeks each, then 2.4 mg once weekly for 52 weeks (68 weeks total). If 2.4 mg was not tolerated, 1.7 mg was permitted to avoid complete discontinuation, with an attempt to re-escalate recommended. [CSR PDF pp. 39-40; Tables 9-1 and 9-2]	
Comparator(s)	Matched placebo injection once weekly using the same pen and escalating volumes for 68 weeks; both groups received diet counselling targeting a 500 kcal/day deficit and ≥ 150 minutes/week physical activity, with counselling every 4 weeks. [CSR PDF pp. 39-42]	No second study in CSR. [CSR PDF p. 1]
Study duration		
• Screening phase	Screening at week -1, randomisation at week 0. [CSR PDF p. 35; Figure 9-1]	No second study in CSR. [CSR PDF p. 1]
• Run-in phase	No separate treatment run-in; a screening interval and food diary requirement preceded randomisation. [CSR PDF pp. 35,38]	No second study in CSR. [CSR PDF p. 1]
• Treatment phase	68 weeks: 16-week escalation plus 52-week maintenance. [CSR PDF pp. 35,40]	No second study in CSR. [CSR PDF p. 1]
• Follow-up phase	7-week off-treatment safety follow-up (week 75); selected participants could enter a planned 52-week off-treatment extension, reported separately. [CSR PDF pp. 35-36]	No second study in CSR. [CSR PDF p. 1]
Outcomes		
Primary End Point	Change in body weight (%) from week 0 to week 68, and achieving $\geq 5\%$ baseline body-weight reduction at week 68. [CSR PDF p. 59; Table 9-8]	No second study in CSR. [CSR PDF p. 1]
Secondary and Exploratory End Points	Secondary: Confirmatory: $\geq 10\%$ and $\geq 15\%$ weight loss at week 68; baseline-to-week-68 change in waist circumference, systolic blood pressure, SF-36 physical functioning and IWQOL-Lite-CT physical function. Supportive: $\geq 20\%$ loss; weight (kg), BMI, diastolic pressure, lipids, CRP, PAI-1, other SF-36/IWQOL scores and physical-function responders, HbA1c, fasting glucose/insulin, leptin and soluble leptin receptor, and DEXA body composition/weight. Safety: TEAEs/SAEs through week 75 and pulse, amylase, lipase, calcitonin change to week 68. [CSR PDF pp. 59-61; Table 9-8] Exploratory: Baseline-to-week-68 glycaemic category, antihypertensive/lipid-lowering medication change, SPS-6 total, fatty liver index category, ICIQ-UI-SF in women; permanent product discontinuation and time to discontinuation through week 68; food diary days and physical	Secondary: No second study in CSR. [CSR PDF p. 1] Exploratory: No second study in CSR. [CSR PDF p. 1]

	STEP 1 (NN9536-4373; NCT03548935) [CSR PDF p. 2]	No second study in CSR. [CSR PDF p. 1]
	activity minutes/week through week 68. [CSR PDF p. 61; Table 9-8]	
Publication status		
Publications	Novo Nordisk. NN9536-4373 (STEP 1), clinical trial report, final version 1.0, 17 August 2020. [CSR PDF pp. 1-2] No STEP 1 journal publication is identified in the supplied report. ClinicalTrials.gov identifier: NCT03548935. [CSR PDF p. 2]	No second study in CSR. [CSR PDF p. 1] No second study in CSR. [CSR PDF p. 1]

AE = adverse event; CI = confidence interval; FAS = full analysis set; OR = odds ratio; SAE = serious adverse event; SD = standard deviation. Terminology follows the CSR. [CSR PDF pp. 25-28]

Source: Novo Nordisk, STEP 1 CSR, final 17 August 2020. Citations use the 1-based PDF page position, not the separate printed text-part page number. [CSR PDF pp. 1-2]

Description of Studies

Included evidence: one supplied CSR for STEP 1; this is not a completed systematic literature review. [CSR PDF pp. 1-2]

Trial objective: compare semaglutide 2.4 mg weekly versus placebo, adjunctive to diet/activity, for weight loss, efficacy and safety in adults with overweight or obesity. [CSR PDF p. 33] A systematic-review objective/protocol is not supplied. STEP 1 compared semaglutide 2.4 mg weekly with placebo, each with lifestyle intervention, for body weight, cardiovascular risk factors, clinical outcome assessments, glucose metabolism, other weight-related factors, safety and tolerability. [CSR PDF p. 33] A systematic-review protocol is not reported. Phase 3a, multicentre, multinational, randomised (2:1), double-blind, placebo-controlled, two-arm trial. [CSR PDF pp. 2,35,42] 129 sites in 16 countries: Argentina, Belgium, Bulgaria, Canada (7 sites), Denmark, Finland, France, Germany, India, Japan, Mexico, Poland, Russian Federation, Taiwan, UK and US. [CSR PDF p. 2] N=1961: semaglutide 1306; placebo 655. [CSR PDF p. 65; Table 10-1] Central allocation used IWRS; subjects, investigators and sponsor remained blinded through treatment/follow-up and database lock. [CSR PDF p. 42] Stratification is not stated in the supplied CSR. Data cut-off: 11 May 2020 except antibodies/pharmacokinetics, cut off 1 July 2020. [CSR PDF p. 2]

Eligibility Criteria

Adults ≥ 18 years with BMI ≥ 30 kg/m², or ≥ 27 kg/m² with ≥ 1 treated or untreated weight-related comorbidity (hypertension, dyslipidaemia, obstructive sleep apnoea or cardiovascular disease), and ≥ 1 self-reported unsuccessful dietary weight-loss effort. [CSR PDF p. 37] Diabetes was excluded; the separate STEP 2 trial was intended to address people with type 2 diabetes. [CSR PDF p. 36] Key exclusions: HbA1c $\geq 6.5\%$; weight change > 5 kg within 90 days; history of type 1/type 2 diabetes; uncontrolled thyroid disease; severe psychiatric disorders/major depression and suicidality criteria; pregnancy/breast-feeding or inadequate contraception. Prior glucose-lowering drugs (90 days), GLP-1 RA (180 days), obesity medication (90 days), and prior/planned bariatric surgery/device were restricted. Randomisation additionally required food diary adherence, PHQ-9 < 15 and no specified suicidal behaviour/ideation. [CSR PDF pp. 37-38,43,209-210]

Interventions

Trial regimen: 0.25 mg once weekly for 4 weeks, then 0.5, 1.0 and 1.7 mg once weekly for 4 weeks each, then 2.4 mg once weekly for 52 weeks (68 weeks total). If 2.4 mg was not tolerated, 1.7 mg was permitted to avoid complete discontinuation, with an attempt to re-escalate recommended. [CSR PDF pp. 39-40; Tables 9-1 and 9-2] Matched placebo injection once weekly using the same pen and escalating volumes for 68 weeks; both groups received diet counselling targeting a 500 kcal/day deficit and ≥ 150 minutes/week physical activity, with counselling every 4 weeks. [CSR PDF pp. 39-42] Products were identical in appearance and packaging. Pen training occurred at randomisation and site visits. Subjects administered weekly injections in thigh, abdomen or upper arm; dose reminders supported escalation. [CSR PDF pp. 40-44] Product discontinuation criteria included safety concerns, calcitonin ≥ 100 ng/L, suspected pancreatitis, pregnancy/intention to conceive, or another investigational trial. Subjects discontinuing product were encouraged to stay in follow-up. [CSR PDF pp. 38-39] Whether the trial pen matches the Canadian marketed device is not reported.

Outcomes

Baseline efficacy assessments were at randomisation unless specified. Weight used a calibrated digital scale, without shoes, with empty bladder and light clothing; BMI was calculated from weight and height; waist was measured midway between lower rib and iliac crest. [CSR PDF p. 45] Change in body weight (%) from week 0 to week 68, and achieving $\geq 5\%$ baseline body-weight reduction at week 68. [CSR PDF p. 59; Table 9-8] Confirmatory: $\geq 10\%$ and $\geq 15\%$ weight loss at week 68; baseline-to-week-68 change in waist circumference, systolic blood pressure, SF-36 physical functioning and IWQOL-Lite-CT physical function. Supportive: $\geq 20\%$ loss; weight (kg), BMI, diastolic pressure, lipids, CRP, PAI-1, other SF-36/IWQOL scores and physical-function responders, HbA1c, fasting glucose/insulin, leptin and soluble leptin receptor, and DEXA body composition/weight. Safety: TEAEs/SAEs through week 75 and pulse, amylase, lipase, calcitonin change to week 68. [CSR PDF pp. 59-61; Table 9-8] SF-36 is a 36-item generic HRQoL measure with 8 domains and physical/mental summaries; IWQOL-Lite-CT is a 20-item weight-related instrument. Higher scores indicate better function; SF-36 uses norm-based T-scores (mean 50, SD 10), IWQOL scores range 0-100. Within-person physical-function responder thresholds were 4.3 (SF-36) and 20 (IWQOL) (prespecified in the CSR); these are not between-group MIDs. [CSR PDF pp. 45-46,112-115,117,120] An independent external EAC adjudicated selected deaths, cardiovascular events, pancreatitis and malignant neoplasms. Treatment-emergent AEs were defined by onset during on-treatment exposure including 49 days after dosing. [CSR PDF pp. 49-54,128-129] Formal surrogate validation and between-group MIDs are not reported.

Table 4: Summary of Outcomes Relevant to the Systematic Review

Outcome Measure	Timepoint	Study 1	Study 2
Change in body weight (%) from week 0 to week 68, and achieving $\geq 5\%$ baseline body-weight reduction at week 68. [CSR PDF p. 59; Table 9-8]	Week 68 versus week 0. [CSR PDF p. 59]	Co-primary*; multiplicity-controlled treatment-policy analyses. [CSR PDF pp. 34,87]	No second study in CSR. [CSR PDF p. 1]
Confirmatory: $\geq 10\%$ and $\geq 15\%$ weight loss at week 68; baseline-to-week-68 change in waist circumference, systolic blood pressure, SF-36 physical functioning and IWQOL-Lite-CT physical function. Supportive: $\geq 20\%$ loss; weight (kg), BMI, diastolic pressure, lipids, CRP, PAI-1, other SF-36/IWQOL scores and physical-function responders, HbA1c, fasting glucose/insulin, leptin and soluble leptin receptor, and DEXA body composition/weight. Safety: TEAEs/SAEs through week 75 and pulse, amylase, lipase, calcitonin change to week 68. [CSR PDF pp. 59-61; Table 9-8] Baseline-to-week-68 glycaemic category,	Week 68 efficacy; week 75 TEAEs/SAEs. [CSR PDF pp. 59-61]	Confirmatory secondary* and supportive secondary/exploratory as specified in this row; * hierarchical testing applies only to confirmatory endpoints. [CSR PDF pp. 59-61,87]	No second study in CSR. [CSR PDF p. 1]

Outcome Measure	Timepoint	Study 1	Study 2
antihypertensive/lipid-lowering medication change, SPS-6 total, fatty liver index category, ICIQ-UI-SF in women; permanent product discontinuation and time to discontinuation through week 68; food diary days and physical activity minutes/week through week 68. [CSR PDF p. 61; Table 9-8]			
No further outcomes beyond those listed in the preceding row. [CSR PDF pp. 59-61]	No further outcomes beyond those listed in the preceding row. [CSR PDF pp. 59-61]	No further outcomes beyond those listed in the preceding row. [CSR PDF pp. 59-61]	No further outcomes beyond those listed in the preceding row. [CSR PDF pp. 59-61]

* Statistical testing for these endpoints was adjusted for multiple comparisons (e.g., hierarchical testing)

AE = adverse event; CI = confidence interval; FAS = full analysis set; OR = odds ratio; SAE = serious adverse event; SD = standard deviation. Terminology follows the CSR. [CSR PDF pp. 25-28]

Source: Novo Nordisk, STEP 1 CSR, final 17 August 2020. Citations use the 1-based PDF page position, not the separate printed text-part page number. [CSR PDF pp. 1-2]

