

Reimbursement Review Sponsor Summary Template

Completed from the supplied STEP 1 CSR only. Citations use the printed "Report body" page number (the "of 6980" sequence), not the separate "Text part" numbering; cited main-report and end-of-text-table pages match PDF page positions. "Not reported" identifies a source gap, not a negative clinical finding; scope citations locate what this CSR covers. Original headings, fields and instructions are retained as requested. (CSR pp. 1-3, 32, 35-36.)

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

No clinical figures added. Figure fields are retained and marked where the source does not provide the requested evidence.

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; CSR = clinical study report; DXA/DEXA = dual-energy X-ray absorptiometry; ETD = estimated treatment difference; GLP-1 = glucagon-like peptide-1; HbA1c = glycated haemoglobin; IWQOL-Lite-CT = Impact of Weight on Quality of Life-Lite for Clinical Trials; MMRM = mixed model for repeated measurements; OR = odds ratio; PRO = patient-reported outcome; SAS = safety analysis set; SF-36 = Short Form-36. (CSR pp. 25-26, 45-46, 58.)

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Section 1. Introduction

Application Summary

Table 1: Submitted for Review

Item	Description
Drug (product)	Semaglutide, solution for subcutaneous injection, maintenance dose 2.4 mg once weekly. The brand name Wegovy is not stated in this CSR. (CSR pp. 2, 39-40.)
Sponsor	Novo Nordisk, Novo Allé, 2880 Bagsvaerd, Denmark. (CSR p. 2.)
Health Canada indication	Not reported in the supplied CSR. (CSR pp. 1, 32, 35-36: report scope.)
Health Canada approval status	Not reported in the supplied CSR. (CSR pp. 1, 32, 35-36: report scope.)
Health Canada review pathway	Not reported in the supplied CSR. (CSR pp. 1, 32, 35-36: report scope.)
NOC date	Not reported in the supplied CSR. (CSR pp. 1, 32, 35-36: report scope.)
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 through reduced energy intake, increased satiety/fullness and reduced hunger. (CSR pp. 31-32.)
Recommended dosage	Trial regimen: semaglutide subcutaneously once weekly, 0.25, 0.5, 1.0 and 1.7 mg for 4 weeks each, then 2.4 mg for 52 weeks. A 1.7 mg maintenance dose was permitted for intolerance, with an attempt to re-escalate recommended. (CSR pp. 39-40, Tables 9-1 and 9-2.) Approved Canadian dosing is not reported. (CSR pp. 39-40.)
Submission type	Not reported in the supplied CSR. (CSR pp. 1, 32, 35-36: report scope.)
Reimbursement request	Not reported in the supplied CSR. (CSR pp. 1, 32, 35-36: report scope.)

Rationale for Filing the Resubmission or Reassessment

Not reported in the supplied CSR. (CSR pp. 1, 32, 35-36: report scope.)

Drug under Review

Indication and Reimbursement Request

The CSR describes weight management in adults with overweight or obesity; it does not provide the Health Canada indication or a reimbursement request. (CSR pp. 2, 32, 36-37.)

Dosing and Administration

Trial regimen: semaglutide subcutaneously once weekly, 0.25, 0.5, 1.0 and 1.7 mg for 4 weeks each, then 2.4 mg for 52 weeks. A 1.7 mg maintenance dose was permitted for intolerance, with an attempt to re-escalate recommended. (CSR pp. 39-40, Tables 9-1 and 9-2.) Both groups received counselling every 4 weeks for a 500 kcal/day deficit and ≥150 minutes/week of physical activity, with daily food/activity records. (CSR p. 41.)

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 through reduced energy intake, increased satiety/fullness and reduced hunger. (CSR pp. 31-32.)

Prescribing

Trial injections were self-administered once weekly in the thigh, abdomen or upper arm, at any time regardless of meals. Canadian prescriber restrictions are not reported. (CSR p. 40, Table 9-1.)

Disease Background

Overview of the Condition

Obesity is associated with increased morbidity, mortality and reduced health-related quality of life; associated conditions include type 2 diabetes, hypertension, dyslipidaemia, sleep apnoea, cardiovascular disease and osteoarthritis. The CSR describes difficulty achieving and maintaining weight loss with lifestyle measures. (CSR p. 31.)

Estimated Disease Prevalence

Canadian provincial/territorial prevalence estimates and uncertainty bounds are not reported. The CSR provides a qualitative global obesity background only. (CSR p. 31.)

Table 2: 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. (CSR p. 31: background.)	Not reported. (CSR p. 31: background.)	Not reported. (CSR p. 31: background.)
Alberta	Not reported. (CSR p. 31: background.)	Not reported. (CSR p. 31: background.)	Not reported. (CSR p. 31: background.)
British Columbia	Not reported. (CSR p. 31: background.)	Not reported. (CSR p. 31: background.)	Not reported. (CSR p. 31: background.)
Manitoba	Not reported. (CSR p. 31: background.)	Not reported. (CSR p. 31: background.)	Not reported. (CSR p. 31: background.)

New Brunswick	Not reported. (CSR p. 31: background.)	Not reported. (CSR p. 31: background.)	Not reported. (CSR p. 31: background.)
Newfoundland and Labrador	Not reported. (CSR p. 31: background.)	Not reported. (CSR p. 31: background.)	Not reported. (CSR p. 31: background.)
Northwest Territories	Not reported. (CSR p. 31: background.)	Not reported. (CSR p. 31: background.)	Not reported. (CSR p. 31: background.)
Nova Scotia	Not reported. (CSR p. 31: background.)	Not reported. (CSR p. 31: background.)	Not reported. (CSR p. 31: background.)
Nunavut	Not reported. (CSR p. 31: background.)	Not reported. (CSR p. 31: background.)	Not reported. (CSR p. 31: background.)
Ontario	Not reported. (CSR p. 31: background.)	Not reported. (CSR p. 31: background.)	Not reported. (CSR p. 31: background.)
Prince Edward Island	Not reported. (CSR p. 31: background.)	Not reported. (CSR p. 31: background.)	Not reported. (CSR p. 31: background.)
Saskatchewan	Not reported. (CSR p. 31: background.)	Not reported. (CSR p. 31: background.)	Not reported. (CSR p. 31: background.)
Yukon	Not reported. (CSR p. 31: background.)	Not reported. (CSR p. 31: background.)	Not reported. (CSR p. 31: background.)
Non-Insured Health Benefits	Not reported. (CSR p. 31: background.)	Not reported. (CSR p. 31: background.)	Not reported. (CSR p. 31: background.)

Diagnosis of the Condition

Diagnostic Testing Requirements

Trial assessment included body weight, height/BMI, waist circumference and laboratory measures including HbA1c and fasting plasma glucose; HbA1c $\geq 6.5\%$ was a key exclusion. Requirements for routine Canadian diagnostic testing are not reported. (CSR pp. 37, 45-46.)

Availability of Diagnostic Testing

Central and specialized laboratories were used in the trial; availability, access barriers and coverage of diagnostic testing in Canadian practice are not reported. (CSR p. 29.)

Health Care Resources

Pre-Treatment Phase

Trial screening assessed eligibility and included a food diary and mental-health randomization criteria. Canadian pre-treatment resource use and costs are not reported. (CSR pp. 37-38.)

Treatment Phase

Both groups received counselling every 4 weeks for a 500 kcal/day deficit and ≥ 150 minutes/week of physical activity, with daily food/activity records. (CSR p. 41.) Trial use of injections and safety assessments is described, but routine-care resource quantities and costs are not reported. (CSR pp. 39-41, 47-55.)

Post-Treatment Phase

A safety follow-up visit was scheduled 7 weeks after treatment; routine Canadian post-treatment resource use and costs are not reported. (CSR pp. 35-36.)

Place in Therapy and Comparators

Current Treatment Paradigm

The CSR describes lifestyle intervention (diet and exercise) as first-line treatment, bariatric surgery as an option for some people with severe obesity, and pharmacotherapy as a potential alternative. It does not set out a Canadian reimbursement algorithm. (CSR pp. 31, 36.)

Unmet Therapeutic Needs

The CSR identifies difficulty sustaining weight loss, biological responses promoting regain, limitations of surgery and a need for safe, effective, convenient therapies supporting weight maintenance and comorbidity management. (CSR p. 31.)

Impact of Drug on Treatment Paradigm

Proposed Place in Therapy

Adults aged ≥ 18 years with BMI ≥ 30 kg/m², or ≥ 27 kg/m² with hypertension, dyslipidaemia, obstructive sleep apnoea or cardiovascular disease, and ≥ 1 unsuccessful dietary weight-loss effort; type 2 diabetes excluded. (CSR pp. 36-37.) Canadian reimbursement positioning is not reported. (CSR pp. 32-37.)

Potential Impact on Currently Reimbursed Treatments

Effects on utilization, displacement or funding of currently reimbursed treatments are not reported. (CSR pp. 31-37: trial rationale and comparator.)

Provisional Algorithm Diagram (oncology drugs)

Not applicable to this weight-management trial; an oncology treatment algorithm is not reported. (CSR pp. 2, 32-37.)

Not applicable to this weight-management trial; an oncology treatment algorithm is not reported. (CSR pp. 2, 32-37.)

Comparators

The randomized comparator was matching subcutaneous placebo plus the same lifestyle intervention. No active-comparator randomized arm is reported. (CSR pp. 37, 39-41.)

Table 3: 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 p. 40.)	Trial: weight management; Canadian indication not reported. (CSR pp. 2, 37.)	Trial regimen: semaglutide subcutaneously once weekly, 0.25, 0.5, 1.0 and 1.7 mg for 4 weeks each, then 2.4 mg for 52 weeks. A 1.7 mg maintenance dose was permitted for intolerance, with an attempt to re-escalate recommended. (CSR pp. 39-40, Tables 9-1 and 9-2.)	NA Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)	NA Not reported in the supplied CSR: no pharmacoeconomic submission is presented. (CSR pp. 1, 32-36: clinical-trial scope.)
Matching placebo. (CSR p. 40.)	Control intervention in STEP 1. (CSR p. 37.)	Subcutaneous once weekly; volume matched to semaglutide escalation and maintenance; same lifestyle counselling. (CSR pp. 39-41.)	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)	Not reported in the supplied CSR: no pharmacoeconomic submission is presented. (CSR pp. 1, 32-36: clinical-trial scope.)
Not reported in the supplied CSR. (CSR pp. 1, 32, 35-36: report scope.)	Not reported in the supplied CSR. (CSR pp. 1, 32, 35-36: report scope.)	Not reported in the supplied CSR. (CSR pp. 1, 32, 35-36: report scope.)	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)	Not reported in the supplied CSR: no pharmacoeconomic submission is presented. (CSR pp. 1, 32-36: clinical-trial scope.)
Add rows as needed Not reported in the supplied CSR. (CSR pp. 1, 32, 35-36: report scope.)	Add rows as needed Not reported in the supplied CSR. (CSR pp. 1, 32, 35-36: report scope.)	Add rows as needed Not reported in the supplied CSR. (CSR pp. 1, 32, 35-36: report scope.)	Add rows as needed Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)	Add rows as needed Not reported in the supplied CSR: no pharmacoeconomic submission is presented. (CSR pp. 1, 32-36: clinical-trial scope.)