Statistical analysis

Clinical Trial Endpoints

Primary treatment-policy estimand uses all randomised subjects regardless of treatment interruptions/discontinuation or other anti-obesity therapy. Week-68 continuous outcomes use ANCOVA with randomised treatment and baseline endpoint covariate; weight-loss responder outcomes use logistic regression with treatment and baseline body weight. Missing values undergo 1000 multiple imputations from retrieved participants in the same arm, grouped using timing of last on-treatment observation. This assumes missing participants resemble the corresponding retrieved participants conditional on imputation predictors. [CSR PDF pp. 33-34,62,93,333] The hypothetical estimand uses on-treatment measurements before first discontinuation or other anti-obesity therapy; MMRM includes treatment and baseline value, nested within visit. Missing-data inference relies on the model; no noninferiority comparison or historical control was used. [CSR PDF pp. 34-36,342] Sensitivity analyses: jump-to-reference imputation from placebo (1000 imputations); single imputation adding 0.3 kg/month regain to last value until baseline, for both arms or semaglutide only; MMRM. The $\geq 5\%$ responder analysis also treats missing responses as nonresponders. Two-way tipping-point penalties ranged -30% to +30% in 1% steps without overturning superiority. [CSR PDF pp. 92,94,334,346] For ratio outcomes such as lipids, ratio-to-baseline and baseline values are log-transformed for ANCOVA; results are back-transformed ratios. [CSR PDF pp. 441-443]

Table 5: Statistical Analysis of Efficacy Endpoints

Endpoint	Statistical Model	Adjustment Factors	Handling of missing data	Sensitivity Analyses
Study 1				
Change in body weight (%) from	ANCOVA for percentage weight	Treatment factor and baseline body-weight	1000 retrieved-participant multiple	Sensitivity analyses: jump-to-reference imputation from

Endpoint	Statistical Model	Adjustment Factors	Handling of missing data	Sensitivity Analyses
week 0 to week 68, and achieving $\geq 5\%$ baseline body-weight reduction at week 68. [CSR PDF p. 59; Table 9-8]	change; binary logistic regression for $\geq 5\%$ response. [CSR PDF pp. 93,333]	covariate. [CSR PDF pp. 93,333]	imputations within treatment arm; timing of last on-treatment observation informs groups. [CSR PDF pp. 62,93,333]	placebo (1000 imputations); single imputation adding 0.3 kg/month regain to last value until baseline, for both arms or semaglutide only; MMRM. The $\geq 5\%$ responder analysis also treats missing responses as nonresponders. Two-way tipping-point penalties ranged -30% to +30% in 1% steps without overturning superiority. [CSR PDF pp. 92,94,334,346]
Confirmatory: $\geq 10\%$ and $\geq 15\%$ weight loss at week 68; baseline-to-week-68 change in waist circumference, systolic blood pressure, SF-36 physical functioning and IWQOL-Lite-CT physical function. Supportive: $\geq 20\%$ loss; weight (kg), BMI, diastolic pressure, lipids, CRP, PAI-1, other SF-36/IWQOL scores and physical-function responders, HbA1c, fasting glucose/insulin, leptin and soluble leptin receptor, and DEXA body composition/weight. Safety: TEAEs/SAEs through week 75 and pulse, amylase, lipase, calcitonin change to week 68. [CSR PDF pp. 59-61; Table 9-8]	Continuous: ANCOVA; binary: logistic regression. [CSR PDF pp. 362,371,400,418,462,488]	Treatment and corresponding baseline value; baseline body weight for weight-loss response. [CSR PDF pp. 362,371,400,418,462,488]	Retrieved-participant multiple imputation (1000 datasets) for confirmatory continuous endpoints. [CSR PDF pp. 371,418,462,488]	Jump-to-reference sensitivity analyses for confirmatory continuous outcomes; hypothetical MMRM as complementary estimand. [CSR PDF pp. 97,107,113-114,117-119]
Study 2				
No second study in CSR. [CSR PDF p. 1]	No second study in CSR. [CSR PDF p. 1]	No second study in CSR. [CSR PDF p. 1]	Not applicable: no second study is	No second study in CSR. [CSR PDF p. 1]

Endpoint	Statistical Model	Adjustment Factors	Handling of missing data	Sensitivity Analyses
1]			reported in this CSR. [CSR PDF pp. 1-2]	

AE = adverse event; CI = confidence interval; FAS = full analysis set; OR = odds ratio; SAE = serious adverse event; SD = standard deviation. Terminology follows the CSR. [CSR PDF pp. 25-28]

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Sample Size and Power Calculation

Planned N=1950 (1300 semaglutide, 650 placebo), driven by safety exposure/regulatory requirements; effective power 99% for the eight hierarchical efficacy endpoints. SAP updated IWQOL physical-function power using trials NN9536-4153 and NN9924-4233 without changing N. [CSR PDF pp. 36,62] Numeric effect/SD/dropout assumptions are not reproduced in the supplied report; it refers to protocol/SAP appendices for calculations.

Statistical Testing

Superiority trial; confirmatory treatment-policy testing used a prespecified hierarchy: percentage weight change, $\geq 5\%$, $\geq 10\%$, $\geq 15\%$ weight-loss response, waist circumference, systolic blood pressure, SF-36 physical functioning, IWQOL physical function. Local two-sided alpha was 0.05 at each reached test, with family-wise error controlled by the hierarchy; reported p-values are unadjusted two-sided values. All eight tests passed. Final main-phase analyses; no interim or post-hoc analyses were performed. [CSR PDF pp. 34-36,63,87] Primary treatment-policy estimand uses all randomised subjects regardless of treatment interruptions/discontinuation or other anti-obesity therapy. Week-68 continuous outcomes use ANCOVA with randomised treatment and baseline endpoint covariate; weight-loss responder outcomes use logistic regression with treatment and baseline body weight. Missing values undergo 1000 multiple imputations from retrieved participants in the same arm, grouped using timing of last on-treatment observation. This assumes missing participants resemble the corresponding retrieved participants conditional on imputation predictors. [CSR PDF pp. 33-34,62,93,333] The hypothetical estimand uses on-treatment measurements before first discontinuation or other anti-obesity therapy; MMRM includes treatment and baseline value, nested within visit. Missing-data inference relies on the model; no noninferiority comparison or historical control was used. [CSR PDF pp. 34-36,342]

Subgroup Analyses

No treatment-by-subgroup efficacy analyses, subgroup multiplicity adjustment or subgroup interaction tests are reported in the supplied CSR. DEXA was a prespecified subpopulation (acceptable screening scan, BMI ≤ 40 kg/m²). [CSR PDF pp. 35,38,58]

Analysis populations

Analysis sets were defined before unblinding: FAS, SAS and DEXA. All 1961 randomised participants were exposed, so FAS and SAS contained the same people. [CSR PDF pp. 58,65-66]

Table 6: Analysis Populations of Study 1 and Study 2

Study	Population	Definition	Application
Study 1	FAS [CSR PDF p. 58]	All randomised participants, evaluated as randomised: 1306 semaglutide; 655 placebo. [CSR PDF pp. 58,65]	Efficacy analyses and baseline summaries. [CSR PDF pp. 58,68-70]
	SAS [CSR PDF p. 58]	All randomised participants receiving ≥ 1 dose, evaluated as treated: 1306 semaglutide; 655 placebo. [CSR PDF pp. 58,65]	Safety analyses. [CSR PDF pp. 58,127-129]
	DEXA analysis set [CSR PDF p. 58]	FAS subset with acceptable baseline DEXA scan: 140 participants (95 semaglutide, 45 placebo).	Body-composition analyses. [CSR PDF pp. 58,102-103]

Study	Population	Definition	Application
		[CSR PDF pp. 58,72]	
Study 2	No second study in CSR. [CSR PDF p. 1]	No second study in CSR. [CSR PDF p. 1]	No second study in CSR. [CSR PDF p. 1]

AE = adverse event; CI = confidence interval; FAS = full analysis set; OR = odds ratio; SAE = serious adverse event; SD = standard deviation. Terminology follows the CSR. [CSR PDF pp. 25-28]

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Patient Population

Baseline characteristics

Baseline is the last eligible observation at or before randomisation; the FAS includes 1306 semaglutide and 655 placebo participants. [CSR PDF pp. 58,69-70]

Table 7: Summary of Baseline Characteristics of Study 1 and Study 2

Characteristic	Study 1		Study 2	
	Semaglutide 2.4 mg [CSR PDF p. 65] (N = 1306 [CSR PDF p. 65])	Placebo [CSR PDF p. 65] (N = 655 [CSR PDF p. 65])	No second study in CSR. [CSR PDF p. 1] (N = No second study in CSR. [CSR PDF p. 1])	No second study in CSR. [CSR PDF p. 1] (N = No second study in CSR. [CSR PDF p. 1])
Age; sex; race (FAS)	Age 46 (SD 13) years; median 46, range 18-86. Female 955 (73.1%); White 973 (74.5%); Asian 181 (13.9%); Black 72 (5.5%). [CSR PDF pp. 69-70; Tables 10-2/10-3]	Age 47 (SD 12) years; median 48, range 18-82. Female 498 (76.0%); White 499 (76.2%); Asian 80 (12.2%); Black 39 (6.0%). [CSR PDF pp. 69-70; Tables 10-2/10-3]	No second study in CSR. [CSR PDF p. 1]	No second study in CSR. [CSR PDF p. 1]
Weight; BMI; waist (FAS), mean (SD)	Weight 105.4 (22.1) kg; median 102.1, range 61.8-245.6. BMI 37.8 (6.7) kg/m ² ; waist 114.6 (14.8) cm; n=1306 each. [CSR PDF p. 70; Table 10-3]	Weight 105.2 (21.5) kg; median 101.3, range 66.3-211.0. BMI 38.0 (6.5) kg/m ² ; waist 114.8 (14.4) cm; n=655 each. [CSR PDF p. 70; Table 10-3]	No second study in CSR. [CSR PDF p. 1]	No second study in CSR. [CSR PDF p. 1]
Glycaemia and comorbidity (FAS)	HbA1c 5.7 (0.3)%, n=1306; fasting glucose 5.3 (0.6) mmol/L, n=1291 (15 missing). Prediabetes approximately 45%. [CSR PDF pp. 68,70] Overall population: dyslipidaemia 37.0%, hypertension 36.0%, knee osteoarthritis 14.0%, sleep apnoea 11.7%. [CSR PDF p. 71]	HbA1c 5.7 (0.3)%, n=655; fasting glucose 5.3 (0.6) mmol/L, n=649 (6 missing). Prediabetes approximately 40%. [CSR PDF pp. 68,70] Comorbidity proportions were similar between arms. [CSR PDF p. 71]	No second study in CSR. [CSR PDF p. 1]	No second study in CSR. [CSR PDF p. 1]

AE = adverse event; CI = confidence interval; FAS = full analysis set; OR = odds ratio; SAE = serious adverse event; SD = standard deviation. Terminology follows the CSR. [CSR PDF pp. 25-28]

Source: Novo Nordisk, STEP 1 CSR, final 17 August 2020. Citations use the 1-based PDF page position, not the separate printed text-part page number. [CSR PDF pp. 1-2]

Patient Disposition

2303 screened, 305 failed screening, 37 withdrew before randomisation; 1961 randomised and exposed. Trial completers: 1240/1306 (94.9%) and 609/655 (93.0%). Treatment completers: 1083 (82.9%) and 508 (77.6%). [CSR PDF pp. 65-66]

Table 8: Sample Table for Patient Disposition

Patient disposition	Study 1		Study 2	
	Semaglutide 2.4 mg [CSR PDF p. 65] (N = 1306 [CSR PDF p. 65])	Placebo [CSR PDF p. 65] (N = 655 [CSR PDF p. 65])	No second study in CSR. [CSR PDF p. 1] (N = No second study in CSR. [CSR PDF p. 1])	No second study in CSR. [CSR PDF p. 1] (N = No second study in CSR. [CSR PDF p. 1])
Screened, N	2303 total before randomisation; not allocated by arm. [CSR PDF p. 65]	2303 total before randomisation; not allocated by arm. [CSR PDF p. 65]	No second study in CSR. [CSR PDF p. 1]	No second study in CSR. [CSR PDF p. 1]
Reason for screening failure, N (%)	305 total (13.2% of 2303 screened); 37 pre-randomisation withdrawals separately. [CSR PDF p. 65]	Pooled screening population, before allocation. [CSR PDF p. 65]	Not applicable: no second study is reported in this CSR. [CSR PDF pp. 1-2]	Not applicable: no second study is reported in this CSR. [CSR PDF pp. 1-2]
HbA1c $\geq 6.5\%$	120/305 screen failures (39.3%), pooled before allocation. [CSR PDF pp. 68,209]	120/305 screen failures (39.3%), pooled before allocation. [CSR PDF pp. 68,209]	No second study in CSR. [CSR PDF p. 1]	No second study in CSR. [CSR PDF p. 1]
Uncontrolled thyroid disease	81/305 (26.6%), pooled before allocation. [CSR PDF pp. 68,209]	81/305 (26.6%), pooled before allocation. [CSR PDF pp. 68,209]	No second study in CSR. [CSR PDF p. 1]	No second study in CSR. [CSR PDF p. 1]
Other screening failures	Investigator concern 38 (12.5%); PHQ-9 ≥ 15 : 18 (5.9%); past suicide attempt 8 (2.6%); reasons may overlap. [CSR	Pooled before allocation; denominator 305 failures. [CSR PDF p. 68]	Not applicable: no second study is reported in this CSR. [CSR PDF pp. 1-2]	Not applicable: no second study is reported in this CSR. [CSR PDF pp. 1-2]

Patient disposition	Study 1		Study 2	
	PDF p. 68]			
Randomized, N (%)	1306 (100%) [CSR PDF pp. 65-66; Table 10-1]	655 (100%) [CSR PDF pp. 65-66; Table 10-1]	No second study in CSR. [CSR PDF p. 1]	No second study in CSR. [CSR PDF p. 1]
Discontinued from study, N (%)	66 (5.1%) [CSR PDF pp. 65-66; Table 10-1]	46 (7.0%) [CSR PDF pp. 65-66; Table 10-1]	No second study in CSR. [CSR PDF p. 1]	No second study in CSR. [CSR PDF p. 1]
Reason for discontinuation, N (%)	Subject withdrawal 26 (2.0%); death 1 (<0.1%). [CSR PDF p. 66]	Subject withdrawal 17 (2.6%); death 1 (0.2%). [CSR PDF p. 66]	Not applicable: no second study is reported in this CSR. [CSR PDF pp. 1-2]	Not applicable: no second study is reported in this CSR. [CSR PDF pp. 1-2]
Adverse events	4 consent withdrawals mentioning AEs, plus 1 death; not systematically collected; primary disposition category is not AE. [CSR PDF pp. 136-137; Table 12-7]	1 consent withdrawal mentioning AEs, plus 1 death; not systematically collected; primary disposition category is not AE. [CSR PDF pp. 136-137; Table 12-7]	No second study in CSR. [CSR PDF p. 1]	No second study in CSR. [CSR PDF p. 1]
Lost to follow-up	39 (3.0%) [CSR PDF pp. 65-66; Table 10-1]	28 (4.3%) [CSR PDF pp. 65-66; Table 10-1]	No second study in CSR. [CSR PDF p. 1]	No second study in CSR. [CSR PDF p. 1]
Permanent product discontinuation	223 (17.1%); AE disposition reason 91 (7.0%). [CSR PDF p. 65]	147 (22.4%); AE disposition reason 21 (3.2%). [CSR PDF p. 65]	Not applicable: no second study is reported in this CSR. [CSR PDF pp. 1-2]	Not applicable: no second study is reported in this CSR. [CSR PDF pp. 1-2]
FAS, N	1306 [CSR PDF pp. 65-66; Table 10-1]	655 [CSR PDF pp. 65-66; Table 10-1]	No second study in CSR. [CSR PDF p. 1]	No second study in CSR. [CSR PDF p. 1]
PP, N	Not applicable: no PP analysis set defined. [CSR PDF p. 58]	Not applicable: no PP analysis set defined. [CSR PDF p. 58]	No second study in CSR. [CSR PDF p. 1]	No second study in CSR. [CSR PDF p. 1]
Safety, N	1306 [CSR PDF pp. 65-66; Table 10-1]	655 [CSR PDF pp. 65-66; Table 10-1]	No second study in CSR. [CSR PDF p. 1]	No second study in CSR. [CSR PDF p. 1]

AE = adverse event; CI = confidence interval; FAS = full analysis set; OR = odds ratio; SAE = serious adverse event; SD = standard deviation. Terminology follows the CSR. [CSR PDF pp. 25-28]

Source: Novo Nordisk, STEP 1 CSR, final 17 August 2020. Citations use the 1-based PDF page position, not the separate printed text-part page number. [CSR PDF pp. 1-2]

Exposure to Interventions

Study treatments

Mean on-treatment exposure was 59.2 versus 57.4 weeks; total exposure 1480.8 versus 720.9 patient-years (semaglutide versus placebo). This efficacy observation definition differs from the +7-week AE exposure window (1706.1 versus 829.6 patient-years). [CSR PDF pp. 58,73,128] At last dose, 89.6% versus 98.0% of treatment completers reached maintenance dose/equivalent placebo volume. Compliance was assessed by missed-dose questioning and diaries. [CSR PDF pp. 73-74]

Table 9: Sample Table for Patient Exposure

Exposure	Study 1		Study 2	
	Semaglutide 2.4 mg [CSR PDF p. 65] (N = 1306 [CSR PDF p. 65])	Placebo [CSR PDF p. 65] (N = 655 [CSR PDF p. 65])	No second study in CSR. [CSR PDF p. 1] (N = No second study in CSR. [CSR PDF p. 1])	No second study in CSR. [CSR PDF p. 1] (N = No second study in CSR. [CSR PDF p. 1])
Total, patient-weeks or patient-years	1480.8 patient-years to first discontinuation; 1570.0 including subsequent on-treatment periods (+14 days). [CSR PDF p. 310; Table 14.1.23]	720.9 patient-years to first discontinuation; 763.1 including subsequent on-treatment periods (+14 days). [CSR PDF p. 310; Table 14.1.23]	No second study in CSR. [CSR PDF p. 1]	No second study in CSR. [CSR PDF p. 1]
Duration, mean (SD)	59.2 (20.2) weeks to first product discontinuation; total on-treatment (+14 days) 62.7 (16.5) weeks. [CSR PDF p. 310; Table 14.1.23]	57.4 (20.6) weeks to first product discontinuation; total on-treatment (+14 days) 60.8 (17.4) weeks. [CSR PDF p. 310; Table 14.1.23]	No second study in CSR. [CSR PDF p. 1]	No second study in CSR. [CSR PDF p. 1]
Duration, median (IQR or range)	69.1 weeks (range 2.1-73.1), first-discontinuation period; IQR not reported. [CSR PDF p. 310; Table 14.1.23]	69.1 weeks (range 0.1-74.7), first-discontinuation period; IQR not reported. [CSR PDF p. 310; Table 14.1.23]	No second study in CSR. [CSR PDF p. 1]	No second study in CSR. [CSR PDF p. 1]
Adherence, %	A single dose-adherence percentage is not reported; 89.6% of treatment completers received 2.4 mg at last dose. [CSR PDF pp.	A single dose-adherence percentage is not reported; 98.0% of treatment completers received maintenance-equivalent volume at last dose. [CSR	No second study in CSR. [CSR PDF p. 1]	No second study in CSR. [CSR PDF p. 1]

	73-74]	PDF pp. 73-74]		
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AE = adverse event; CI = confidence interval; FAS = full analysis set; OR = odds ratio; SAE = serious adverse event; SD = standard deviation. Terminology follows the CSR. [CSR PDF pp. 25-28]

Source: Novo Nordisk, STEP 1 CSR, final 17 August 2020. Citations use the 1-based PDF page position, not the separate printed text-part page number. [CSR PDF pp. 1-2]

Concomitant medications and co-interventions

Matched placebo injection once weekly using the same pen and escalating volumes for 68 weeks; both groups received diet counselling targeting a 500 kcal/day deficit and ≥ 150 minutes/week physical activity, with counselling every 4 weeks. [CSR PDF pp. 39-42] Baseline medications overall included renin-angiotensin agents 23.6%, anti-inflammatory/antirheumatic drugs 21.5%, lipid-modifying agents 18.5%, psychoanaleptics 14.7%, analgesics 14.3%, diuretics 11.1%, beta blockers 10.6%. Initiated after randomisation (semaglutide/placebo): acid-related drugs 26.2%/13.0%, functional GI drugs 13.8%/4.6%, antidiarrheals 10.0%/3.7%, constipation drugs 8.4%/4.1%, antiemetics 8.2%/3.1%. [CSR PDF pp. 71-72] New anti-obesity therapy was prohibited and participants starting it were instructed to stop it; changes in concomitant treatment were recorded at visits. [CSR PDF p. 43]

Subsequent treatment (if applicable)

No protocol crossover. Other anti-obesity medication was used by 5 (0.4%) versus 10 (1.5%) participants and bariatric surgery by 2 (0.2%) versus 3 (0.5%) during the trial (semaglutide/placebo), despite restrictions. [CSR PDF pp. 43,72]

Table Number: Sample Table for Subsequent Treatment

Exposure	Study 1		Study 2	
	Semaglutide 2.4 mg [CSR PDF p. 65] (N = 1306 [CSR PDF p. 65])	Placebo [CSR PDF p. 65] (N = 655 [CSR PDF p. 65])	No second study in CSR. [CSR PDF p. 1] (N = No second study in CSR. [CSR PDF p. 1])	No second study in CSR. [CSR PDF p. 1] (N = No second study in CSR. [CSR PDF p. 1])
Received subsequent therapy, n (%)	Combined unique-person total across medication and surgery not reported; components below. [CSR PDF p. 72]	Combined unique-person total across medication and surgery not reported; components below. [CSR PDF p. 72]	No second study in CSR. [CSR PDF p. 1]	No second study in CSR. [CSR PDF p. 1]
Other anti-obesity medication, n (%)	5 (0.4%) [CSR PDF p. 72]	10 (1.5%) [CSR PDF p. 72]	No second study in CSR. [CSR PDF p. 1]	No second study in CSR. [CSR PDF p. 1]
Bariatric surgery, n (%)	2 (0.2%) [CSR PDF p. 72]	3 (0.5%) [CSR PDF p. 72]	No second study in CSR. [CSR PDF p. 1]	No second study in CSR. [CSR PDF p. 1]
Additional subsequent therapies	Not reported in the supplied CSR.	Not reported in the supplied CSR.	Not applicable: no second study is reported in this CSR. [CSR PDF pp. 1-2]	Not applicable: no second study is reported in this CSR. [CSR PDF pp. 1-2]

AE = adverse event; CI = confidence interval; FAS = full analysis set; OR = odds ratio; SAE = serious adverse event; SD = standard deviation. Terminology follows the CSR. [CSR PDF pp. 25-28]

Source: Novo Nordisk, STEP 1 CSR, final 17 August 2020. Citations use the 1-based PDF page position, not the separate printed text-part page number. [CSR PDF pp. 1-2]

Results

Efficacy

At week 68, treatment-policy estimated weight change was -14.85% with semaglutide and -2.41% with placebo: difference -12.44 percentage points (95% CI -13.37 to -11.51), $p < 0.0001$. FAS $n = 1306/655$; observed week-68 weight $n = 1212/577$. [CSR PDF p. 333; Table 14.2.9] Observed week-68 $\geq 5\%$ loss: 1047/1212 (86.4%) versus 182/577 (31.5%); adjusted treatment-policy OR 11.22 (95% CI 8.88-14.19), $p < 0.0001$. Observed $\geq 10\%$, $\geq 15\%$, $\geq 20\%$ responses were 69.1%, 50.5%, 32.0% versus 12.0%, 4.9%, 1.7%. [CSR PDF pp. 87,344-345; Tables 11-1, 14.2.24-25] Confirmatory week-68 treatment-policy differences: waist -9.42 cm (95% CI -10.30 to -8.53), systolic BP -5.10 mmHg (-6.34 to -3.87), SF-36 physical functioning +1.80 (1.18-2.42), IWQOL physical function +9.43 (7.50-11.35); all $p < 0.0001$. $\geq 10\%$ and $\geq 15\%$ weight-loss ORs were 14.68 (11.08-19.44) and 19.26 (12.89-28.76). [CSR PDF p. 87; Table 11-1]

Summary of efficacy outcomes

At week 68, treatment-policy estimated weight change was -14.85% with semaglutide and -2.41% with placebo: difference -12.44 percentage points (95% CI -13.37 to -11.51), $p < 0.0001$. FAS $n = 1306/655$; observed week-68 weight $n = 1212/577$. [CSR PDF p. 333; Table 14.2.9]

Not reported: overall-survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]

The CSR reports continuous treatment differences and response odds ratios with 95% CIs; absolute risk differences with CIs are not reported. [CSR PDF pp. 87,333,345]

Table 10: Sample table for key efficacy outcomes

	Study 1 Semaglutide 2.4 mg [CSR PDF p. 65] (N = 1306 [CSR PDF p. 65])	Study 1 Placebo [CSR PDF p. 65] (N = 655 [CSR PDF p. 65])	Study 2 No second study in CSR. [CSR PDF p. 1] (N = No second study in CSR. [CSR PDF p. 1])	Study 2 No second study in CSR. [CSR PDF p. 1] (N = No second study in CSR. [CSR PDF p. 1])
Percentage body-weight change at week 68 [CSR PDF p. 59]				
Number of patients contributing to the analysis	1306 FAS; 1212 observed [CSR PDF p. 333]	655 FAS; 577 observed [CSR PDF p. 333]	No second study in CSR. [CSR PDF p. 1]	No second study in CSR. [CSR PDF p. 1]
Baseline, mean (SD)	105.4 (22.1) kg; percentage change defined relative to this baseline. [CSR PDF p. 70]	105.2 (21.5) kg; percentage change defined relative to this baseline. [CSR PDF p. 70]	No second study in CSR. [CSR PDF p. 1]	No second study in CSR. [CSR PDF p. 1]
Change from baseline, mean (95% CI preferred; SE if not available)	-14.85%; arm CI/SE not reported in this analysis table. [CSR PDF p. 333]	-2.41%; arm CI/SE not reported in this analysis table. [CSR PDF p. 333]	No second study in CSR. [CSR PDF p. 1]	No second study in CSR. [CSR PDF p. 1]
Treatment group difference versus control (95% CI)	-12.44 percentage points (95% CI -13.37 to -11.51) [CSR PDF p. 333]	Reference comparator [CSR PDF p. 333]	No second study in CSR. [CSR PDF p. 1]	No second study in CSR. [CSR PDF p. 1]
P value	< 0.0001 ; hierarchical test,	Reference comparator;	No second study in CSR. [CSR PDF p.	No second study in CSR.