Source: Source for completed entries: reference 1, STEP 1 CSR; specific page/table citations appear in each completed field. No other evidence source was used.

Proposed Reimbursement Conditions

Proposed initiation, renewal, discontinuation and prescribing reimbursement conditions and their rationales are not reported; trial eligibility and stopping rules are not reimbursement conditions. (CSR pp. 37-39.)

Table 4: Proposed Reimbursement Conditions for the Drug Under Review

Proposed reimbursement condition	Reason
Initiation	
1. Not reported in CSR: reimbursement condition/rationale. (CSR pp. 37-39: trial criteria only.)	Not reported in CSR: reimbursement condition/rationale. (CSR pp. 37-39: trial criteria only.)
2. Not reported in CSR: reimbursement condition/rationale. (CSR pp. 37-39: trial criteria only.)	Not reported in CSR: reimbursement condition/rationale. (CSR pp. 37-39: trial criteria only.)
Add or delete rows as needed Not reported in CSR: reimbursement condition/rationale. (CSR pp. 37-39: trial criteria only.)	Not reported in CSR: reimbursement condition/rationale. (CSR pp. 37-39: trial criteria only.)
Renewal	
3. Not reported in CSR: reimbursement condition/rationale. (CSR pp. 37-39: trial criteria only.)	Not reported in CSR: reimbursement condition/rationale. (CSR pp. 37-39: trial criteria only.)
4. Not reported in CSR: reimbursement condition/rationale. (CSR pp. 37-39: trial criteria only.)	Not reported in CSR: reimbursement condition/rationale. (CSR pp. 37-39: trial criteria only.)
Add or delete rows as needed Not reported in CSR: reimbursement condition/rationale. (CSR pp. 37-39: trial criteria only.)	Not reported in CSR: reimbursement condition/rationale. (CSR pp. 37-39: trial criteria only.)
Discontinuation	
5. Not reported in CSR: reimbursement condition/rationale. (CSR pp. 37-39: trial criteria only.)	Not reported in CSR: reimbursement condition/rationale. (CSR pp. 37-39: trial criteria only.)
Add or delete rows as needed Not reported in CSR: reimbursement condition/rationale. (CSR pp. 37-39: trial criteria only.)	Not reported in CSR: reimbursement condition/rationale. (CSR pp. 37-39: trial criteria only.)
Prescribing	
6. Not reported in CSR: reimbursement condition/rationale. (CSR pp. 37-39: trial criteria only.)	Not reported in CSR: reimbursement condition/rationale. (CSR pp. 37-39: trial criteria only.)
Add or delete rows as needed Not reported in CSR: reimbursement condition/rationale. (CSR pp. 37-39: trial criteria only.)	Not reported in CSR: reimbursement condition/rationale. (CSR pp. 37-39: trial criteria only.)

AE = adverse event; CI = confidence interval; FAS = full analysis set; OR = odds ratio; SAE = serious adverse event. (CSR pp. 25-26, 58.)

Section 2. Systematic Review

Objectives and Methods

No systematic review is reported in the CSR. The available clinical evidence summarized here is STEP 1, whose primary objective was comparison of weight change with semaglutide versus placebo, both with lifestyle intervention. (CSR pp. 1, 32-33.)

Review Protocol

Not reported in the supplied CSR: no systematic-review methods or results are provided. (CSR pp. 1, 32-36: single-trial scope.)

Population

Adults aged ≥ 18 years with BMI ≥ 30 kg/m², or ≥ 27 kg/m² with hypertension, dyslipidaemia, obstructive sleep apnoea or cardiovascular disease, and ≥ 1 unsuccessful dietary weight-loss effort; type 2 diabetes excluded. (CSR pp. 36-37.) Systematic-review population criteria and subgroups are not reported. (CSR pp. 32-37.)

Intervention

Trial regimen: semaglutide subcutaneously once weekly, 0.25, 0.5, 1.0 and 1.7 mg for 4 weeks each, then 2.4 mg for 52 weeks. A 1.7 mg maintenance dose was permitted for intolerance, with an attempt to re-escalate recommended. (CSR pp. 39-40, Tables 9-1 and 9-2.)

Comparator(s)

Matching placebo plus lifestyle intervention. Systematic-review comparator criteria are not reported. (CSR pp. 37, 39-41.)

Outcomes

Co-primary: percentage change in body weight and $\geq 5\%$ weight loss at week 68. Confirmatory secondary: $\geq 10\%$ and $\geq 15\%$ weight loss; changes in waist circumference, systolic blood pressure, SF-36 physical functioning and IWQOL-Lite-CT physical function at week 68. All eight endpoints were in the multiplicity-controlled hierarchy. (CSR pp. 59-61, 87, Tables 9-8 and 11-1.)

Study design

STEP 1 (NN9536-4373; NCT03548935) was a phase 3a, multicentre, multinational, randomized, double-blind, placebo-controlled trial; 1,961 participants were randomized 2:1 (semaglutide 1,306; placebo 655). It included 68 weeks of treatment and 7 weeks of safety follow-up. (CSR pp. 2, 35, 65-66.)

Table 5: Inclusion criteria for the systematic review

Criteria	Description
Population	Adults aged ≥ 18 years with BMI ≥ 30 kg/m ² , or ≥ 27 kg/m ² with hypertension, dyslipidaemia, obstructive sleep apnoea or cardiovascular disease, and ≥ 1 unsuccessful dietary weight-loss effort; type 2 diabetes excluded. (CSR pp. 36-37.) Systematic-review criteria/subgroups: not reported. (CSR pp. 32-37.) Subgroups: Systematic-review subgroups not reported. (CSR pp. 32-37.)
Intervention	Trial regimen: semaglutide subcutaneously once weekly, 0.25, 0.5, 1.0 and 1.7 mg for 4 weeks each, then 2.4 mg for 52 weeks. A 1.7 mg maintenance dose was permitted for intolerance, with an attempt to re-escalate recommended. (CSR pp. 39-40, Tables 9-1 and 9-2.)
Comparator	Matching placebo plus lifestyle intervention. Systematic-review comparator criteria are not reported. (CSR pp. 37, 39-41.)
Outcomes	Efficacy outcomes: Co-primary: percentage change in body weight and $\geq 5\%$ weight loss at week 68. Confirmatory secondary: $\geq 10\%$ and $\geq 15\%$ weight loss; changes in waist circumference, systolic blood pressure, SF-36 physical functioning and IWQOL-Lite-CT physical function at week 68. All eight endpoints were in the multiplicity-controlled hierarchy. (CSR pp. 59-61, 87, Tables 9-8 and 11-1.) Harms outcomes: AEs, SAEs, fatal events, discontinuations, and safety focus areas. (CSR pp. 61, 128-129.)
Study Designs	STEP 1 (NN9536-4373; NCT03548935) was a phase 3a, multicentre, multinational, randomized, double-blind, placebo-controlled trial; 1,961 participants were randomized 2:1 (semaglutide 1,306; placebo 655). It included 68 weeks of treatment and 7 weeks of safety follow-up. (CSR pp. 2, 35, 65-66.) Systematic-review design eligibility not reported. (CSR pp. 32-36.)

AE = adverse event; CI = confidence interval; FAS = full analysis set; OR = odds ratio; SAE = serious adverse event. (CSR pp. 25-26, 58.)

Literature Search and Study Selection

Literature Search Methodology

Systematic-review information not reported in supplied CSR. (CSR pp. 1, 32-36.)

Searching bibliographic databases

Searching clinical trial registries

Reporting of the literature search

Example of Reporting Clinical Literature Search Methods

Intervention search: not reported. (CSR pp. 1, 32-36.) Population search: not reported. (CSR pp. 1, 32-36.)

Systematic-review information not reported in supplied CSR. (CSR pp. 1, 32-36.)

Study Selection

Figure Not reported: PRISMA Flow Diagram

Systematic-review information not reported in supplied CSR. (CSR pp. 1, 32-36.)

Included Studies

Table 6: Details of Included Studies

Study identifier	STEP 1 / NN9536-4373. (CSR p. 2.)	Second study not reported. (CSR pp. 1, 32.)
Designs & Populations		
Study Design	STEP 1 (NN9536-4373; NCT03548935) was a phase 3a, multicentre, multinational, randomized, double-blind, placebo-controlled trial; 1,961 participants were randomized 2:1 (semaglutide 1,306; placebo 655). It included 68 weeks of treatment and 7 weeks of safety follow-up. (CSR pp. 2, 35, 65-66.)	Second study not reported. (CSR pp. 1, 32.)
Locations	129 sites / 16 countries; 7 Canadian sites. (CSR p. 2.)	Second study not reported. (CSR pp. 1, 32.)
Patient Enrolment Dates:	Start date: 4 June 2018 (trial initiated). (CSR p. 2.) End date: Last enrollment date not reported. (CSR p. 2: trial dates.)	Start date: Second study not reported. (CSR pp. 1, 32.) End date: Second study not reported. (CSR pp. 1, 32.)
Randomized (N)	1,961: semaglutide 1,306; placebo 655. (CSR p. 65.)	Second study not reported. (CSR pp. 1, 32.)
Inclusion Criteria	Adults aged ≥ 18 years with BMI ≥ 30 kg/m ² , or ≥ 27 kg/m ² with hypertension, dyslipidaemia, obstructive sleep apnoea or cardiovascular disease, and ≥ 1 unsuccessful dietary weight-loss effort; type 2 diabetes excluded. (CSR pp. 36-37.)	Second study not reported. (CSR pp. 1, 32.)
Exclusion Criteria	Adults aged ≥ 18 years with BMI ≥ 30 kg/m ² , or ≥ 27 kg/m ² with hypertension, dyslipidaemia, obstructive sleep apnoea or cardiovascular disease, and ≥ 1 unsuccessful dietary weight-loss effort; type 2 diabetes excluded. (CSR pp. 36-37.) Additional reported exclusions include HbA1c $\geq 6.5\%$, >5 kg weight change within 90 days, uncontrolled thyroid disease, PHQ-9 ≥ 15 at screening and lifetime suicide attempt. Randomization required food-diary completion, PHQ-9 < 15 and no specified suicidal behaviour/ideation. The full protocol exclusion list is referenced but not reproduced in the supplied report. (CSR pp. 37-38, 68.)	Second study not reported. (CSR pp. 1, 32.)
Drugs		