	Study 1 Semaglutide 2.4 mg [CSR PDF p. 65] (N = 1306 [CSR PDF p. 65])	Study 1 Placebo [CSR PDF p. 65] (N = 655 [CSR PDF p. 65])	Study 2 No second study in CSR. [CSR PDF p. 1] (N = No second study in CSR. [CSR PDF p. 1])	Study 2 No second study in CSR. [CSR PDF p. 1] (N = No second study in CSR. [CSR PDF p. 1])
	local alpha 0.05. [CSR PDF pp. 87,333]	between-arm p<0.0001. [CSR PDF pp. 87,333]	1]	[CSR PDF p. 1]
≥5% baseline body-weight loss at week 68 [CSR PDF p. 59]				
n (%)	1047/1212 (86.4%), observed [CSR PDF p. 344]	182/577 (31.5%), observed [CSR PDF p. 344]	No second study in CSR. [CSR PDF p. 1]	No second study in CSR. [CSR PDF p. 1]
OR/RR (95% CI)	OR 11.22 (95% CI 8.88-14.19) [CSR PDF p. 345]	Reference comparator [CSR PDF p. 345]	No second study in CSR. [CSR PDF p. 1]	No second study in CSR. [CSR PDF p. 1]
RD (95% CI)	Risk difference and CI not reported; observed response proportions shown above. [CSR PDF pp. 344-345]	Risk difference and CI not reported; observed response proportions shown above. [CSR PDF pp. 344-345]	No second study in CSR. [CSR PDF p. 1]	No second study in CSR. [CSR PDF p. 1]
P value	<0.0001; hierarchical test, local alpha 0.05. [CSR PDF pp. 87,345]	Reference comparator; between-arm p<0.0001. [CSR PDF pp. 87,345]	No second study in CSR. [CSR PDF p. 1]	No second study in CSR. [CSR PDF p. 1]
Overall survival (template time-to-event fields)				
Events, n (%)	Not reported: overall-survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]	Not reported: overall-survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]	Not reported: overall-survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]	Not reported: overall-survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]
Censored, n (%)	Not reported: overall-survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]	Not reported: overall-survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]	Not reported: overall-survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]	Not reported: overall-survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]
Censoring reason 1 (add rows as needed), n (%)	Not reported: overall-survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]	Not reported: overall-survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]	Not reported: overall-survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]	Not reported: overall-survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]

	Study 1 Semaglutide 2.4 mg [CSR PDF p. 65] (N = 1306 [CSR PDF p. 65])	Study 1 Placebo [CSR PDF p. 65] (N = 655 [CSR PDF p. 65])	Study 2 No second study in CSR. [CSR PDF p. 1] (N = No second study in CSR. [CSR PDF p. 1])	Study 2 No second study in CSR. [CSR PDF p. 1] (N = No second study in CSR. [CSR PDF p. 1])
				PDF pp. 59-61]
Overall survival (months), median (95% CI)	Not reported: overall-survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]	Not reported: overall-survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]	Not reported: overall-survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]	Not reported: overall-survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]
HR (95% CI)	Not reported: overall-survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]	Not reported: overall-survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]	Not reported: overall-survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]	Not reported: overall-survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]
P value	Not reported: overall-survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]	Not reported: overall-survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]	Not reported: overall-survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]	Not reported: overall-survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]
Survival probability (%) at Not applicable months (95% CI)	Not reported: overall-survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]	Not reported: overall-survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]	Not reported: overall-survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]	Not reported: overall-survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]
Difference in survival probability (%) (95% CI)	Not reported: overall-survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]	Not reported: overall-survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]	Not reported: overall-survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]	Not reported: overall-survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]
Other confirmatory efficacy outcomes at week 68				
See other confirmatory outcomes in the treatment cells.	Confirmatory week-68 treatment-policy differences: waist -9.42 cm (95% CI -10.30 to -8.53), systolic BP -5.10 mmHg (-6.34 to -3.87), SF-36	Placebo reference; both groups received lifestyle intervention. [CSR PDF pp. 41,87]	No second study in CSR. [CSR PDF p. 1]	No second study in CSR. [CSR PDF p. 1]

	Study 1 Semaglutide 2.4 mg [CSR PDF p. 65] (N = 1306 [CSR PDF p. 65])	Study 1 Placebo [CSR PDF p. 65] (N = 655 [CSR PDF p. 65])	Study 2 No second study in CSR. [CSR PDF p. 1] (N = No second study in CSR. [CSR PDF p. 1])	Study 2 No second study in CSR. [CSR PDF p. 1] (N = No second study in CSR. [CSR PDF p. 1])
	physical functioning +1.80 (1.18-2.42), IWQOL physical function +9.43 (7.50-11.35); all p<0.0001. ≥10% and ≥15% weight-loss ORs were 14.68 (11.08-19.44) and 19.26 (12.89-28.76). [CSR PDF p. 87; Table 11-1]			

AE = adverse event; CI = confidence interval; FAS = full analysis set; OR = odds ratio; SAE = serious adverse event; SD = standard deviation. Terminology follows the CSR. [CSR PDF pp. 25-28]

* Specify if the P-value has been adjusted for multiple testing using a superscript 'a'

Source: Novo Nordisk, STEP 1 CSR, final 17 August 2020. Citations use the 1-based PDF page position, not the separate printed text-part page number. [CSR PDF pp. 1-2]

Percentage body-weight change

At week 68, treatment-policy estimated weight change was -14.85% with semaglutide and -2.41% with placebo: difference -12.44 percentage points (95% CI -13.37 to -11.51), p<0.0001. FAS n=1306/655; observed week-68 weight n=1212/577. [CSR PDF p. 333; Table 14.2.9] Hypothetical estimand: -16.86% versus -2.44%; difference -14.42 points (95% CI -15.29 to -13.55). Sensitivity differences ranged -11.94 to -12.83 points, all p<0.0001; tipping-point analysis did not overturn superiority over the examined penalty range. [CSR PDF pp. 90,92,334]

Weight-loss responder outcomes

Observed week-68 ≥5% loss: 1047/1212 (86.4%) versus 182/577 (31.5%); adjusted treatment-policy OR 11.22 (95% CI 8.88-14.19), p<0.0001. Observed ≥10%, ≥15%, ≥20% responses were 69.1%, 50.5%, 32.0% versus 12.0%, 4.9%, 1.7%. [CSR PDF pp. 87,344-345; Tables 11-1, 14.2.24-25] ≥5% sensitivity ORs ranged 10.22-14.65 (all p<0.0001), including nonresponder imputation OR 10.56 (8.48-13.14). [CSR PDF p. 346]

Other efficacy and patient-reported outcomes

Confirmatory week-68 treatment-policy differences: waist -9.42 cm (95% CI -10.30 to -8.53), systolic BP -5.10 mmHg (-6.34 to -3.87), SF-36 physical functioning +1.80 (1.18-2.42), IWQOL physical function +9.43 (7.50-11.35); all p<0.0001. ≥10% and ≥15% weight-loss ORs were 14.68 (11.08-19.44) and 19.26 (12.89-28.76). [CSR PDF p. 87; Table 11-1] SF-36 ≥4.3-point responders: observed 26.6% versus 17.1%, OR 2.11 (1.53-2.91). IWQOL ≥20-point responders: 39.6% versus 25.6%, OR 2.46 (1.90-3.18). [CSR PDF pp. 115,120] Supportive treatment-policy weight change was -15.33 versus -2.61 kg (difference -12.71, 95% CI -13.68 to -11.74); BMI difference -4.61 kg/m² (-4.96 to -4.27); HbA1c difference -0.29 percentage points (-0.32 to -0.26). [CSR PDF pp. 336,362,400] DEXA observed fat-mass reduction was 9.3 versus 1.5 kg and lean-mass reduction 5.8 versus 1.8 kg. Work productivity and urinary incontinence showed only minor differences; glycaemic category improved more with semaglutide. [CSR PDF pp. 102-103,122-124] Other HRQoL scores: week-68 changes favoured semaglutide for all other SF-36 domains and component summaries,

and IWQOL physical/psychosocial/total scores; these are supportive analyses. [CSR PDF pp. 116,121]

Cardiometabolic outcomes: systolic BP changes -6.16/-1.06 mmHg; diastolic BP -2.83/-0.42 mmHg, difference -2.41 (95% CI -3.25 to -1.57). All fasting lipid changes favoured semaglutide. CRP ratio to baseline 0.47/0.85, treatment ratio 0.56 (0.51-0.61); PAI-1 treatment ratio 0.75 (0.71-0.79), with caution because the CSR notes possible laboratory-level drift. [CSR PDF pp. 108,111-112,126]

Glucose: fasting plasma glucose change -0.46/-0.03 mmol/L, difference -0.44 (95% CI -0.50 to -0.37); fasting insulin ratios 0.74/0.93, treatment ratio 0.79 (0.74-0.83). Among baseline prediabetes participants, 84%/48% became normoglycaemic and 0.5%/3.0% developed diabetes at week 68 (observed). [CSR PDF pp. 123-124]

Exploratory medication outcomes among users: antihypertensive reduction/stopping 34%/16%, increase 12%/22%; lipid-lowering reduction/stopping 22%/17%, increase 10%/20%. Among baseline fatty liver index ≥ 60 , improvement to <30 occurred in 24%/1%, and to 30- <60 in 22%/11%. [CSR PDF pp. 101,108,110-111]

SPS-6 mean remained 26/26; ICIQ-UI-SF in women changed from 2.7/2.9 to 2.3/3.3. The CSR describes no overall between-treatment difference for these exploratory measures. Mean physical activity exceeded 150 minutes/week in both arms; food-diary recording declined in both. [CSR PDF pp. 74,122]

DEXA treatment-policy differences at week 68: fat-mass proportion -3.29 points (95% CI -4.94 to -1.65), lean-mass proportion +2.94 (1.40-4.49), visceral-fat proportion -1.98 (-3.69 to -0.27). These proportional changes coexist with loss of absolute lean mass. [CSR PDF pp. 103,125-126]

Table Number: Sample table for efficacy outcome

	Semaglutide 2.4 mg [CSR PDF p. 65] (N = 1306 (FAS) [CSR PDF p. 65])	Placebo [CSR PDF p. 65] (N = 655 (FAS) [CSR PDF p. 65])
Body weight (kg), week 68; treatment-policy estimand		
Number of patients contributing to the analysis	1306 FAS; 1212 observed [CSR PDF p. 336]	655 FAS; 577 observed [CSR PDF p. 336]
Baseline, mean (SD)	105.4 (22.1) kg [CSR PDF p. 70]	105.2 (21.5) kg [CSR PDF p. 70]
End of treatment time point (specify), mean (SE)	90.01 kg; SE not reported. [CSR PDF p. 336]	102.72 kg; SE not reported. [CSR PDF p. 336]
Change from baseline, mean (SE)	-15.33 kg; SE not reported. [CSR PDF p. 336]	-2.61 kg; SE not reported. [CSR PDF p. 336]
Treatment group difference versus control (95% CI)	-12.71 kg (95% CI - 13.68 to -11.74) [CSR PDF p. 336]	Reference comparator [CSR PDF p. 336]
P value	<0.0001 (supportive; not in confirmatory hierarchy) [CSR PDF p. 336]	Reference comparator [CSR PDF p. 336]
$\geq 10\%$ body-weight loss, week 68		
n (%)	838/1212 (69.1%), observed [CSR PDF p. 344]	69/577 (12.0%), observed [CSR PDF p. 344]
OR/RR (95% CI)	OR 14.68 (95% CI 11.08-19.44) [CSR PDF p. 87]	Reference comparator [CSR PDF p. 87]
RD (95% CI)	Risk difference/CI not reported. [CSR PDF p.	Risk difference/CI not reported. [CSR

	Semaglutide 2.4 mg [CSR PDF p. 65] (N = 1306 (FAS) [CSR PDF p. 65])	Placebo [CSR PDF p. 65] (N = 655 (FAS) [CSR PDF p. 65])
	87]	PDF p. 87]
P value	<0.0001; hierarchical test, alpha 0.05. [CSR PDF p. 87]	Reference comparator [CSR PDF p. 87]
Overall survival (template time-to-event fields)		
Events, n (%)	Not reported: overall- survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]	Not reported: overall- survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]
Overall survival (months), median (95% CI)	Not reported: overall- survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]	Not reported: overall- survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]
HR (95% CI)	Not reported: overall- survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]	Not reported: overall- survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]
P value	Not reported: overall- survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]	Not reported: overall- survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]
Survival probability (%) at Not applicable months (95% CI)	Not reported: overall- survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]	Not reported: overall- survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]
Difference in survival probability (%) (95% CI)	Not reported: overall- survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]	Not reported: overall- survival efficacy analysis is not an endpoint in this CSR. [CSR PDF pp. 59-61]

AE = adverse event; CI = confidence interval; FAS = full analysis set; OR = odds ratio; SAE = serious adverse event; SD = standard deviation. Terminology follows the CSR. [CSR PDF pp. 25-28]

Source: Novo Nordisk, STEP 1 CSR, final 17 August 2020. Citations use the 1-based PDF page position, not the separate printed text-part page number. [CSR PDF pp. 1-2]

Harms

STEP 1 SAS: 1306 semaglutide and 655 placebo. TEAEs occurred in 1171 (89.7%) versus 566 (86.4%); SAEs in 128 (9.8%) versus 42 (6.4%); AEs leading to permanent treatment discontinuation in 92 (7.0%) versus 20 (3.1%). In-trial deaths: 1 (0.1%) versus 1 (0.2%). [CSR PDF p. 128; Table 12-1] Common GI preferred terms, semaglutide/placebo n (%): nausea 577 (44.2)/114 (17.4); diarrhoea 412 (31.5)/104 (15.9); vomiting 324 (24.8)/43 (6.6); constipation 306 (23.4)/62 (9.5); dyspepsia 135 (10.3)/23 (3.5); abdominal pain 130 (10.0)/36 (5.5); upper abdominal pain 125 (9.6)/35

(5.3); eructation 112 (8.6)/3 (0.5); abdominal distension 96 (7.4)/31 (4.7); reflux 82 (6.3)/20 (3.1); flatulence 65 (5.0)/21 (3.2). [CSR PDF p. 141; Table 12-10]

Table Number: Sample table for key harms data

Adverse events	Semaglutide 2.4 mg [CSR PDF p. 128] (N = 1306 [CSR PDF p. 128])	Placebo [CSR PDF p. 128] (N = 655 [CSR PDF p. 128])
Most common adverse events, n (%)		
≥ 1 adverse event	1171 (89.7%) [CSR PDF p. 128]	566 (86.4%) [CSR PDF p. 128]
Nausea	577 (44.2%) [CSR PDF p. 141]	114 (17.4%) [CSR PDF p. 141]
Diarrhoea	412 (31.5%) [CSR PDF p. 141]	104 (15.9%) [CSR PDF p. 141]
Vomiting; constipation	324 (24.8%); 306 (23.4%) [CSR PDF p. 141]	43 (6.6%); 62 (9.5%) [CSR PDF p. 141]
Serious adverse events, n (%)		
Patients with ≥ 1 SAE	128 (9.8%) [CSR PDF p. 128]	42 (6.4%) [CSR PDF p. 128]
Serious gastrointestinal disorders (SOC)	18 (1.4%) [CSR PDF p. 135]	0 [CSR PDF p. 135]
Serious hepatobiliary disorders (SOC)	17 (1.3%) [CSR PDF p. 135]	1 (0.2%) [CSR PDF p. 135]
Serious infections (SOC)	27 (2.1%) [CSR PDF p. 135]	10 (1.5%) [CSR PDF p. 135]
Patients who stopped treatment due to adverse events, n (%)		
Patients who stopped	92 (7.0%); permanent product discontinuation, AE form. [CSR PDF p. 137]	20 (3.1%); permanent product discontinuation, AE form. [CSR PDF p. 137]
Gastrointestinal disorders (SOC)	59 (4.5%) [CSR PDF p. 137]	5 (0.8%) [CSR PDF p. 137]
Psychiatric disorders (SOC)	7 (0.5%) [CSR PDF p. 137]	3 (0.5%) [CSR PDF p. 137]
AE-related temporary interruption	126 (9.6%) [CSR PDF p. 138]	26 (4.0%) [CSR PDF p. 138]
Deaths, n (%)		
Patients who died	1 (0.1%), in-trial [CSR PDF p. 128]	1 (0.2%), in-trial [CSR PDF p. 128]
Death details	EAC: sudden cardiac death, day 311; product stopped day 198. [CSR PDF p. 134]	EAC: malignancy, day 145; fatal events included aspiration pneumonia and sepsis. Some details redacted. [CSR PDF p. 134]

Additional deaths	No additional in-trial deaths. [CSR PDF p. 128]	No additional in-trial deaths. [CSR PDF p. 128]
Adverse events of special interest, n (%)		
Gallbladder disorders; adjudicated acute pancreatitis, n (%)	34 (2.6%); 3 (0.2%), respectively. [CSR PDF p. 129]	8 (1.2%); 0, respectively. [CSR PDF p. 129]
Other safety focus areas	Safety focus areas, semaglutide/placebo n (%): GI 969 (74.2)/314 (47.9); gallbladder 34 (2.6)/8 (1.2); adjudicated acute pancreatitis 3 (0.2)/0; cardiovascular (in-trial) 107 (8.2)/75 (11.5); malignant neoplasms (in-trial) 14 (1.1)/7 (1.1); hepatic 31 (2.4)/20 (3.1); acute renal failure 3 (0.2)/2 (0.3); hypoglycaemia 8 (0.6)/5 (0.8); injection-site reactions 65 (5.0)/44 (6.7); allergy 96 (7.4)/54 (8.2); psychiatric 124 (9.5)/83 (12.7). [CSR PDF p. 129; Table 12-2]	Placebo results included in parallel summary in this row. [CSR PDF p. 129]

AE = adverse event; CI = confidence interval; FAS = full analysis set; OR = odds ratio; SAE = serious adverse event; SD = standard deviation. Terminology follows the CSR. [CSR PDF pp. 25-28]

Source: Novo Nordisk, STEP 1 CSR, final 17 August 2020. Citations use the 1-based PDF page position, not the separate printed text-part page number. [CSR PDF pp. 1-2]

Safety Evaluation Plan

SAS analysed as treated: all 1961 randomised/exposed participants (1306/655). AE summaries use onset within the on-treatment window, including 49 days after dosing. Deaths, cardiovascular events and neoplasms use in-trial follow-up. Selected events underwent independent EAC adjudication; MedDRA 22.1 coding was used. Clinical/laboratory safety assessments used the specified observation periods. This is STEP 1 safety, not a pooled development-programme analysis. [CSR PDF pp. 49-54,58,128-129]

SAS analysed as treated: all 1961 randomised/exposed participants (1306/655). AE summaries use onset within the on-treatment window, including 49 days after dosing. Deaths, cardiovascular events and neoplasms use in-trial follow-up. Selected events underwent independent EAC adjudication; MedDRA 22.1 coding was used. Clinical/laboratory safety assessments used the specified observation periods. This is STEP 1 safety, not a pooled development-programme analysis. [CSR PDF pp. 49-54,58,128-129]

Overview of Safety

STEP 1 SAS: 1306 semaglutide and 655 placebo. TEAEs occurred in 1171 (89.7%) versus 566 (86.4%); SAEs in 128 (9.8%) versus 42 (6.4%); AEs leading to permanent treatment discontinuation in 92 (7.0%) versus 20 (3.1%). In-trial deaths: 1 (0.1%) versus 1 (0.2%). [CSR PDF p. 128; Table 12-1] Common-event threshold in the CSR is $\geq 5\%$ in either arm. [CSR PDF p. 131]

STEP 1 SAS: 1306 semaglutide and 655 placebo. TEAEs occurred in 1171 (89.7%) versus 566 (86.4%); SAEs in 128 (9.8%) versus 42 (6.4%); AEs leading to permanent treatment discontinuation in 92 (7.0%) versus 20 (3.1%). In-trial deaths: 1 (0.1%) versus 1 (0.2%). [CSR PDF p. 128; Table 12-1] Common-event threshold in the CSR is $\geq 5\%$ in either arm. [CSR PDF p. 131]

Adverse Events

STEP 1 SAS: 1306 semaglutide and 655 placebo. TEAEs occurred in 1171 (89.7%) versus 566 (86.4%); SAEs in 128 (9.8%) versus 42 (6.4%); AEs leading to permanent treatment discontinuation in 92 (7.0%) versus 20 (3.1%). In-trial deaths: 1 (0.1%) versus 1 (0.2%). [CSR PDF p. 128; Table 12-1] Common GI preferred terms, semaglutide/placebo n (%): nausea 577 (44.2)/114 (17.4); diarrhoea 412 (31.5)/104 (15.9); vomiting 324 (24.8)/43 (6.6); constipation 306 (23.4)/62 (9.5); dyspepsia 135 (10.3)/23 (3.5); abdominal pain 130 (10.0)/36 (5.5); upper abdominal pain 125 (9.6)/35 (5.3); eructation 112 (8.6)/3 (0.5); abdominal distension 96 (7.4)/31 (4.7); reflux 82 (6.3)/20 (3.1); flatulence 65 (5.0)/21 (3.2). [CSR PDF p. 141; Table 12-10]

STEP 1 SAS: 1306 semaglutide and 655 placebo. TEAEs occurred in 1171 (89.7%) versus 566 (86.4%); SAEs in 128 (9.8%) versus 42 (6.4%); AEs leading to permanent treatment discontinuation in 92 (7.0%) versus 20 (3.1%). In-trial deaths: 1 (0.1%) versus 1 (0.2%). [CSR PDF p. 128; Table 12-1] Common GI preferred terms, semaglutide/placebo n (%): nausea 577 (44.2)/114 (17.4); diarrhoea 412 (31.5)/104 (15.9); vomiting 324 (24.8)/43 (6.6); constipation 306 (23.4)/62 (9.5); dyspepsia 135 (10.3)/23 (3.5); abdominal pain 130 (10.0)/36 (5.5); upper abdominal pain 125 (9.6)/35 (5.3); eructation 112 (8.6)/3 (0.5); abdominal distension 96 (7.4)/31 (4.7); reflux 82 (6.3)/20 (3.1); flatulence 65 (5.0)/21 (3.2). [CSR PDF p. 141; Table 12-10]

Serious Adverse Events

On-treatment SAEs: 128/1306 (9.8%; 164 events) versus 42/655 (6.4%; 53 events). Serious GI disorders: 18 (1.4%) versus 0; serious hepatobiliary disorders: 17 (1.3%) versus 1 (0.2%). [CSR PDF pp. 128,135]

On-treatment SAEs: 128/1306 (9.8%; 164 events) versus 42/655 (6.4%; 53 events). Serious GI disorders: 18 (1.4%) versus 0; serious hepatobiliary disorders: 17 (1.3%) versus 1 (0.2%). [CSR PDF pp. 128,135]