Study identifier	STEP 1 / NN9536-4373. (CSR p. 2.)	Second study not reported. (CSR pp. 1, 32.)
Intervention	Trial regimen: semaglutide subcutaneously once weekly, 0.25, 0.5, 1.0 and 1.7 mg for 4 weeks each, then 2.4 mg for 52 weeks. A 1.7 mg maintenance dose was permitted for intolerance, with an attempt to re-escalate recommended. (CSR pp. 39-40, Tables 9-1 and 9-2.) Both groups received counselling every 4 weeks for a 500 kcal/day deficit and ≥150 minutes/week of physical activity, with daily food/activity records. (CSR p. 41.)	Second study not reported. (CSR pp. 1, 32.)
Comparator(s)	Matching placebo plus lifestyle intervention. Systematic-review comparator criteria are not reported. (CSR pp. 37, 39-41.)	Second study not reported. (CSR pp. 1, 32.)
Study duration		
• Screening phase	1 week (week -1 to week 0). (CSR p. 35, Figure 9-1.)	Second study not reported. (CSR pp. 1, 32.)
• Run-in phase	No separate run-in phase described. (CSR pp. 35-39.)	Second study not reported. (CSR pp. 1, 32.)
• Treatment phase	68 weeks: 16-week escalation + 52-week maintenance. (CSR p. 35.)	Second study not reported. (CSR pp. 1, 32.)
• Follow-up phase	7 weeks off treatment; extension planned separately. (CSR pp. 35-36.)	Second study not reported. (CSR pp. 1, 32.)
Outcomes		
Primary End Point	Percentage body-weight change and ≥5% weight loss at week 68. (CSR pp. 59, 87.)	Second study not reported. (CSR pp. 1, 32.)
Secondary and Exploratory End Points	Secondary: Confirmatory: ≥10%/≥15% weight loss, waist, systolic BP, SF-36 physical functioning and IWQOL-Lite-CT physical function at week 68. Supportive: other weight, metabolic, PRO and safety endpoints. (CSR pp. 59-61.) Exploratory: Glycaemic category, antihypertensive/lipid medication use, productivity, permanent treatment discontinuation/time to discontinuation, fatty liver index, urinary incontinence, diet/activity. (CSR p. 61.)	Secondary: Second study not reported. (CSR pp. 1, 32.) Exploratory: Second study not reported. (CSR pp. 1, 32.)
Publication status		
Publications	STEP 1 journal publication not reported. Final CSR dated 17 August 2020. (CSR p. 2.) NCT03548935. (CSR p. 2.)	Second study not reported. (CSR pp. 1, 32.) Second study not reported. (CSR pp. 1, 32.)

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Description of Studies

See the adjacent response in this field. (CSR pp. 2, 35-36.)

STEP 1 (NN9536-4373; NCT03548935) was a phase 3a, multicentre, multinational, randomized, double-blind, placebo-controlled trial; 1,961 participants were randomized 2:1 (semaglutide 1,306; placebo 655). It included 68 weeks of treatment and 7 weeks of safety follow-up. (CSR pp. 2, 35, 65-66.) It was conducted at 129 sites in 16 countries, including 7 Canadian sites and 63 Canadian participants. Trial initiation was 4 June 2018; primary completion 30 March 2020; completion 19 April 2020. (CSR pp. 2, 69.)

Eligibility Criteria

Adults aged ≥ 18 years with BMI ≥ 30 kg/m², or ≥ 27 kg/m² with hypertension, dyslipidaemia, obstructive sleep apnoea or cardiovascular disease, and ≥ 1 unsuccessful dietary weight-loss effort; type 2 diabetes excluded. (CSR pp. 36-37.) Additional reported exclusions include HbA1c $\geq 6.5\%$, >5 kg weight change within 90 days, uncontrolled thyroid disease, PHQ-9 ≥ 15 at screening and lifetime suicide attempt. Randomization required food-diary completion, PHQ-9 < 15 and no specified suicidal behaviour/ideation. The full protocol exclusion list is referenced but not reproduced in the supplied report. (CSR pp. 37-38, 68.)

Interventions

Trial regimen: semaglutide subcutaneously once weekly, 0.25, 0.5, 1.0 and 1.7 mg for 4 weeks each, then 2.4 mg for 52 weeks. A 1.7 mg maintenance dose was permitted for intolerance, with an attempt to re-escalate recommended. (CSR pp. 39-40, Tables 9-1 and 9-2.) Both groups received counselling every 4 weeks for a 500 kcal/day deficit and ≥ 150 minutes/week of physical activity, with daily food/activity records. (CSR p. 41.) Allocation was centralized via IWRS, with subjects, investigators and sponsor blinded; products had identical appearance. (CSR p. 42.)

Outcomes

Co-primary: percentage change in body weight and $\geq 5\%$ weight loss at week 68. Confirmatory secondary: $\geq 10\%$ and $\geq 15\%$ weight loss; changes in waist circumference, systolic blood pressure, SF-36 physical functioning and IWQOL-Lite-CT physical function at week 68. All eight endpoints were in the multiplicity-controlled hierarchy. (CSR pp. 59-61, 87, Tables 9-8 and 11-1.) Supportive/exploratory endpoints included $\geq 20\%$ weight loss, BMI, lipids, glucose measures, body composition, other quality-of-life scores, medication use, work productivity, urinary incontinence and treatment discontinuation; safety included AEs and SAEs through week 75. (CSR pp. 59-61.) Body weight was measured with standardized digital scales; waist circumference with a standardized tape. SF-36 has 36 items, 8 domains and 2 summaries; IWQOL-Lite-CT has 20 items. Higher physical-function scores indicate better function. Prespecified within-person responder thresholds were +4.3 for SF-36 and +20 for IWQOL-Lite-CT; these are not between-group MIDs. A complete scale-range/MID-validation account is not provided here. (CSR pp. 45-46, 115, 120.)

The summary table below is required for all applications. When identifying primary and secondary endpoints, include a “*” and footnote identifying which endpoints were adjusted for multiple comparisons in the statistical analyses.

Table 7: Summary of Outcomes Relevant to the Systematic Review

Outcome Measure	Timepoint	Study 1	Study 2
Body-weight change (%) and $\geq 5\%$ loss* (CSR pp. 59-61, 87.)	Week 68 (CSR pp. 59-61, 87.)	Co-primary* (CSR pp. 59-61, 87.)	Second study not reported. (CSR pp. 1, 32.)
$\geq 10\%/\geq 15\%$ loss; waist circumference; systolic BP* (CSR pp. 59-61, 87.)	Week 68 (CSR pp. 59-61, 87.)	Confirmatory secondary* (CSR pp. 59-61, 87.)	Second study not reported. (CSR pp. 1, 32.)

Outcome Measure	Timepoint	Study 1	Study 2
Add rows as necessary SF-36 physical functioning and IWQOL-Lite-CT physical function*; safety (CSR pp. 59-61, 87.)	Week 68; AEs/SAEs through week 75 (CSR pp. 59-61, 87.)	PROs: confirmatory secondary*; safety: supportive (CSR pp. 59-61, 87.)	No second study reported. (CSR pp. 1, 32.)

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

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Statistical analysis

Clinical Trial Endpoints

Percentage weight change used ANCOVA with randomized treatment and baseline weight; $\geq 5\%$ response used logistic regression with the same factor/covariate. Missing week-68 outcomes were multiply imputed 1,000 times using retrieved participants in the same treatment arm. (CSR p. 93, Table 11-2; CSR p. 333, Table 14.2.9.) The primary treatment-policy estimand included all randomized subjects irrespective of treatment discontinuation or other anti-obesity therapy; the hypothetical estimand assumed adherence and no other anti-obesity therapy. (CSR pp. 33-34.)

Table 8: Statistical Analysis of Efficacy Endpoints

Endpoint	Statistical Model	Adjustment Factors	Handling of missing data	Sensitivity Analyses
Study 1 STEP 1. (CSR p. 2.)				
Body-weight change (%) (CSR pp. 93, 333-334, 346.)	ANCOVA (CSR pp. 93, 333-334, 346.)	Treatment factor; baseline weight covariate (CSR pp. 93, 333-334, 346.)	Retrieved-dropout multiple imputation $\times 1,000$ (CSR pp. 93, 333-334, 346.)	Jump-to-reference; single imputation with weight regain; MMRM; tipping-point analysis (CSR pp. 93, 333-334, 346.)
$\geq 5\%$ weight loss (CSR pp. 93, 333-334, 346.)	Binary logistic regression (CSR pp. 93, 333-334, 346.)	Treatment factor; baseline weight covariate (CSR pp. 93, 333-334, 346.)	Retrieved-dropout multiple imputation $\times 1,000$ (CSR pp. 93, 333-334, 346.)	As above; non-responder analysis also reported (CSR pp. 93, 333-334, 346.)
Study 2 No second study reported. (CSR pp. 1, 32.)				
Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)	No second study reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Sample Size and Power Calculation

Planned N=1,950 (1,300 semaglutide; 650 placebo), chosen to support safety exposure/regulatory requirements; reported effective power was 99% for eight hierarchical efficacy endpoints. The IWQOL-Lite-CT power calculation was

updated before unblinding without changing sample size. Detailed effect-size/variance assumptions are referenced to the protocol/SAP but not provided in the supplied report. (CSR pp. 36, 58, 62.)

Statistical Testing

Superiority was tested for eight endpoints in the pre-specified hierarchy at local two-sided alpha 0.05. All passed ($p < 0.0001$). Table 11-1 labels the displayed p-values as unadjusted; multiplicity control was through the hierarchy, not numerical p-value adjustment. No safety inference or interim analysis was planned. (CSR pp. 34, 36, 87, Table 11-1.)

Subgroup Analyses

No efficacy subgroup effect estimates or subgroup interaction tests are reported in the supplied CSR. The DEXA sub-study was a prespecified subset, with 140 participants (95 semaglutide; 45 placebo), not an efficacy interaction analysis. (CSR pp. 35, 72, 84-85.)

Analysis populations

FAS: all randomized, analyzed as randomized. SAS: randomized participants exposed to ≥ 1 dose, analyzed as treated; FAS and SAS were identical (1,306 versus 655). DXA: FAS subset with acceptable baseline DEXA scans. No per-protocol population is defined. (CSR pp. 58, 65, 72, 84.)

Table 9: Analysis Populations of Study 1 and Study 2

Study	Population	Definition	Application
Study 1	FAS (CSR pp. 58, 65, 72, 84.)	All randomized, as randomized; 1,306 / 655 (CSR pp. 58, 65, 72, 84.)	Efficacy (CSR pp. 58, 65, 72, 84.)
	SAS (CSR pp. 58, 65, 72, 84.)	All randomized with ≥ 1 dose, as treated; 1,306 / 655 (CSR pp. 58, 65, 72, 84.)	Safety (CSR pp. 58, 65, 72, 84.)
	DXA (CSR pp. 58, 65, 72, 84.)	FAS subset with acceptable baseline scan; 95 / 45 (CSR pp. 58, 65, 72, 84.)	Body-composition sub-study (CSR pp. 58, 65, 72, 84.)
Study 2	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Patient Population

Baseline characteristics

Baseline characteristics are tabulated below for the FAS. Females: 955/1,306 (73.1%) versus 498/655 (76.0%); White race: 973 (74.5%) versus 499 (76.2%). Waist circumference mean (SD): 114.6 (14.8) versus 114.8 (14.4) cm; HbA1c: 5.7 (0.3)% in both groups. (CSR pp. 69-70, Tables 10-2 and 10-3.)