Withdrawals Due to Adverse Events

AE-form permanent product discontinuations were 92 (7.0%) versus 20 (3.1%), including GI disorders 59 (4.5%) versus 5 (0.8%). Disposition-form AE discontinuations were 91 (7.0%) versus 21 (3.2%); the CSR explicitly attributes the one-person-per-arm discrepancy to different forms. Temporary interruptions due to AEs: 126 (9.6%) versus 26 (4.0%); dose reductions: 124 (9.5%) versus 4 (0.6%). These are product changes, distinct from complete trial withdrawal. [CSR PDF pp. 137-138; Table 12-8] AE-related trial-withdrawal information was not systematically collected; Table 12-7 lists 4 semaglutide and 1 placebo subject withdrawing consent for reasons mentioning AEs, plus one death in each arm. The accompanying prose contains inconsistent counts. [CSR PDF pp. 136-137; Tables 12-6/12-7]

AE-form permanent product discontinuations were 92 (7.0%) versus 20 (3.1%), including GI disorders 59 (4.5%) versus 5 (0.8%). Disposition-form AE discontinuations were 91 (7.0%) versus 21 (3.2%); the CSR explicitly attributes the one-person-per-arm discrepancy to different forms. Temporary interruptions due to AEs: 126 (9.6%) versus 26 (4.0%); dose reductions: 124 (9.5%) versus 4 (0.6%). These are product changes, distinct from complete trial withdrawal. [CSR PDF pp. 137-138; Table 12-8] AE-related trial-withdrawal information was not systematically collected; Table 12-7 lists 4 semaglutide and 1 placebo subject withdrawing consent for reasons mentioning AEs, plus one death in each arm. The accompanying prose contains inconsistent counts. [CSR PDF pp. 136-137; Tables 12-6/12-7]

Adverse Events of Special Interest

Safety focus areas, semaglutide/placebo n (%): GI 969 (74.2)/314 (47.9); gallbladder 34 (2.6)/8 (1.2); adjudicated acute pancreatitis 3 (0.2)/0; cardiovascular (in-trial) 107 (8.2)/75 (11.5); malignant neoplasms (in-trial) 14 (1.1)/7 (1.1); hepatic 31 (2.4)/20 (3.1); acute renal failure 3 (0.2)/2 (0.3); hypoglycaemia 8 (0.6)/5 (0.8); injection-site reactions 65 (5.0)/44 (6.7); allergy 96 (7.4)/54 (8.2); psychiatric 124 (9.5)/83 (12.7). [CSR PDF p. 129; Table 12-2] Dose escalation/lower maintenance dose supported GI tolerability; suspected pancreatitis required stopping product with protocol-defined resumption rules. [CSR PDF pp. 38-40]

Safety focus areas, semaglutide/placebo n (%): GI 969 (74.2)/314 (47.9); gallbladder 34 (2.6)/8 (1.2); adjudicated acute pancreatitis 3 (0.2)/0; cardiovascular (in-trial) 107 (8.2)/75 (11.5); malignant neoplasms (in-trial) 14 (1.1)/7 (1.1); hepatic 31 (2.4)/20 (3.1); acute renal failure 3 (0.2)/2 (0.3); hypoglycaemia 8 (0.6)/5 (0.8); injection-site reactions 65 (5.0)/44 (6.7); allergy 96 (7.4)/54 (8.2); psychiatric 124 (9.5)/83 (12.7). [CSR PDF p. 129; Table 12-2] Dose escalation/lower maintenance dose supported GI tolerability; suspected pancreatitis required stopping product with protocol-defined resumption rules. [CSR PDF pp. 38-40]

Sponsor Summary and Conclusion

The CSR confirms superiority for all eight confirmatory efficacy endpoints, with more gastrointestinal adverse events on semaglutide. [CSR PDF pp. 87,129]

At week 68, treatment-policy estimated weight change was -14.85% with semaglutide and -2.41% with placebo: difference -12.44 percentage points (95% CI -13.37 to -11.51), $p < 0.0001$. FAS $n = 1306/655$; observed week-68 weight $n = 1212/577$. [CSR PDF p. 333; Table 14.2.9] Confirmatory week-68 treatment-policy differences: waist -9.42 cm (95% CI -10.30 to -8.53), systolic BP -5.10 mmHg (-6.34 to -3.87), SF-36 physical functioning +1.80 (1.18-2.42), IWQOL physical function +9.43 (7.50-11.35); all $p < 0.0001$. $\geq 10\%$ and $\geq 15\%$ weight-loss ORs were 14.68 (11.08-19.44) and 19.26 (12.89-28.76). [CSR PDF p. 87; Table 11-1] STEP 1 SAS: 1306 semaglutide and 655 placebo. TEAEs occurred in 1171 (89.7%) versus 566 (86.4%); SAEs in 128 (9.8%) versus 42 (6.4%); AEs leading to permanent treatment discontinuation in 92 (7.0%) versus 20 (3.1%). In-trial deaths: 1 (0.1%) versus 1 (0.2%). [CSR PDF p. 128; Table 12-1] GI and gallbladder events were more frequent with semaglutide; most GI events were non-serious, mild/moderate and recovered. [CSR PDF pp. 129,141]

Sponsor Identified Gaps in the Evidence

Evidence gaps concern active comparators, excluded populations and longer follow-up. [CSR PDF pp. 35-37]

CSR scope limits: no active-drug comparison; adults without diabetes; main treatment duration 68 weeks plus safety follow-up to week 75; extension results excluded. Thus comparative efficacy against other drugs, effects in excluded populations and longer-term durability cannot be established from this CSR. [CSR PDF pp. 35-37] No sponsor-authored gap assessment or separate gap-addressing report is supplied.

Section 3. Long-Term Extension Studies

Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]

Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]

Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]

Description of Studies

Study Design and Objectives

Planned 52-week open-label off-treatment extension of STEP 1; approximately 300 selected main-phase completers from Canada, Germany, Japan, UK and US. Extension results were to be reported separately. [CSR PDF pp. 32,35-36]

Eligibility criteria

Subset completing main phase on maintenance-dose semaglutide 2.4 mg or matching placebo, at selected sites/countries. [CSR PDF p. 35] Full extension eligibility details are not reported in the supplied CSR.

Interventions

No study drug and no structured lifestyle intervention during the 52-week off-treatment extension. [CSR PDF p. 35]

Outcomes

Planned evaluation of change after end of treatment in body weight, cardiovascular risk factors and glucose metabolism. [CSR PDF pp. 35-36]

Statistical analysis

Extension statistical methods and baseline definitions are not reported in this CSR. Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]

Patient Population

Baseline characteristics

Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]

Table Number: Summary of Baseline Characteristics

Characteristic	Study 1		Study 2	
	Extension results not reported. [CSR PDF pp. 35-36] (N = Extension results not reported. [CSR PDF pp. 35-36])	Extension results not reported. [CSR PDF pp. 35-36] (N = Extension results not reported. [CSR PDF pp. 35-36])	Extension results not reported. [CSR PDF pp. 35-36] (N = Extension results not reported. [CSR PDF pp. 35-36])	Extension results not reported. [CSR PDF pp. 35-36] (N = Extension results not reported. [CSR PDF pp. 35-36])
Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]

Characteristic	Study 1		Study 2	
	Extension results not reported. [CSR PDF pp. 35-36] (N = Extension results not reported. [CSR PDF pp. 35-36])	Extension results not reported. [CSR PDF pp. 35-36] (N = Extension results not reported. [CSR PDF pp. 35-36])	Extension results not reported. [CSR PDF pp. 35-36] (N = Extension results not reported. [CSR PDF pp. 35-36])	Extension results not reported. [CSR PDF pp. 35-36] (N = Extension results not reported. [CSR PDF pp. 35-36])
Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]
Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]

AE = adverse event; CI = confidence interval; FAS = full analysis set; OR = odds ratio; SAE = serious adverse event; SD = standard deviation. Terminology follows the CSR. [CSR PDF pp. 25-28]

Source: Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]

Patient Disposition

Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]

Exposure to study treatments

Study treatments

Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]

Table Number: Sample Table for Patient Exposure

Exposure	Study 1		Study 2	
	Extension results not reported. [CSR PDF pp. 35-36] (N = Extension results not reported. [CSR PDF pp. 35-36])	Extension results not reported. [CSR PDF pp. 35-36] (N = Extension results not reported. [CSR PDF pp. 35-36])	Extension results not reported. [CSR PDF pp. 35-36] (N = Extension results not reported. [CSR PDF pp. 35-36])	Extension results not reported. [CSR PDF pp. 35-36] (N = Extension results not reported. [CSR PDF pp. 35-36])
Total, patient-weeks or patient-years	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]
Duration, mean (SD)	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]
Duration, median (IQR or range)	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]

Adherence, %	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]
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AE = adverse event; CI = confidence interval; FAS = full analysis set; OR = odds ratio; SAE = serious adverse event; SD = standard deviation. Terminology follows the CSR. [CSR PDF pp. 25-28]

Source: Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]

Concomitant medications and co-interventions

No structured lifestyle intervention during the extension. [CSR PDF p. 35] Extension concomitant-medication results are not reported.

Subsequent treatment (if applicable)

Off-treatment follow-up after the main phase; no extension switch to active therapy is described. [CSR PDF pp. 35-36] Subsequent-treatment results are not reported.

Table 11: Sample Table for Subsequent Treatment

Exposure	Study 1		Study 2	
	Extension results not reported. [CSR PDF pp. 35-36] (N = Extension results not reported. [CSR PDF pp. 35-36])	Extension results not reported. [CSR PDF pp. 35-36] (N = Extension results not reported. [CSR PDF pp. 35-36])	Extension results not reported. [CSR PDF pp. 35-36] (N = Extension results not reported. [CSR PDF pp. 35-36])	Extension results not reported. [CSR PDF pp. 35-36] (N = Extension results not reported. [CSR PDF pp. 35-36])
Received subsequent therapy, n (%)	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]
Extension results not reported. [CSR PDF pp. 35-36], n (%)	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]
Extension results not reported. [CSR PDF pp. 35-36], n (%)	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]
Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]	Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]	Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]	Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]	Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]

AE = adverse event; CI = confidence interval; FAS = full analysis set; OR = odds ratio; SAE = serious adverse event; SD = standard deviation. Terminology follows the CSR. [CSR PDF pp. 25-28]

Source: Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]

Results

Efficacy

Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]

Body weight (extension results not reported)

Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]

Cardiovascular risk factors (extension results not reported)

Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]

Glucose metabolism (extension results not reported)

Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]

Harms

Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]

Table 12: Summary of Harms

Adverse events	Extension results not reported. [CSR PDF pp. 35-36] (N = Extension results not reported. [CSR PDF pp. 35-36])	Extension results not reported. [CSR PDF pp. 35-36] (N = Extension results not reported. [CSR PDF pp. 35-36])
Most common adverse events, n (%)		
≥ 1 adverse event	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]
Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]
Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]
Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]	Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]	Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]
Serious adverse events, n (%)		
Patients with ≥ 1 SAE	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]
Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]

	pp. 35-36]	pp. 35-36]
Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]
Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]	Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]	Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]
Patients who stopped treatment due to adverse events, n (%)		
Patients who stopped	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]
Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]
Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]
Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]	Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]	Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]
Deaths, n (%)		
Patients who died	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]
Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]
Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]	Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]	Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]
Adverse events of special interest, n (%)		
Extension results not reported. [CSR PDF pp. 35-36], n (%)	Extension results not reported. [CSR PDF pp. 35-36]	Extension results not reported. [CSR PDF pp. 35-36]
Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]	Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]	Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]

AE = adverse event; CI = confidence interval; FAS = full analysis set; OR = odds ratio; SAE = serious adverse event; SD = standard deviation. Terminology follows the CSR. [CSR PDF pp. 25-28]

Source: Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]

Sponsor Summary and Conclusion

Planned 52-week open-label off-treatment extension of STEP 1; approximately 300 selected main-phase completers from Canada, Germany, Japan, UK and US. Extension results were to be reported separately. [CSR PDF pp. 32,35-36]
Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]

Planned 52-week open-label off-treatment extension of STEP 1; approximately 300 selected main-phase completers from Canada, Germany, Japan, UK and US. Extension results were to be reported separately. [CSR PDF pp. 32,35-36]
Not reported: extension results are outside this CSR and were to be reported separately. [CSR PDF pp. 35-36]

Sponsor Identified Gaps in the Evidence

Durability after withdrawal and longer-term outcomes cannot be assessed because extension results are outside this report. [CSR PDF pp. 35-36]

Durability after withdrawal and longer-term outcomes cannot be assessed because extension results are outside this report. [CSR PDF pp. 35-36]

Section 4. Indirect Evidence

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

- **Rationale for why no indirect comparisons have been included in the application.**

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Description of Indirect Comparison(s)

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Objectives

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Study Selection Methods

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Table Number: Study Selection Criteria and Methods for Indirect Comparisons

Characteristics	Indirect Comparison
Population	No indirect comparison reported. [CSR PDF pp. 35-37]
Intervention	No indirect comparison reported. [CSR PDF pp. 35-37]
Comparator	No indirect comparison reported. [CSR PDF pp. 35-37]
Outcome	No indirect comparison reported. [CSR PDF pp. 35-37]
Study designs	No indirect comparison reported. [CSR PDF pp. 35-37]
Publication characteristics	No indirect comparison reported. [CSR PDF pp. 35-37]
Exclusion criteria	No indirect comparison reported. [CSR PDF pp. 35-37]
Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]	No indirect comparison reported. [CSR PDF pp. 35-37]
Selection process	No indirect comparison reported. [CSR PDF pp. 35-37]
Data extraction process	No indirect comparison reported. [CSR PDF pp. 35-37]
Quality assessment	No indirect comparison reported. [CSR PDF pp. 35-37]

AE = adverse event; CI = confidence interval; FAS = full analysis set; OR = odds ratio; SAE = serious adverse event; SD = standard deviation. Terminology follows the CSR. [CSR PDF pp. 25-28]

Source: Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Indirect comparison analysis methods

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

o Convergence diagnostics, burn-in period, number of iterations and number of chains should also be described.