Summarize relevant baseline demographic and clinical characteristics of the population for each study using a table (example table below). Indicate in the table which analysis set the baseline characteristics have been summarized for (e.g., FAS set)

- 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 10: Summary of Baseline Characteristics of Study 1 and Study 2

Characteristic	Study 1		Study 2	
	Semaglutide 2.4 mg (CSR p. 65.) (N1,306 (CSR p. 65.)=)	Placebo (CSR p. 65.) (N655 (CSR p. 65.)=)	Second study not reported. (CSR pp. 1, 32.) (NSecond study not reported. (CSR pp. 1, 32.)=)	Second study not reported. (CSR pp. 1, 32.) (N =Second study not reported. (CSR pp. 1, 32.))
Age (years), mean (SD); median [range] (CSR p. 70, Table 10-3.)	46 (13); 46 [18-86] (CSR p. 70, Table 10-3.)	47 (12); 48 [18-82] (CSR p. 70, Table 10-3.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)

Characteristic	Study 1		Study 2	
	Semaglutide 2.4 mg (CSR p. 65.) (N1,306 (CSR p. 65.)=)	Placebo (CSR p. 65.) (N655 (CSR p. 65.)=)	Second study not reported. (CSR pp. 1, 32.) (N=Second study not reported. (CSR pp. 1, 32.)=)	Second study not reported. (CSR pp. 1, 32.) (N=Second study not reported. (CSR pp. 1, 32.)=)
Weight (kg), mean (SD); median [range] (CSR p. 70, Table 10-3.)	105.4 (22.1); 102.1 [61.8-245.6] (CSR p. 70, Table 10-3.)	105.2 (21.5); 101.3 [66.3-211.0] (CSR p. 70, Table 10-3.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)
BMI (kg/m ²), mean (SD); median [range] (CSR p. 70, Table 10-3.)	37.8 (6.7); 36.7 [26.5-83.0] (CSR p. 70, Table 10-3.)	38.0 (6.5); 36.5 [27.5-67.0] (CSR p. 70, Table 10-3.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Patient Disposition

Please summarize the patient disposition for each included study using a table.

Table 11: Sample Table for Patient Disposition

Patient disposition	Study 1		Study 2	
	Semaglutide 2.4 mg (CSR p. 65.) (N =1,306 (CSR p. 65.))	Placebo (CSR p. 65.) (N =655 (CSR p. 65.))	Second study not reported. (CSR pp. 1, 32.) (N =Second study not reported. (CSR pp. 1, 32.))	Second study not reported. (CSR pp. 1, 32.) (N =Second study not reported. (CSR pp. 1, 32.))
Screened, N	2,303 overall; not assigned by arm. (CSR pp. 58, 65-68.)	2,303 overall; not assigned by arm. (CSR pp. 58, 65-68.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)
Reason for screening failure, N (%)	305 overall; reasons below use screen-failure denominator. (CSR pp. 58, 65-68.)	305 overall; not arm-specific. (CSR pp. 58, 65-68.)	No second study reported. (CSR pp. 1, 32.)	No second study reported. (CSR pp. 1, 32.)

	Study 1		Study 2	
Screen-failure reason (overall). (CSR p. 68.) Patient disposition	HbA1c $\geq$ 6.5%: 120 (39.3%) overall. (CSR pp. 58, 65-68.)	Not arm-specific. (CSR pp. 58, 65-68.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)
Screen-failure reason (overall). (CSR p. 68.)	Thyroid criteria: 81 (26.6%) overall. (CSR pp. 58, 65-68.)	Not arm-specific. (CSR pp. 58, 65-68.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)
Add rows as required	Other safety/compliance: 38 (12.5%); PHQ-9 $\geq$ 15: 18 (5.9%); suicide attempt: 8 (2.6%), overall. (CSR pp. 58, 65-68.)	Reasons can overlap; not arm-specific. (CSR pp. 58, 65-68.)	No second study reported. (CSR pp. 1, 32.)	No second study reported. (CSR pp. 1, 32.)
Randomized, N (%)	1,306 (100%) (CSR pp. 58, 65-68.)	655 (100%) (CSR pp. 58, 65-68.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)
Discontinued from study, N (%)	66 (5.1%) (CSR pp. 58, 65-68.)	46 (7.0%) (CSR pp. 58, 65-68.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)
Reason for discontinuation, N (%)	Withdrawal by subject: 26 (2.0%) (CSR pp. 58, 65-68.)	Withdrawal by subject: 17 (2.6%) (CSR pp. 58, 65-68.)	No second study reported. (CSR pp. 1, 32.)	No second study reported. (CSR pp. 1, 32.)
Adverse events	4 consent withdrawals mentioning AEs; not systematically collected. (CSR pp. 136-137, Table 12-7.)	1 consent withdrawal mentioning AEs; not systematically collected. (CSR pp. 136-137, Table 12-7.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)
Lost to follow-up	39 (3.0%) (CSR pp. 58, 65-68.)	28 (4.3%) (CSR pp. 58, 65-68.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)

	Study 1		Study 2	
Add rows as required Patient disposition	Death: 1 (<0.1%) (CSR pp. 58, 65-68.)	Death: 1 (0.2%) (CSR pp. 58, 65-68.)	No second study reported. (CSR pp. 1, 32.)	No second study reported. (CSR pp. 1, 32.)
FAS, N	1,306 (CSR pp. 58, 65-68.)	655 (CSR pp. 58, 65-68.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)
PP, N	Not defined. (CSR pp. 58, 65-68.)	Not defined. (CSR pp. 58, 65-68.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)
Safety, N	1,306 (CSR pp. 58, 65-68.)	655 (CSR pp. 58, 65-68.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Exposure to Interventions

Study treatments

The exposure table uses time to first treatment discontinuation (including temporary interruption), consistent with the CSR narrative. AE summaries use the separate 49-day ascertainment window (1,706.1 versus 829.6 patient-years). These denominators are not interchangeable. (CSR pp. 73, 128, 310; Tables 12-1 and 14.1.23.)

Table 12: Sample Table for Patient Exposure

Exposure	Study 1		Study 2	
	Semaglutide 2.4 mg (CSR p. 65.) (N =1,306 (CSR p. 65.))	Placebo (CSR p. 65.) (N =655 (CSR p. 65.))	Second study not reported. (CSR pp. 1, 32.) (N =Second study not reported. (CSR pp. 1, 32.))	Second study not reported. (CSR pp. 1, 32.) (N =Second study not reported. (CSR pp. 1, 32.))
Total, patient-weeks or patient-years	1,480.8 patient-years (CSR p. 310, Table 14.1.23; time to first discontinuation.)	720.9 patient-years (CSR p. 310, Table 14.1.23; time to first discontinuation.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)

Duration, mean (SD)	59.2 (20.2) weeks (CSR p. 310, Table 14.1.23; time to first discontinuation.)	57.4 (20.6) weeks (CSR p. 310, Table 14.1.23; time to first discontinuation.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)
Duration, median (IQR or range)	69.1 weeks [2.1-73.1] (CSR p. 310, Table 14.1.23; time to first discontinuation.)	69.1 weeks [0.1-74.7] (CSR p. 310, Table 14.1.23; time to first discontinuation.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)
Adherence, %	Overall adherence % not reported; 89.6% of completers had 2.4 mg at last dose. (CSR pp. 73-74.)	Overall adherence % not reported; 98.0% of completers had matching maintenance volume. (CSR pp. 73-74.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Concomitant medications and co-interventions

Both groups received counselling every 4 weeks for a 500 kcal/day deficit and ≥ 150 minutes/week of physical activity, with daily food/activity records. (CSR p. 41.) Baseline concomitant use included renin-angiotensin-system agents (23.6%) and lipid-modifying agents (18.5%) overall. During trial, acid-related-disorder drugs were initiated in 26.2% versus 13.0%, and functional-GI-disorder drugs in 13.8% versus 4.6%. Other anti-obesity medication was used by 5 (0.4%) versus 10 (1.5%), and bariatric surgery by 2 (0.2%) versus 3 (0.5%). (CSR pp. 71-72.)

Subsequent treatment (if applicable)

Other anti-obesity medication during trial: 5 (0.4%) versus 10 (1.5%); bariatric surgery: 2 (0.2%) versus 3 (0.5%). No randomized cross-over is described. Detailed subsequent-therapy regimens and a combined unique-patient total are not reported. (CSR pp. 35, 72.)

Table 13: Sample Table for Subsequent Treatment

Exposure	Study 1		Study 2	
	Semaglutide 2.4 mg (CSR p. 65.) (N = 1,306 (CSR p. 65.))	Placebo (CSR p. 65.) (N = 655 (CSR p. 65.))	Second study not reported. (CSR pp. 1, 32.) (N = Second study not reported. (CSR pp. 1, 32.))	Second study not reported. (CSR pp. 1, 32.) (N =)Second study not reported. (CSR pp. 1, 32.)

Received subsequent therapy, n (%)	Combined unique-patient total not reported. (CSR p. 72.)	Combined unique-patient total not reported. (CSR p. 72.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)
Other anti-obesity medication (during trial). (CSR p. 72.), n (%)	5 (0.4%). (CSR p. 72.)	10 (1.5%). (CSR p. 72.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)
Bariatric surgery (during trial). (CSR p. 72.), n (%)	2 (0.2%). (CSR p. 72.)	3 (0.5%). (CSR p. 72.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)
Add rows as required	Post-trial therapy not reported. (CSR pp. 35-36, 72.)	Post-trial therapy not reported. (CSR pp. 35-36, 72.)	No second study reported. (CSR pp. 1, 32.)	No second study reported. (CSR pp. 1, 32.)

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Results

Efficacy

At week 68, treatment-policy estimated mean body-weight change was -14.85% with semaglutide versus -2.41% with placebo; difference -12.44 percentage points (95% CI -13.37 to -11.51; $p < 0.0001$). The $\geq 5\%$ weight-loss odds ratio was 11.22 (95% CI 8.88 to 14.19; $p < 0.0001$). (CSR pp. 87, 89, 93; Tables 11-1 and 11-2.)

Summary of efficacy outcomes

Results below distinguish imputed treatment-policy estimates from observed responder proportions. The main data cut-off was 11 May 2020; PK and antibody data cut-off was 1 July 2020. (CSR pp. 2, 58, 87-94.)

Provide a table similar to the example below summarizing key efficacy outcomes for the studies. For any included figures, indicate the data source including citation (and corresponding figure number in the clinical study report where applicable).

For time-to-event analyses overall frequency of events, number of patients censored, and time of follow-up (e.g., total days of follow-up, median or mean time of follow-up) for each stratum should be presented descriptively.

In addition to any relevant relative differences in effects (e.g., odds ratio, relative risk, hazard ratio), absolute differences in effects with confidence intervals should be presented in the data tables when possible, even if they are not part of the statistical analysis plan. These include mean difference for continuous outcomes, risk difference for dichotomous outcomes, and difference in survival probability at relevant time points for outcomes from time-to-event analyses. Absolute effects and their confidence intervals are essential for the review team's appraisal of the clinical importance of the reported effects.

Table 14: Sample table for key efficacy outcomes

STEP 1 main phase. (CSR pp. 35-36.)	Study 1 Semaglutide 2.4 mg (CSR p. 65.) 1,306 (CSR p. 65.)	Study 1 Placebo (CSR p. 65.) 655 (CSR p. 65.)	Study 2 Second study not reported. (CSR pp. 1, 32.) Second study not reported. (CSR pp. 1, 32.)	Study 2 Second study not reported. (CSR pp. 1, 32.) Second study not reported. (CSR pp. 1, 32.)
Body-weight change (%) at week 68* (CSR p. 87.)				
Number of patients contributing to the analysis	FAS 1,306; observed at week 68: 1,212 (CSR pp. 87, 93, 333, 344; Tables 11-1, 11-2, 14.2.9, 14.2.24.)	FAS 655; observed at week 68: 577 (CSR pp. 87, 93, 333, 344; Tables 11-1, 11-2, 14.2.9, 14.2.24.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)
Baseline, mean (SD)	Body weight: 105.4 (22.1) kg (CSR p. 70.)	Body weight: 105.2 (21.5) kg (CSR p. 70.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)
Change from baseline, mean (95% CI preferred; SE if not available)	-14.85%; arm-specific CI/SE not reported in primary analysis table. (CSR pp. 87, 93, 333, 344; Tables 11-1, 11-2, 14.2.9, 14.2.24.)	-2.41%; arm-specific CI/SE not reported in primary analysis table. (CSR pp. 87, 93, 333, 344; Tables 11-1, 11-2, 14.2.9, 14.2.24.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)
Treatment group difference versus control (95% CI)	-12.44 percentage points (95% CI -13.37 to -11.51) (CSR pp. 87, 93, 333, 344; Tables 11-1, 11-2, 14.2.9, 14.2.24.)	Reference (CSR pp. 87, 93, 333, 344; Tables 11-1, 11-2, 14.2.9, 14.2.24.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)

STEP 1 main phase. (CSR pp. 35-36.)	Study 1 Semaglutide 2.4 mg (CSR p. 65.) 1,306 (CSR p. 65.)	Study 1 Placebo (CSR p. 65.) 655 (CSR p. 65.)	Study 2 Second study not reported. (CSR pp. 1, 32.) Second study not reported. (CSR pp. 1, 32.)	Study 2 Second study not reported. (CSR pp. 1, 32.) Second study not reported. (CSR pp. 1, 32.)
P value	<0.0001; unadjusted p; hierarchy controlled* (CSR pp. 87, 93, 333, 344; Tables 11-1, 11-2, 14.2.9, 14.2.24.)	Same comparison (CSR pp. 87, 93, 333, 344; Tables 11-1, 11-2, 14.2.9, 14.2.24.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)
≥5% weight loss at week 68* (CSR p. 87.)				
n (%)	1,047/1,212 (86.4%), observed (CSR pp. 87, 93, 333, 344; Tables 11-1, 11-2, 14.2.9, 14.2.24.)	182/577 (31.5%), observed (CSR pp. 87, 93, 333, 344; Tables 11-1, 11-2, 14.2.9, 14.2.24.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)
OR/RR (95% CI)	OR 11.22 (95% CI 8.88-14.19), treatment-policy analysis (CSR pp. 87, 93, 333, 344; Tables 11-1, 11-2, 14.2.9, 14.2.24.)	Reference (CSR pp. 87, 93, 333, 344; Tables 11-1, 11-2, 14.2.9, 14.2.24.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)
RD (95% CI)	RD and 95% CI not reported in CSR analysis table. (CSR pp. 87, 93, 333, 344; Tables 11-1, 11-2, 14.2.9, 14.2.24.)	RD and 95% CI not reported in CSR analysis table. (CSR pp. 87, 93, 333, 344; Tables 11-1, 11-2, 14.2.9, 14.2.24.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)

STEP 1 main phase. (CSR pp. 35-36.)	Study 1 Semaglutide 2.4 mg (CSR p. 65.) 1,306 (CSR p. 65.)	Study 1 Placebo (CSR p. 65.) 655 (CSR p. 65.)	Study 2 Second study not reported. (CSR pp. 1, 32.) Second study not reported. (CSR pp. 1, 32.)	Study 2 Second study not reported. (CSR pp. 1, 32.) Second study not reported. (CSR pp. 1, 32.)
P value	<0.0001; unadjusted p; hierarchy controlled* (CSR pp. 87, 93, 333, 344; Tables 11-1, 11-2, 14.2.9, 14.2.24.)	Same comparison (CSR pp. 87, 93, 333, 344; Tables 11-1, 11-2, 14.2.9, 14.2.24.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)
Survival efficacy: not evaluated. (CSR pp. 59-61.)				
Events, n (%)	Not reported; survival efficacy not evaluated. (CSR pp. 59-61.)	Not reported; survival efficacy not evaluated. (CSR pp. 59-61.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)
Censored, n (%)	Not reported; survival efficacy not evaluated. (CSR pp. 59-61.)	Not reported; survival efficacy not evaluated. (CSR pp. 59-61.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)
Censoring reason 1 (add rows as needed), n (%)	Not reported; survival efficacy not evaluated. (CSR pp. 59-61.)	Not reported; survival efficacy not evaluated. (CSR pp. 59-61.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)
Overall survival (months), median (95% CI)	Not reported; survival efficacy not evaluated. (CSR pp. 59-61.)	Not reported; survival efficacy not evaluated. (CSR pp. 59-61.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)
HR (95% CI)	Not reported; survival efficacy not evaluated. (CSR pp. 59-61.)	Not reported; survival efficacy not evaluated. (CSR pp. 59-61.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)

STEP 1 main phase. (CSR pp. 35-36.)	Study 1 Semaglutide 2.4 mg (CSR p. 65.) 1,306 (CSR p. 65.)	Study 1 Placebo (CSR p. 65.) 655 (CSR p. 65.)	Study 2 Second study not reported. (CSR pp. 1, 32.) Second study not reported. (CSR pp. 1, 32.)	Study 2 Second study not reported. (CSR pp. 1, 32.) Second study not reported. (CSR pp. 1, 32.)
P value	Not reported; survival efficacy not evaluated. (CSR pp. 59-61.)	Not reported; survival efficacy not evaluated. (CSR pp. 59-61.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)
Survival probability (%) at Not applicable months (95% CI)	Not reported; survival efficacy not evaluated. (CSR pp. 59-61.)	Not reported; survival efficacy not evaluated. (CSR pp. 59-61.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)
Difference in survival probability (%) (95% CI)	Not reported; survival efficacy not evaluated. (CSR pp. 59-61.)	Not reported; survival efficacy not evaluated. (CSR pp. 59-61.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)
Additional outcomes summarized in text. (CSR pp. 87, 97, 114, 119.)				
As above	Not reported; survival efficacy not evaluated. (CSR pp. 59-61.)	Not reported; survival efficacy not evaluated. (CSR pp. 59-61.)	Second study not reported. (CSR pp. 1, 32.)	Second study not reported. (CSR pp. 1, 32.)

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; FAS = full analysis set; RR = relative risk; OR = odds ratio.

^aSpecify if the P-value has been adjusted for multiple testing using a superscript 'a'

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Body-weight change (%) at week 68 (CSR p. 87.)

Body-weight change (%) at week 68. At week 68, treatment-policy estimated mean body-weight change was -14.85% with semaglutide versus -2.41% with placebo; difference -12.44 percentage points (95% CI -13.37 to -11.51; $p < 0.0001$). The $\geq 5\%$ weight-loss odds ratio was 11.22 (95% CI 8.88 to 14.19; $p < 0.0001$). (CSR pp. 87, 89, 93; Tables 11-1 and 11-2.) Sensitivity ETDs: jump-to-reference -11.94 (95% CI -12.83 to -11.04); single-imputation S1 -12.46 (-13.32 to -11.61); S2 -12.35 (-13.21 to -11.50); MMRM -12.83 (-13.70 to -11.96), all $p < 0.0001$. No tipping point was reached over tested penalties -30% to +30%. Hypothetical-estimand ETD: -14.42 (-15.29 to -13.55). (CSR pp. 90-92, 334, Table 14.2.11.)

Please avoid the following when presenting results:

- Interpreting the difference between two groups as being statistically significant based upon nonoverlapping confidence intervals for the individual within groups change (rather than a statistical test of the difference between groups).

- Interpreting the clinical relevance of statistically nonsignificant findings.
- Focusing on the clinical relevance of within groups changes rather than the clinical relevance of the difference in the between groups change when there is a comparison group or historical control.

For time-to-event analyses overall frequency of events, number of patients censored, and time of follow-up (e.g., total days of follow-up, median or mean time of follow-up) for each stratum should be presented descriptively.

In addition to any relevant relative differences in effects (e.g., odds ratio, relative risk, hazard ratio), absolute differences in effects with confidence intervals should be presented in the data tables when possible, even if they are not part of the statistical analysis plan. These include mean difference for continuous outcomes, risk difference for dichotomous outcomes, and difference in survival probability for outcomes from time-to-event analyses. Absolute effects are essential for the review team's appraisal of the clinical importance of the reported effects.

Report the results from key sensitivity analyses and subgroup analyses under each of the outcomes. Subgroup analyses should reflect those that are specified within the systematic review protocol.

If data within the report are derived from different cut-off dates, please ensure that the dates are clearly specified when reporting the results.

Weight-loss response at week 68 (CSR pp. 87, 344.)

Body-weight response at week 68. Observed $\geq 5\%$ loss: 1,047/1,212 (86.4%) versus 182/577 (31.5%). Sensitivity ORs: jump-to-reference 10.22 (95% CI 8.10-12.89), S1 12.38 (9.90-15.48), S2 12.10 (9.68-15.11), MMRM 14.65 (11.65-18.42) and non-responder imputation 10.56 (8.48-13.14), all $p < 0.0001$. (CSR pp. 344, 346, Tables 14.2.24 and 14.2.27.) For $\geq 10\%$ loss, observed 838/1,212 (69.1%) versus 69/577 (12.0%); OR 14.68 (11.08-19.44). For $\geq 15\%$ loss, 612/1,212 (50.5%) versus 28/577 (4.9%); OR 19.26 (12.89-28.76); both $p < 0.0001$ within the hierarchy. $\geq 20\%$ loss was supportive: 388/1,212 (32.0%) versus 10/577 (1.7%). (CSR pp. 87, 344.)

Please use a separate subheading for each endpoint.

Other confirmatory endpoints (CSR p. 87.)

Other confirmatory outcomes at week 68. Waist change: -13.54 versus -4.13 cm; difference -9.42 (95% CI -10.30 to -8.53). Systolic BP difference: -5.10 mmHg (-6.34 to -3.87). SF-36 physical functioning change: +2.21 versus +0.41; difference +1.80 (1.18-2.42). IWQOL-Lite-CT physical function change: +14.67 versus +5.25; difference +9.43 (7.50-11.35). All $p < 0.0001$ within the hierarchy. Reported sensitivity analyses supported the conclusions for waist circumference and the two PRO outcomes. (CSR pp. 87, 97, 114, 119.)

Please use a separate subheading for each endpoint.

Table 15: Sample table for efficacy outcome

Waist circumference at week 68* (CSR p. 87.)	Semaglutide 2.4 mg (CSR p. 65.) N = 1,306 (CSR p. 65.)	Placebo (CSR p. 65.) N = 655 (CSR p. 65.)
Waist circumference (cm), week 68* (CSR pp. 87, 371.)		
Number of patients contributing to the analysis	FAS 1,306; observed 1,210 (CSR p. 371, Table 14.2.54.)	FAS 655; observed 575 (CSR p. 371, Table 14.2.54.)