- Matching-adjusting indirect comparison (MAIC):

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

o Specify whether an anchored or unanchored MAIC was conducted

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

- Discuss any steps taken to address potential sources of heterogeneity (e.g., excluding studies, doses, or timepoints from the analysis) or meta-regression analyses.

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

- For Network Meta-Analyses, describe how nodes in the network were constructed, how different doses, different routes of administration, different drugs within the same class, and comparators were handled (separate nodes or pooled analysis).

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

- List which outcomes were analyzed and the rationale for excluding any of those that were pre-planned for analyses.

- The table below provides an example of how the key data element may be described using a table format. The sample table is focussed on describing Bayesian NMA methods and likely needs modification for other approaches. Add or delete rows as appropriate. As methods may vary for different types of outcomes (continuous, dichotomous) or by network or population, additional columns may be added as needed.

Table Number: Indirect Comparison Analysis Methods

Methods	Description
Analysis methods	No indirect comparison reported. [CSR PDF pp. 35-37]

Methods	Description
Priors	No indirect comparison reported. [CSR PDF pp. 35-37]
Assessment of Model fit	No indirect comparison reported. [CSR PDF pp. 35-37]
Assessment of Consistency	No indirect comparison reported. [CSR PDF pp. 35-37]
Assessment of Convergence	No indirect comparison reported. [CSR PDF pp. 35-37]
Outcomes	No indirect comparison reported. [CSR PDF pp. 35-37]
Follow-up timepoints	No indirect comparison reported. [CSR PDF pp. 35-37]
Construction of nodes	No indirect comparison reported. [CSR PDF pp. 35-37]
Sensitivity analyses	No indirect comparison reported. [CSR PDF pp. 35-37]
Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]	No indirect comparison reported. [CSR PDF pp. 35-37]
Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]	No indirect comparison reported. [CSR PDF pp. 35-37]

AE = adverse event; CI = confidence interval; FAS = full analysis set; OR = odds ratio; SAE = serious adverse event; SD = standard deviation. Terminology follows the CSR. [CSR PDF pp. 25-28]

Source: Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Results

Summary of included studies

The table below is an example of what may be used to provide a description of important differences across trials for key characteristics. The list of characteristics are examples; please add rows as appropriate (and delete a row only if the characteristic is irrelevant). No evidence of effect modification may be added as a comment, if appropriate.

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Consider: Dosage, treatment duration, route of administration, supportive care as well as information on treatment titration, induction or maintenance treatment. Highlight the differences between trials, if any.

Table Number: Sample Table for Assessment of Homogeneity

Characteristics	Description and handling of potential effect modifiers
Disease severity	No indirect comparison reported. [CSR PDF pp. 35-37]
Treatment history	No indirect comparison reported. [CSR PDF pp. 35-37]
Trial eligibility criteria	No indirect comparison reported. [CSR PDF pp. 35-37]
Dosing of comparators	No indirect comparison reported. [CSR PDF pp. 35-37]
Placebo response	No indirect comparison reported. [CSR PDF pp. 35-37]
Definitions of endpoints	No indirect comparison reported. [CSR PDF pp. 35-37]
Timing of endpoint evaluation	No indirect comparison reported. [CSR PDF pp. 35-37]
Withdrawal frequency	No indirect comparison reported. [CSR PDF pp. 35-37]
Clinical trial setting	No indirect comparison reported. [CSR PDF pp. 35-37]
Study design	No indirect comparison reported. [CSR PDF pp. 35-37]

AE = adverse event; CI = confidence interval; FAS = full analysis set; OR = odds ratio; SAE = serious adverse event; SD = standard deviation. Terminology follows the CSR. [CSR PDF pp. 25-28]

Source: Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Evidence Networks

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Efficacy

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Table Number: ITC Sample Data Table for Continuous Outcomes (e.g., Summary of NMA Results for Efficacy Results, [Treatment] Versus Comparators)

Comparator	No indirect comparison reported. [CSR PDF pp. 35-37]	No indirect comparison reported. [CSR PDF pp. 35-37]
No indirect comparison reported. [CSR PDF pp. 35-37]	No indirect comparison reported. [CSR PDF pp. 35-37]	No indirect comparison reported. [CSR PDF pp. 35-37]
No indirect comparison reported. [CSR PDF pp. 35-37]	No indirect comparison reported. [CSR PDF pp. 35-37]	No indirect comparison reported. [CSR PDF pp. 35-37]
No indirect comparison reported. [CSR PDF pp. 35-37]	No indirect comparison reported. [CSR PDF pp. 35-37]	No indirect comparison reported. [CSR PDF pp. 35-37]

AE = adverse event; CI = confidence interval; FAS = full analysis set; OR = odds ratio; SAE = serious adverse event; SD = standard deviation. Terminology follows the CSR. [CSR PDF pp. 25-28]

Source: Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Table Number: ITC Sample Data Table for Dichotomous Outcomes (e.g., Summary of NMA Results for Efficacy Results, [Treatment] Versus Comparators)

Comparator	No indirect comparison reported. [CSR PDF pp. 35-37]	No indirect comparison reported. [CSR PDF pp. 35-37]
No indirect comparison reported. [CSR PDF pp. 35-37]	No indirect comparison reported. [CSR PDF pp. 35-37]	No indirect comparison reported. [CSR PDF pp. 35-37]
No indirect comparison reported. [CSR PDF pp. 35-37]	No indirect comparison reported. [CSR PDF pp. 35-37]	No indirect comparison reported. [CSR PDF pp. 35-37]
No indirect comparison reported. [CSR PDF pp. 35-37]	No indirect comparison reported. [CSR PDF pp. 35-37]	No indirect comparison reported. [CSR PDF pp. 35-37]

AE = adverse event; CI = confidence interval; FAS = full analysis set; OR = odds ratio; SAE = serious adverse event; SD = standard deviation. Terminology follows the CSR. [CSR PDF pp. 25-28]

Source: Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Harms

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Sponsor Summary and Conclusion

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Not reported in this CSR; it reports a direct placebo-controlled trial, not an indirect comparison. [CSR PDF pp. 35-37]

Section 5. Studies Addressing Gaps in the Pivotal and RCT Evidence

No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]

No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]

Summary of Gaps in the Evidence

Table Number: Summary of Gaps in the Evidence

Gap in Pivotal and RCT Evidence	Studies that Address Gaps	
	Study Description	Summary of Key Results
CSR scope limits: no active-drug comparison; adults without diabetes; main treatment duration 68 weeks plus safety follow-up to week 75; extension results excluded. Thus comparative efficacy against other drugs, effects in excluded populations and longer-term durability cannot be established from this CSR. [CSR PDF pp. 35-37] No sponsor-authored gap assessment or separate gap-addressing report is supplied.e.g. Describe the populations and/outcomes that were not studied in the pivotal studies or other RCTs	No additional study reported. [CSR PDF pp. 1,35-36]Briefly describe (e.g., 52-week, prospective observational study)	No additional study reported. [CSR PDF pp. 1,35-36]Briefly describe the key results focusing on how the evidence addresses the important gap in the evidence

No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]	No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]	No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]
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No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]

Description of No additional gap-addressing study is reported in this CSR; its scope is the STEP 1 main phase. [CSR PDF pp. 1,32,35-36]

No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]

Study Design and Objectives

No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]

No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]

Eligibility criteria

No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]

Interventions

No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]

Outcomes

No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]

Statistical analysis

No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]

Patient Population

Baseline characteristics

No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]

- for discrete data please report as n (%)
- for continuous data please report the mean (SD); where continuous data are skewed also report the median (IQR or range)

More than one table can be created if all studies do not fit in a single table.

Table Number: Summary of Baseline Characteristics of Study 1 and Study 2

Characteristic	Study 1		Study 2	
	No additional study reported. [CSR PDF pp. 1,35-36] (N = No additional study reported. [CSR PDF pp. 1,35-36])	No additional study reported. [CSR PDF pp. 1,35-36] (N = No additional study reported. [CSR PDF pp. 1,35-36])	No additional study reported. [CSR PDF pp. 1,35-36] (N = No additional study reported. [CSR PDF pp. 1,35-36])	No additional study reported. [CSR PDF pp. 1,35-36] (N = No additional study reported. [CSR PDF pp. 1,35-36])
No additional study	No additional study	No additional study	No additional study	No additional study

Characteristic	Study 1		Study 2	
	No additional study reported. [CSR PDF pp. 1,35-36] (N = No additional study reported. [CSR PDF pp. 1,35-36])	No additional study reported. [CSR PDF pp. 1,35-36] (N = No additional study reported. [CSR PDF pp. 1,35-36])	No additional study reported. [CSR PDF pp. 1,35-36] (N = No additional study reported. [CSR PDF pp. 1,35-36])	No additional study reported. [CSR PDF pp. 1,35-36] (N = No additional study reported. [CSR PDF pp. 1,35-36])
reported. [CSR PDF pp. 1,35-36]	reported. [CSR PDF pp. 1,35-36]	reported. [CSR PDF pp. 1,35-36]	reported. [CSR PDF pp. 1,35-36]	reported. [CSR PDF pp. 1,35-36]
No additional study reported. [CSR PDF pp. 1,35-36]	No additional study reported. [CSR PDF pp. 1,35-36]	No additional study reported. [CSR PDF pp. 1,35-36]	No additional study reported. [CSR PDF pp. 1,35-36]	No additional study reported. [CSR PDF pp. 1,35-36]
No additional study reported. [CSR PDF pp. 1,35-36]	No additional study reported. [CSR PDF pp. 1,35-36]	No additional study reported. [CSR PDF pp. 1,35-36]	No additional study reported. [CSR PDF pp. 1,35-36]	No additional study reported. [CSR PDF pp. 1,35-36]

AE = adverse event; CI = confidence interval; FAS = full analysis set; OR = odds ratio; SAE = serious adverse event; SD = standard deviation. Terminology follows the CSR. [CSR PDF pp. 25-28]

Source: No additional gap-addressing study is reported in this CSR; its scope is the STEP 1 main phase. [CSR PDF pp. 1,32,35-36]

Patient disposition

No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]

Exposure to Interventions

Study treatments

No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]

Table Number: Sample Table for Patient Exposure

Exposure	Study 1		Study 2	
	No additional study reported. [CSR PDF pp. 1,35-36] (N = No additional study reported. [CSR PDF pp. 1,35-36])	No additional study reported. [CSR PDF pp. 1,35-36] (N = No additional study reported. [CSR PDF pp. 1,35-36])	No additional study reported. [CSR PDF pp. 1,35-36] (N = No additional study reported. [CSR PDF pp. 1,35-36])	No additional study reported. [CSR PDF pp. 1,35-36] (N = No additional study reported. [CSR PDF pp. 1,35-36])
Total, patient-weeks or patient-years	No additional study reported. [CSR PDF pp. 1,35-36]	No additional study reported. [CSR PDF pp. 1,35-36]	No additional study reported. [CSR PDF pp. 1,35-36]	No additional study reported. [CSR PDF pp. 1,35-36]
Duration, mean (SD)	No additional study reported. [CSR PDF pp. 1,35-36]	No additional study reported. [CSR PDF pp. 1,35-36]	No additional study reported. [CSR PDF pp. 1,35-36]	No additional study reported. [CSR PDF pp. 1,35-36]
Duration, median (IQR or range)	No additional study reported. [CSR PDF pp. 1,35-36]	No additional study reported. [CSR PDF pp. 1,35-36]	No additional study reported. [CSR PDF pp. 1,35-36]	No additional study reported. [CSR PDF pp. 1,35-36]

Adherence, %	No additional study reported. [CSR PDF pp. 1,35-36]	No additional study reported. [CSR PDF pp. 1,35-36]	No additional study reported. [CSR PDF pp. 1,35-36]	No additional study reported. [CSR PDF pp. 1,35-36]
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AE = adverse event; CI = confidence interval; FAS = full analysis set; OR = odds ratio; SAE = serious adverse event; SD = standard deviation. Terminology follows the CSR. [CSR PDF pp. 25-28]

Source: No additional gap-addressing study is reported in this CSR; its scope is the STEP 1 main phase. [CSR PDF pp. 1,32,35-36]

Concomitant medications and co-interventions

No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]

Within the text, describe any concomitant medications or cointerventions required or permitted during the study. If concomitant medication doses were lowered or treatment stopped, describe the schedule as applicable (e.g., tapering corticosteroids).