Waist circumference at week 68* (CSR p. 87.)	Semaglutide 2.4 mg (CSR p. 65.) N = 1,306 (CSR p. 65.)	Placebo (CSR p. 65.) N = 655 (CSR p. 65.)
Baseline, mean (SD)	114.6 (14.8) cm (CSR p. 70.)	114.8 (14.4) cm (CSR p. 70.)
End of treatment time point (specify), mean (SE)	101.13 cm; SE not reported in primary table (CSR p. 371, Table 14.2.54.)	110.55 cm; SE not reported in primary table (CSR p. 371, Table 14.2.54.)
Change from baseline, mean (SE)	-13.54 cm; SE not reported in primary table (CSR p. 371, Table 14.2.54.)	-4.13 cm; SE not reported in primary table (CSR p. 371, Table 14.2.54.)
Treatment group difference versus control (95% CI)	-9.42 cm (95% CI -10.30 to -8.53) (CSR p. 371, Table 14.2.54.)	Reference (CSR p. 371, Table 14.2.54.)
P value	<0.0001; unadjusted p, hierarchy controlled* (CSR p. 371, Table 14.2.54.)	Same comparison (CSR p. 371, Table 14.2.54.)
Dichotomous outcome: not applicable to waist. (CSR pp. 59-61.)		
n (%)	Not applicable to waist circumference. (CSR pp. 59-61, 371.)	Not applicable to waist circumference. (CSR pp. 59-61, 371.)
OR/RR (95% CI)	Not applicable to waist circumference. (CSR pp. 59-61, 371.)	Not applicable to waist circumference. (CSR pp. 59-61, 371.)
RD (95% CI)	Not applicable to waist circumference. (CSR pp. 59-61, 371.)	Not applicable to waist circumference. (CSR pp. 59-61, 371.)
P value	Not applicable to waist circumference. (CSR pp. 59-61, 371.)	Not applicable to waist circumference. (CSR pp. 59-61, 371.)

Waist circumference at week 68* (CSR p. 87.)	Semaglutide 2.4 mg (CSR p. 65.) N = 1,306 (CSR p. 65.)	Placebo (CSR p. 65.) N = 655 (CSR p. 65.)
Survival outcome: not evaluated. (CSR pp. 59-61.)		
Events, n (%)	Not applicable to waist circumference. (CSR pp. 59-61, 371.)	Not applicable to waist circumference. (CSR pp. 59-61, 371.)
Overall survival (months), median (95% CI)	Not applicable to waist circumference. (CSR pp. 59-61, 371.)	Not applicable to waist circumference. (CSR pp. 59-61, 371.)
HR (95% CI)	Not applicable to waist circumference. (CSR pp. 59-61, 371.)	Not applicable to waist circumference. (CSR pp. 59-61, 371.)
P value	Not applicable to waist circumference. (CSR pp. 59-61, 371.)	Not applicable to waist circumference. (CSR pp. 59-61, 371.)
Survival probability (%) at Not applicable months (95% CI)	Not applicable to waist circumference. (CSR pp. 59-61, 371.)	Not applicable to waist circumference. (CSR pp. 59-61, 371.)
Difference in survival probability (%) (95% CI)	Not applicable to waist circumference. (CSR pp. 59-61, 371.)	Not applicable to waist circumference. (CSR pp. 59-61, 371.)

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Harms

On-treatment AEs occurred in 1,171/1,306 (89.7%) versus 566/655 (86.4%); SAEs in 128 (9.8%) versus 42 (6.4%); and AEs leading to permanent treatment discontinuation in 92 (7.0%) versus 20 (3.1%), for semaglutide versus placebo. There was 1 death in each group during the in-trial period. (CSR p. 128, Table 12-1.)

Table 16: Sample table for key harms data

Adverse events	Semaglutide 2.4 mg (CSR p. 65.) (N = 1,306 (CSR p. 65.))	Placebo (CSR p. 65.) (N = 655 (CSR p. 65.))
Most common adverse events, n (%)		
≥ 1 adverse event	1,171 (89.7%) (CSR p. 128.)	566 (86.4%) (CSR p. 128.)
Nausea (CSR p. 141.)	Nausea: 577 (44.2%) (CSR p. 141.)	Nausea: 114 (17.4%) (CSR p. 141.)
Diarrhoea (CSR p. 141.)	Diarrhoea: 412 (31.5%) (CSR p. 141.)	Diarrhoea: 104 (15.9%) (CSR p. 141.)
Add rows as required	Vomiting: 324 (24.8%); constipation: 306 (23.4%) (CSR p. 141.)	Vomiting: 43 (6.6%); constipation: 62 (9.5%) (CSR p. 141.)
Serious adverse events, n (%)		
Patients with ≥ 1 SAE	128 (9.8%) (CSR p. 135.)	42 (6.4%) (CSR p. 135.)
GI disorders (CSR p. 135.)	GI: 18 (1.4%) (CSR p. 135.)	GI: 0 (CSR p. 135.)
Hepatobiliary disorders (CSR p. 135.)	Hepatobiliary: 17 (1.3%) (CSR p. 135.)	Hepatobiliary: 1 (0.2%) (CSR p. 135.)
Add rows as required	Infections: 27 (2.1%) (CSR p. 135.)	Infections: 10 (1.5%) (CSR p. 135.)
Patients who stopped treatment due to adverse events, n (%)		
Patients who stopped	92 (7.0%); AE form (CSR p. 137.)	20 (3.1%); AE form (CSR p. 137.)
GI disorders (CSR p. 137.)	GI: 59 (4.5%) (CSR p. 137.)	GI: 5 (0.8%) (CSR p. 137.)

Psychiatric disorders (CSR p. 137.)	Psychiatric: 7 (0.5%) (CSR p. 137.)	Psychiatric: 3 (0.5%) (CSR p. 137.)
Add rows as required	Skin: 5 (0.4%) (CSR p. 137.)	Skin: 2 (0.3%) (CSR p. 137.)
Deaths, n (%)		
Patients who died	1 (0.1%), in-trial (CSR p. 128.)	1 (0.2%), in-trial (CSR p. 128.)
Adjudicated causes of death. (CSR p. 134.)	Sudden cardiac death adjudicated; off treatment (CSR p. 134.)	Malignancy adjudicated; off treatment (CSR p. 134.)
Add rows as required	1 fatal event in 1 participant (CSR p. 128.)	3 fatal events in 1 participant (CSR p. 128.)
Adverse events of special interest, n (%)		
Gallbladder disorders; adjudicated pancreatitis. (CSR p. 129.), n (%)	Gallbladder: 34 (2.6%); adjudicated pancreatitis: 3 (0.2%) (CSR p. 129.)	Gallbladder: 8 (1.2%); adjudicated pancreatitis: 0 (CSR p. 129.)
Add rows as required	GI: 969 (74.2%); cardiovascular (in-trial): 107 (8.2%) (CSR p. 129.)	GI: 314 (47.9%); cardiovascular (in-trial): 75 (11.5%) (CSR p. 129.)

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Safety Evaluation Plan

Safety used the SAS. AEs/SAEs generally used on-treatment exposure with a 49-day window; deaths and selected long-latency events used the in-trial period. Selected events were independently adjudicated, and MedDRA 22.1 was used for coding. Safety was descriptive. (CSR pp. 30, 36, 47-51, 58, 127-129.)

See the adjacent response in this field. (CSR pp. 128-137.)

Overview of Safety

See the adjacent response in this field. (CSR pp. 128-137.)

On-treatment AEs occurred in 1,171/1,306 (89.7%) versus 566/655 (86.4%); SAEs in 128 (9.8%) versus 42 (6.4%); and AEs leading to permanent treatment discontinuation in 92 (7.0%) versus 20 (3.1%), for semaglutide versus placebo. There was 1 death in each group during the in-trial period. (CSR p. 128, Table 12-1.)

Adverse Events

Gastrointestinal AEs occurred in 969 (74.2%) versus 314 (47.9%); nausea 577 (44.2%) versus 114 (17.4%), diarrhoea 412 (31.5%) versus 104 (15.9%), vomiting 324 (24.8%) versus 43 (6.6%), and constipation 306 (23.4%) versus 62 (9.5%). Most GI events were non-serious and mild/moderate. (CSR p. 141, Table 12-10.)

See the adjacent response in this field. (CSR pp. 128-137.)

Serious Adverse Events

SAEs affected 128 (9.8%) versus 42 (6.4%); 164 versus 53 events, or 9.6 versus 6.4 events per 100 patient-years. Serious GI disorders occurred in 18 (1.4%) versus 0; hepatobiliary disorders in 17 (1.3%) versus 1 (0.2%). (CSR pp. 134-135, Table 12-5.)

See the adjacent response in this field. (CSR pp. 128-137.)

Withdrawals Due to Adverse Events

See the adjacent response in this field. (CSR pp. 128-137.)

AE-form counts for permanent treatment discontinuation were 92 (7.0%) versus 20 (3.1%); end-of-trial-form counts were 91 (7.0%) versus 21 (3.2%). The CSR explicitly explains this one-participant-per-arm discrepancy. Trial withdrawal is separate: Table 12-7 lists 4 semaglutide and 1 placebo participants withdrawing consent with reasons mentioning AEs, plus 1 death per arm; AE-related trial withdrawal was not systematically collected. (CSR pp. 65, 136-137, Tables 12-7 and 12-8.)

Adverse Events of Special Interest

Safety focus areas included GI and gallbladder disorders, pancreatitis, cardiovascular disorders, neoplasms, hepatic events, renal failure, hypoglycaemia, injection-site/allergic reactions, psychiatric disorders and medication errors. Gallbladder disorders: 34 (2.6%) versus 8 (1.2%); adjudicated pancreatitis: 3 (0.2%) versus 0. (CSR p. 129, Table 12-2.) Pulse-rate difference at week 68 was +4.26 beats/min (95% CI 3.38 to 5.15). (CSR p. 187.)

See the adjacent response in this field. (CSR pp. 128-137.)

Sponsor Summary and Conclusion

See the adjacent response in this field. (CSR pp. 87, 128, 188-190.)

The sponsor concluded that semaglutide was superior to placebo for both primary and all confirmatory secondary endpoints, with sensitivity analyses supporting robustness. Gastrointestinal adverse effects and treatment discontinuation were more frequent with semaglutide. This describes the CSR conclusion and does not establish reimbursement or comparative efficacy against active treatments. (CSR pp. 87, 128, 188-190.)

Sponsor Identified Gaps in the Evidence

See the adjacent response in this field. (CSR pp. 32, 35-37.)



The CSR does not provide a CDA-AMC sponsor gap assessment. Source limitations relevant here are a placebo-only comparator, exclusion of type 2 diabetes, 68-week treatment duration, and separately reported extension results. The SF-36 baseline ceiling limited potential improvement. (CSR pp. 35-37, 115.)

Section 3. Long-Term Extension Studies

This section should provide a brief summary of long-term extension studies that are completed or have interim analyses at the time of filing the application with CDA-AMC.

- If there are multiple studies, please summarize each study separately.
- If any information in the sections below is the same as the parent study and described previously in the template, please state this, and refer the reader to the appropriate sections of the report. Do not repeat the information in this section.

Description of Studies

Study Design and Objectives

Planned 52-week, open-label, off-treatment STEP 1 extension, without structured lifestyle intervention, targeting approximately 300 maintenance-dose completers from Canada, Germany, Japan, UK and US. Objective: assess post-treatment change in weight, cardiovascular risk factors and glucose metabolism. Results are outside this CSR. (CSR pp. 32, 35-36.)

Eligibility criteria

Planned subset completing the main phase on semaglutide 2.4 mg or matching placebo maintenance dose, from selected countries; target approximately 300 participants. Detailed extension eligibility is not reported here. (CSR pp. 35-36.)

Interventions

No trial product and no structured lifestyle intervention during the planned extension. (CSR p. 35.)

Outcomes

Planned evaluation of body-weight change, cardiovascular risk factors and glucose metabolism after treatment ended; detailed extension endpoint definitions and results are not reported. (CSR pp. 35-36.)

Statistical analysis

Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)

Patient Population

Baseline characteristics

Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)

Table 17: Summary of Baseline Characteristics

Characteristic	Study 1		Study 2	
	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.) (N = Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.))	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.) (N = Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.))	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.) (N = Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.))	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.) (N =)Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)
Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)
Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)
Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Patient Disposition

Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)

Exposure to study treatments

Study treatments

Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)

Table 18: Sample Table for Patient Exposure

Exposure	Study 1	Study 2
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	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.) (N = Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.))	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.) (N = Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.))	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.) (N = Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.))	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.) (N =)Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)
Total, patient-weeks or patient-years	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)
Duration, mean (SD)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)
Duration, median (IQR or range)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)
Adherence, %	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Concomitant medications and co-interventions

Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)

Subsequent treatment (if applicable)

Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)

Table 19: Sample Table for Subsequent Treatment

Exposure	Study 1	Study 2
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	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.) (N =Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.))	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.) (N =Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.))	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.) (N =Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.))	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.) (N =Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.))
Received subsequent therapy, n (%)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)
Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.), n (%)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)
Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.), n (%)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)
Add rows as required				

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Results

Efficacy

Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)

Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)

Please use a separate subheading for each endpoint.

Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)

Please use a separate subheading for each endpoint.

Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)

Please use a separate subheading for each endpoint.

Harms

Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)

Table 20: Summary of Harms

Adverse events	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.) (N = Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.))	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.) (N = Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.))
Most common adverse events, n (%)		
≥ 1 adverse event	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)
Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)
Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)
Add rows as required		Not reported in the supplied CSR; extension results are to be reported separately. (CSR pp. 32, 35-36.)
Serious adverse events, n (%)		
Patients with ≥ 1 SAE	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)

Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)
Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)
Add rows as required		
Patients who stopped treatment due to adverse events, n (%)		
Patients who stopped	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)
Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)
Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)
Add rows as required		
Deaths, n (%)		
Patients who died	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)
Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)
Add rows as required		
Adverse events of special interest, n (%)		



Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.), n (%)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)	Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)
Add rows as required		

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Sponsor Summary and Conclusion

Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)

Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)

Sponsor Identified Gaps in the Evidence

Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)

Extension results not reported in supplied CSR. (CSR pp. 32, 35-36.)

Section 4. Indirect Evidence

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).

If no indirect comparisons are included in the application, please provide the following:

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

Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)

- If a feasibility assessment was performed and the sponsor concluded that an indirect comparison was not possible based on the available information, please clearly describe the assessment and the barriers that precluded the indirect comparison.

Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)

Description of Indirect Comparison(s)

In this section the sponsor should summarize the methods and results of all indirect comparisons included in the application.

Objectives

Indirect comparison not reported in supplied CSR. (CSR pp. 32-37.)

Study Selection Methods

Indirect comparison not reported in supplied CSR. (CSR pp. 32-37.)

Table 21: Study Selection Criteria and Methods for Indirect Comparisons

Characteristics	Indirect Comparison
Population	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.) Briefly state the population(s) of interest for the indirect comparison
Intervention	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.) List intervention including dosing information
Comparator	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.) List comparators including dosing information
Outcome	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.) List outcomes including time points
Study designs	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.) Briefly describe the study designs included in the indirect comparison
Publication characteristics	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.) Specify inclusion of published and/or unpublished studies
Exclusion criteria	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.) Briefly describe the exclusion criteria used for selecting studies
Databases searched	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.) Briefly list databases included in the literature search

Characteristics	Indirect Comparison
Selection process	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.) Briefly describe the review methods (e.g., articles screened independently by 2 researchers)
Data extraction process	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.) Briefly describe the review methods
Quality assessment	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.) Briefly describe the methods used to assess the quality of studies (e.g., appraisal tools)

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation.

Indirect comparison analysis methods

Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)

- Describe the statistical model and the justification in the selection of the methods.

Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)

- Describe the feasibility assessment and how well the underlying assumptions of the methods were supported.

Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)

- Describe how model fit was assessed. If multiple models were run, describe how the model selected as the primary analysis was chosen. If only 1 model was used, please provide the reason(s).

Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)

- Please note the following for Bayesian models:
 - o Describe prior distributions for modeling parameters.

Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)

- o Describe justification for use of informative priors, and whether sensitivity analyses were done to assess the impact of the priors selected.

Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)

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

Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)

- Matching-adjusting indirect comparison (MAIC):
 - o Describe the justification conducting a MAIC and for the comparator chosen.

Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)

- o Specify whether an anchored or unanchored MAIC was conducted

Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)

- o Describe sources of heterogeneity that were identified between trials in the comparison. Specify whether any methods were used to account for heterogeneity prior to the weighting process including whether any patients were excluded from the trial.

Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)

- o Describe any processes used to identify baseline characteristics that are potential effect modifiers and, for unanchored comparisons, prognostic factors.

Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)

- o Describe what characteristics were identified in the variable selection process, and which of these variables were ultimately adjusted for in the weighting process. Specify the justification for excluding any variable identified in the variable selection process.

Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)

- o Describe the method used to calculate the weight of individual patient data.

Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)

- o Describe the approach used to estimate the parameters of the model.

Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)

- o Describe if effective sample size measures and any other weight assessments were reported.

Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)

- Describe how homogeneity was assessed. Please ensure to address clinical, methodological, and statistical heterogeneity.

Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)

- 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 the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)

- Provide rationale for sensitivity analysis with description of methods used.

Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)

- Provide rationale for subgroup analysis with description of methods used.

Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)

- Describe how consistency between direct and indirect comparisons were evaluated if relevant (e.g., inconsistency modelling, simple direct versus indirect, or if it was not possible to assess consistency due to the lack of a closed loops)

Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)

- Describe methods used to conduct standard pairwise meta-analysis (if conducted).

Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)

- 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 the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)

- Describe (where appropriate) methods used for rescaling or conversion of results to a common scale, in cases where studies reported different scales or measures. Discuss appropriateness of any methods for reconstructing individual patient data from summary data.

Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)

- Describe (where appropriate) which set of analysis results have been used where studies have conducted multiple analyses of a given endpoint (e.g., multiple approaches to dealing with missing data).
- 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 22: Indirect Comparison Analysis Methods

Methods	Description
Analysis methods	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.) Briefly describe the methods
Priors	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.) As above
Assessment of Model fit	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.) As above
Assessment of Consistency	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.) As above
Assessment of Convergence	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.) As above
Outcomes	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.) As above
Follow-up timepoints	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.) As above
Construction of nodes	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.) As above
Sensitivity analyses	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.) As above
Subgroup analysis	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.) As above
Methods for pairwise meta-analysis	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.) As above

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation.

Results

Summary of included studies

Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)

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.

Describe the trials included in the systematic review, and the indirect comparison analysis (including number of trials and patients), highlighting any potential sources of heterogeneity (e.g., in the patients, interventions, outcomes, study design or follow up time). Please ensure that features that could lead to differences in treatment effect modifiers are addressed (e.g., patients recruited to studies of A versus B have less advanced disease than those in A versus C).

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 23: Sample Table for Assessment of Homogeneity

Characteristics	Description and handling of potential effect modifiers
Disease severity	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.) Comment on similarities and differences across studies and note if there were any relevant adjustments or sensitivity analyses. Indicate when the information required to compare across studies is missing (i.e., not reported).
Treatment history	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.) As above
Trial eligibility criteria	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.) As above
Dosing of comparators	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.) As above
Placebo response	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.) As above
Definitions of endpoints	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.) As above
Timing of endpoint evaluation	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.) As above
Withdrawal frequency	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.) As above
Clinical trial setting	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.) As above
Study design	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.) As above

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation.

Evidence Networks

Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)

Provide a graphical depiction of the evidence network for each outcome of interest, if available. If a graphical description is not available, briefly describe the network, including the overall number of studies and number of studies contributing to the direct and indirect estimates for important comparisons. For any included figures, indicate the corresponding figure number in the technical report.

Efficacy

Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)

Provide a summary of the indirect comparison results for efficacy outcomes, including point estimates and 95% confidence intervals and/or credible intervals (as appropriate for the method of analysis) for pairwise comparisons of interest to the review. The focus should be on comparisons with relevant comparators, particularly those not assessed in the systematic review evidence. If appropriate, present a tabular summary of the results that contains only the results for the most relevant interventions and outcomes). The tables below provide example formats that may be used to summarize results.

- Describe the results relating to how well the selected model(s) fits the data
- Describe the results of any assessments that were conducted such as assessments of heterogeneity, consistency, and, for MAICs, an assessment of weights. An assessment of weights for a MAIC should at minimum include reporting the effective sample size, both overall and as a percentage of the original sample size of the trial after exclusions.
- Provide a brief summary of the results of subgroup analyses and/or meta-regression, if relevant. Only if relevant/necessary, present the results of one or more sensitivity analyses. It is often sufficient to state that the results of all sensitivity analysis were consistent with the base case (if the methods used for the sensitivity analyses are appropriate and described adequately).

Table 24: ITC Sample Data Table for Continuous Outcomes (e.g., Summary of NMA Results for Efficacy Results, [Treatment] Versus Comparators)

Comparator	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)
Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)
Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)
Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)

Abbreviations must be listed under the table in alphabetical order. For example, CrI =, credible interval; OR = odds ratio; NA = not applicable; NMA = network meta-analysis.

Source: Indicate data source including citation (and corresponding table number[s] in the technical report where applicable).

Table 25: ITC Sample Data Table for Dichotomous Outcomes (e.g., Summary of NMA Results for Efficacy Results, [Treatment] Versus Comparators)

Comparator	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)
Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)
Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)
Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)	Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)

Abbreviations must be listed under the table in alphabetical order. For example, CrI =, credible interval; OR = odds ratio; NA = not applicable; NMA = network meta-analysis.

Source: Indicate data source including citation (and corresponding table number[s] in the technical report where applicable).

Indirect comparison not reported in supplied CSR. (CSR pp. 32-37.)

Please use a separate subheading for each endpoint.

Indirect comparison not reported in supplied CSR. (CSR pp. 32-37.)

Please use a separate subheading for each endpoint.

Indirect comparison not reported in supplied CSR. (CSR pp. 32-37.)

Please use a separate subheading for each endpoint.

Not reported in the supplied CSR: no indirect comparison is presented. (CSR pp. 32-37: direct placebo-controlled trial.)