Subsequent treatment (if applicable)

No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]

Table Number: Sample Table for Subsequent Treatment

Exposure	Study 1		Study 2	
	No additional study reported. [CSR PDF pp. 1,35-36] (N = No additional study reported. [CSR PDF pp. 1,35-36])	No additional study reported. [CSR PDF pp. 1,35-36] (N = No additional study reported. [CSR PDF pp. 1,35-36])	No additional study reported. [CSR PDF pp. 1,35-36] (N = No additional study reported. [CSR PDF pp. 1,35-36])	No additional study reported. [CSR PDF pp. 1,35-36] (N = No additional study reported. [CSR PDF pp. 1,35-36])
Received subsequent therapy, n (%)	No additional study reported. [CSR PDF pp. 1,35-36]	No additional study reported. [CSR PDF pp. 1,35-36]	No additional study reported. [CSR PDF pp. 1,35-36]	No additional study reported. [CSR PDF pp. 1,35-36]
No additional study reported. [CSR PDF pp. 1,35-36], n (%)	No additional study reported. [CSR PDF pp. 1,35-36]	No additional study reported. [CSR PDF pp. 1,35-36]	No additional study reported. [CSR PDF pp. 1,35-36]	No additional study reported. [CSR PDF pp. 1,35-36]
No additional study reported. [CSR PDF pp. 1,35-36], n (%)	No additional study reported. [CSR PDF pp. 1,35-36]	No additional study reported. [CSR PDF pp. 1,35-36]	No additional study reported. [CSR PDF pp. 1,35-36]	No additional study reported. [CSR PDF pp. 1,35-36]
No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]	No additional gap-addressing study is reported in this CSR; its scope is the STEP 1 main phase. [CSR PDF pp. 1,32,35-36]	No additional gap-addressing study is reported in this CSR; its scope is the STEP 1 main phase. [CSR PDF pp. 1,32,35-36]	No additional gap-addressing study is reported in this CSR; its scope is the STEP 1 main phase. [CSR PDF pp. 1,32,35-36]	No additional gap-addressing study is reported in this CSR; its scope is the STEP 1 main phase. [CSR PDF pp. 1,32,35-36]

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AE = adverse event; CI = confidence interval; FAS = full analysis set; OR = odds ratio; SAE = serious adverse event; SD = standard deviation. Terminology follows the CSR. [CSR PDF pp. 25-28]

Source: No additional gap-addressing study is reported in this CSR; its scope is the STEP 1 main phase. [CSR PDF pp. 1,32,35-36]

Results

Efficacy

No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]

Efficacy endpoint 1

No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]

No additional gap-addressing study is reported in this CSR; its scope is the STEP 1 main phase. [CSR PDF pp. 1,32,35-36]

No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]

No additional gap-addressing study is reported in this CSR; its scope is the STEP 1 main phase. [CSR PDF pp. 1,32,35-36]

No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]

Harms

No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]

Studies of Other Design

No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]

Description of No additional gap-addressing study is reported in this CSR; its scope is the STEP 1 main phase. [CSR PDF pp. 1,32,35-36]

Study Design and Objectives

No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]

Eligibility criteria

No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]

Interventions and Exposures

Not reported in the supplied CSR: no additional study of this design is provided. [CSR PDF pp. 1,35-36]

Outcomes

Not reported in the supplied CSR: no additional study of this design is provided. [CSR PDF pp. 1,35-36]

Statistical analysis

No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]
No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]
No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]
No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]
No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]
No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]
No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]
No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]
No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]
No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]

Patient Population

Participant Characteristics

No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]

Participant eligibility

No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]

Exposure to Interventions

Exposures

No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]

Concomitant medications, co-interventions, confounding treatments

No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]

Results

Efficacy

No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]

No additional gap-addressing study is reported in this CSR; its scope is the STEP 1 main phase. [CSR PDF pp. 1,32,35-36]

No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]

Efficacy endpoint 2

No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]

Efficacy endpoint 3

No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]

Harms



No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]

Sponsor Summary and Conclusion

No additional study is reported in the supplied CSR. [CSR PDF pp. 1,35-36]

Section 6. Summary of the Sponsor's Pharmacoeconomic Submission

Not reported in the supplied CSR: no economic evaluation.

Key Components of the Sponsor's Economic Evaluation

Component	Description
Treatment information	
Drug under review (DUR)	Semaglutide 2.4 mg once weekly, subcutaneous solution for injection. Trial products: 1.0 and 3.0 mg/mL in a 3 mL PDS290 pre-filled pen-injector. [CSR PDF pp. 39-40; Table 9-1] The Wegovy brand and marketed Canadian presentations are not established in this CSR. Canadian recommended monograph regimen is not supplied.
Submitted price of drug under review	Not reported in the supplied CSR: no sponsor economic evaluation is provided.
Regimen	Economic-model regimen is not reported. Trial regimen: 0.25 mg once weekly for 4 weeks, then 0.5, 1.0 and 1.7 mg once weekly for 4 weeks each, then 2.4 mg once weekly for 52 weeks (68 weeks total). If 2.4 mg was not tolerated, 1.7 mg was permitted to avoid complete discontinuation, with an attempt to re-escalate recommended. [CSR PDF pp. 39-40; Tables 9-1 and 9-2] Matched placebo injection once weekly using the same pen and escalating volumes for 68 weeks; both groups received diet counselling targeting a 500 kcal/day deficit and ≥ 150 minutes/week physical activity, with counselling every 4 weeks. [CSR PDF pp. 39-42]
Annual cost, per-cycle cost, or one-time cost of drug under review	Not reported in the supplied CSR: no sponsor economic evaluation is provided.
Model information	
Type of economic evaluation	Not reported in the supplied CSR: no sponsor economic evaluation is provided.
Treatment	Model treatment is not reported. Semaglutide 2.4 mg once weekly, subcutaneous solution for injection. Trial products: 1.0 and 3.0 mg/mL in a 3 mL PDS290 pre-filled pen-injector. [CSR PDF pp. 39-40; Table 9-1] The Wegovy brand and marketed Canadian presentations are not established in this CSR.
Included comparator(s)	Model comparator(s) are not reported. Matched placebo injection once weekly using the same pen and escalating volumes for 68 weeks; both groups received diet counselling targeting a 500 kcal/day deficit and ≥ 150 minutes/week physical activity, with counselling every 4 weeks. [CSR PDF pp. 39-42]
Perspective	Not reported in the supplied CSR: no sponsor economic evaluation is provided.
Time horizon	Not reported in the supplied CSR: no sponsor economic evaluation is provided.
Cycle length	Not reported in the supplied CSR: no sponsor economic evaluation is provided.
Modelled population(s)	Model population is not reported. Trial population: Adults ≥ 18 years with BMI ≥ 30 kg/m ² , or ≥ 27 kg/m ² with ≥ 1 treated or untreated weight-related comorbidity (hypertension, dyslipidaemia, obstructive sleep apnoea or cardiovascular disease), and ≥ 1 self-reported

Component	Description
	unsuccessful dietary weight-loss effort. [CSR PDF p. 37]
Characteristics of modelled population	Model starting characteristics are not reported. Trial overall baseline: age 46 (SD 13) years; female 74.1%; weight 105.3 (21.9) kg; BMI 37.9 (6.7) kg/m ² . [CSR PDF pp. 68-70]
Model health states	Not reported in the supplied CSR: no sponsor economic evaluation is provided.
Duration of treatment	Model treatment duration is not reported. Trial treatment: 68 weeks, with 7-week safety follow-up. [CSR PDF p. 35]
Data sources	
Comparative efficacy	Economic-model selection, assumptions and extrapolation are not reported. Available trial evidence: At week 68, treatment-policy estimated weight change was -14.85% with semaglutide and -2.41% with placebo: difference -12.44 percentage points (95% CI -13.37 to -11.51), $p < 0.0001$. FAS $n = 1306/655$; observed week-68 weight $n = 1212/577$. [CSR PDF p. 333; Table 14.2.9] Confirmatory week-68 treatment-policy differences: waist -9.42 cm (95% CI -10.30 to -8.53), systolic BP -5.10 mmHg (-6.34 to -3.87), SF-36 physical functioning +1.80 (1.18-2.42), IWQOL physical function +9.43 (7.50-11.35); all $p < 0.0001$. $\geq 10\%$ and $\geq 15\%$ weight-loss ORs were 14.68 (11.08-19.44) and 19.26 (12.89-28.76). [CSR PDF p. 87; Table 11-1]
Natural history and/or clinical pathway	Model natural-history inputs/transition assumptions are not reported. Obesity is described as a disease with substantial medical, societal and economic impact, reduced health-related quality of life, and increased morbidity and mortality. Associated complications include type 2 diabetes, hypertension, dyslipidaemia, sleep apnoea, cardiovascular disease, osteoarthritis, urinary incontinence, non-alcoholic steatohepatitis and some cancers. Risk increases with BMI; 5%-10% weight loss can improve comorbidities, physical symptoms and quality of life. Lifestyle-induced weight loss is opposed by increased appetite and reduced energy expenditure, contributing to regain. [CSR PDF p. 31] Canadian incidence/prevalence, formal staging and quantified survival estimates are not reported. <i>o disease natural history, population demographics, epidemiological parameters</i> <i>o health state transitions</i>
Health-related utilities and disutilities	Health-state utility/disutility values and mapping are not reported. The CSR reports SF-36 and IWQOL-Lite-CT HRQoL measures; these should not be substituted for utilities. [CSR PDF pp. 112-120]
Costs	Not reported in the supplied CSR: no sponsor economic evaluation is provided.
Summary of the submitted results	
Base case results	Not reported in the supplied CSR: no sponsor economic evaluation is provided.
Scenario analysis results	Not reported in the supplied CSR: no sponsor economic evaluation is provided.

ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life-years; *[add as required]*.

Model Structure

Not reported in the supplied CSR: no economic evaluation.

Not reported in the supplied CSR: no economic evaluation.

Not reported in the supplied CSR: no economic evaluation.



Figure 1: Model Structure

Not reported in the supplied CSR: no economic evaluation.

Appendix 1: Literature Search Strategy

Not reported in the supplied CSR: no systematic literature search or review-selection process is provided.

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Database Search Strategies

Not reported in the supplied CSR: no systematic literature search or review-selection process is provided.

Clinical Trials Registries

Not reported in the supplied CSR: no systematic literature search or review-selection process is provided.

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Not reported in the supplied CSR: no systematic literature search or review-selection process is provided.

Appendix 2: List of Excluded Studies

Table Number: Excluded Studies

Reference	Reason for Exclusion
Not reported in the supplied CSR: no systematic literature search or review-selection process is provided.	Not reported in the supplied CSR: no systematic literature search or review-selection process is provided.
Not reported in the supplied CSR: no systematic literature search or review-selection process is provided.	Not reported in the supplied CSR: no systematic literature search or review-selection process is provided.
Not reported in the supplied CSR: no systematic literature search or review-selection process is provided.	Not reported in the supplied CSR: no systematic literature search or review-selection process is provided.

References

Citations throughout identify exact pages in the supplied 4120-page PDF. "CSR PDF p." means the 1-based page position in that file; its main-text printed pagination differs after inserted contents pages.

1. Novo Nordisk. Effect and safety of semaglutide 2.4 mg once-weekly in subjects with overweight or obesity. NN9536-4373 (STEP 1). Clinical trial report, main phase. Version 1.0, final, 17 August 2020. Supplied file: Phase3a-STEP1-report(3).pdf. [CSR PDF pp. 1-2]

Only the supplied CSR was used to complete the evidence fields; no external clinical evidence or Canadian regulatory/economic assumptions were added.

"Not reported" identifies information unavailable in the supplied CSR; it does not imply that the information does not exist elsewhere.