Harms

Provide a summary of the indirect comparison results for harms outcomes using the guidance provided above. If no harms endpoints were evaluated in the indirect comparison, please state this within this section (i.e., do not delete the section heading in the absence of comparative harms data).

Sponsor Summary and Conclusion

Indirect comparison not reported in supplied CSR. (CSR pp. 32-37.)

In this section the sponsor may provide a brief summary and their conclusions regarding the evidence from the indirect comparisons. **This section must not exceed 1 page.**

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

In this section the sponsor may summarize evidence from additional studies that address important gaps in the evidence presented in sections 2 to 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. Justification for the inclusion of real-world evidence must be provided; this should cover, as relevant, the reasons for the absence of randomized evidence, the limitations of existing trials, and the ability to produce meaningful real-world evidence for the specific research question.

If no additional evidence is provided, this section can be deleted.

Summary of Gaps in the Evidence

The summary table below is required for all applications where the sponsor chooses to include additional evidence.

Table 26: Summary of Gaps in the Evidence

Gap in Pivotal and RCT Evidence	Studies that Address Gaps	
	Study Description	Summary of Key Results
No active comparator; type 2 diabetes excluded; extension results separate. (CSR pp. 32, 35-37.) e.g. Describe the populations and/outcomes that were not studied in the pivotal studies or other RCTs	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.) Briefly describe (e.g., 52-week, prospective observational study)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.) Briefly describe the key results focusing on how the evidence addresses the important gap in the evidence
Add rows as required Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	As above Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	As above Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

If multiple studies are included, report the format below for each study under the appropriate subsection (either Clinical Trials or Studies of Other Designs). The Clinical Trials section may include trials that did not meet the inclusion criteria of the systematic review protocol but are included in Section 5 to fill a gap in the evidence and should be placed under a separate subsection from Studies of Other Designs (e.g., observational designs including real-world evidence studies). The Clinical Trials subsection may be further subdivided based on study design (e.g., Phase II RCTs, single-arm trials, RWE). Clinical trials of similar design may be summarized together with a subsection. Please delete the Clinical Trials or Studies of Other Designs subsection if no evidence is included in that subsection.

Description of Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

If multiple studies are included, report the format below for each study.

Study Design and Objectives

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

Provide a brief overview of the study including study description (name, type, design).

For clinical trials included in Section 5, provide a brief overview of the study including a study description (e.g., study name, key design features, patient type, sample size (N), locations including number of sites in Canada, intervention, and comparator).

Eligibility criteria

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

For clinical trials included in Section 5, briefly describe the inclusion and exclusion criteria. Emphasize any key inclusion/exclusion criteria that are of importance to the condition or may identify a niche patient population.

Interventions

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

For clinical trials included in Section 5, briefly describe the interventions and comparators (if relevant) used in each study and use of concomitant medications and/or treatments.

Outcomes

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

Provide a brief summary of the efficacy and safety outcomes that will be included in this summary, with a focus on those outcomes that fill gaps in pivotal and phase 3 clinical trial evidence.

Statistical analysis

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

Provide a brief summary of the key components of any statistical analyses.

Patient Population

Baseline characteristics

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

Summarize relevant baseline demographic and clinical characteristics of each study using a table (example below). Where multiple clinical trials of the same design have been included in a subsection, this information can be summarized in a single table. Indicate in the table which analysis set the baseline characteristics have been summarized for (e.g., FAS set).

- 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 27: Summary of Baseline Characteristics of Study 1 and Study 2

Characteristic	Study 1		Study 2	
	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.) (N = Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.))	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.) (N = Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.))	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.) (N = Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.))	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.) (N =)Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)
Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)
Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)
Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Patient disposition

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

Summarize patient disposition for each additional study using a summary table (if appropriate). Where multiple clinical trials of the same design have been included in a subsection, this information can be summarized in a single table.

Exposure to Interventions

Study treatments

Summarize exposure using a table (example provided below). Within the text, please describe any discrepancies between treatment groups. Include information on adherence to treatment where relevant. Where multiple clinical trials of the same design have been included in a subsection, this information can be summarized in a single table.

Table 28: Sample Table for Patient Exposure

Exposure	Study 1		Study 2	
	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.) (N = Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.))	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.) (N = Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.))	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.) (N = Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.))	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.) (N =)Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)
Total, patient-weeks or patient-years	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)
Duration, mean (SD)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)
Duration, median (IQR or range)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

Adherence, %	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)
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Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Concomitant medications and co-interventions

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

Provide a table summarizing relevant concomitant medications used during the studies.

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)

Please describe any protocols for managing cross-over to other treatment groups (e.g., placebo to active treatment) or the provision of additional therapies or interventions during the treatment period or follow-up phase (e.g., additional anticancer medication or surgery upon documented disease progression). Consider adding a table to summarize the overall use of subsequent treatments and provide a breakdown of specific treatments and/or interventions.

Table 29: Sample Table for Subsequent Treatment

Exposure	Study 1		Study 2	
	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.) (N = Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.))	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.) (N = Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.))	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.) (N = Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.))	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.) (N =)Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

Received subsequent therapy, n (%)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)
Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.), n (%)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)
Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.), n (%)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)
Add rows as required Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)	Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

Abbreviations must be listed under the table in alphabetical order. For example, CI = confidence interval; OR = odds ratio

Source: For all tables reporting information from included studies, indicate data source including citation (and corresponding table number[s] in the clinical study report where applicable). Data should reflect the results reported in the clinical study report(s) whenever possible.

Results

Efficacy

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

Present the efficacy outcomes in a table or figure, highlighting only key results in the text. For all analyses clearly define when the baseline assessments were performed (e.g., at the outset of the parent study or the beginning of the extension study).

Efficacy endpoint 1

Please use a separate subheading for each endpoint.

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

Please use a separate subheading for each endpoint.

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

Please use a separate subheading for each endpoint.

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

Harms

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

Present the safety outcomes in a table and summarize key findings in the text. Include AEs, SAEs, WDAEs, deaths, and adverse events of special interest. Make sure to use data from treatment-emergent adverse events.

Studies of Other Design

If multiple studies of other designs are included in Section 5, report the format below for each study sequentially. Modify the heading as appropriate (e.g., Real-World Evidence).

Description of Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

Study Design and Objectives

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

For studies of other designs included in Section 5 (e.g., observational designs including real-world evidence studies) briefly describe the specific objectives, any prespecified hypotheses, and key elements of study design. Key elements of study design may include setting, locations, and relevant study dates, including periods of recruitment, exposure, follow-up, and data collection. The data source should be specified, including linkages between datasets if relevant. For prospective studies, methods of follow-up should be described.

Eligibility criteria

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

Report the eligibility criteria for participant selection, taking into consideration the specific study design. Provide the sources and methods for selection of participants or case ascertainment (as relevant according to the specific study design). Diagnostic criteria or algorithms used to identify or classify participants or cases should be described. When matching is a design feature, criteria for matching (for example, selecting controls to match to cases) should be described.

Interventions and Exposures

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

Sponsor Summary of Evidence

Include clear definitions of exposures to treatment and to potential confounders. Clear descriptions of the assumptions and algorithms used to classify exposures to the intervention, comparator, any concomitant treatments (where relevant) and potential confounders should be provided. The time window during which an individual is considered exposed to an intervention should be described, as well as the approach used to handle individuals with more than one relevant drug exposure during the study period. Where multiple data sources have been combined, the comparability across data sets or groups should be described.

Outcomes

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

Clearly define all relevant efficacy and safety outcomes with a focus on those that are reported to fill gaps in pivotal and phase 3 clinical trial evidence. Include clear descriptions of the assumptions and algorithms used to define outcome variables where applicable. If data are obtained from more than one source, the comparability across data sets or groups should be described.

Statistical analysis

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

For studies of other designs included in Section 5 (e.g., observational designs including real-world evidence studies), the description of the statistical analysis will be specific to the study design but generally should include a description or explanation of the following (where relevant):

- How the sample size was determined

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

- The statistical models and tests including all covariates or confounders adjusted for.

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

- Methods to control for confounding

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

- Handling of quantitative variables in the analysis

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

- Methods for matching

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

- Handling of missing data and data imputation

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

- How loss to follow-up was addressed for cohort studies

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

- Methods used to control for multiple comparisons

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

- Sensitivity analysis

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

- Subgroup analysis

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

Patient Population

Participant Characteristics

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

Summarize the characteristics of the eligible participants (e.g., demographic, clinical, social) and provide information on exposures and potential confounders. A table adapted to fit the specific study design should be included. Indicate the number of participants with missing data for each variable of interest. For cohort studies, the follow-up time (e.g., average and total amount) should also be reported.

Participant eligibility

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

Report the numbers of individuals at each stage of study—e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. The reasons for non-participation at each stage should be reported. Consider use of a flow diagram for reporting.

Exposure to Interventions

Exposures

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

For studies of other design that are included in Section 5 (e.g., observational designs including real-world evidence studies), the exposure(s) should be summarized in a table designed to fit the specific study design.

Concomitant medications, co-interventions, confounding treatments

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

Please summarize any concomitant or subsequent treatments.

Results

Efficacy

Present the efficacy outcomes in a table or figure, highlighting only key results in the text. Provide both unadjusted estimates and, if applicable, confounder-adjusted or covariate-adjusted estimates and their precision (e.g., 95% confidence interval). Report the results of key sensitivity analyses and subgroup analyses if relevant.

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

Please use a separate subheading for each endpoint.

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

Efficacy endpoint 2

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

Please use a separate subheading for each endpoint.

Efficacy endpoint 3

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

Please use a separate subheading for each endpoint.

Harms

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

Report the available or relevant adverse events which may include AEs, SAEs, deaths, and adverse events of special interest. Availability of harms data may be related to the specific design and may be reported as percent of population who experience one or more event, frequency of adverse events, or as rate (e.g., per patient-year)

Sponsor Summary and Conclusion

Not reported in the supplied CSR: no additional study report is provided for this field. (CSR pp. 1, 32, 35-36.)

In this section the sponsor may provide a brief summary and their conclusions regarding the evidence from additional studies. **This must not exceed 1 page.**

Section 6. Summary of the Sponsor's Pharmacoeconomic Submission

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.

In this section of the template the sponsor must summarize the key methods and results of the pharmacoeconomic submission. The information is intended to be a summary and additional relevant details should be included in the economic evaluation technical report.

- The total length of this template cannot exceed 6 pages.
- Provide all references to source documentation.
- A RIS file containing all references used in this template must be submitted.

Key Components of the Sponsor's Economic Evaluation

Component	Description
Treatment information	
Drug under review (DUR)	• Clinical-trial product: semaglutide solution for injection (1.0 or 3.0 mg/mL in 3 mL pens), target 2.4 mg once weekly plus lifestyle intervention. Canadian marketed strengths, brand, monograph recommendations and model inputs are not reported. (CSR pp. 39-41, Tables 9-1 and 9-2.) <i>State the generic name (Brand) of DUR, dosage form, and all strengths/concentrations as relevant.</i> • <i>Note if DUR is to be used in addition to other treatment(s), if relevant</i> • <i>Summarize the recommended dosage of DUR per the product monograph.</i>
Submitted price of drug under review	• Not reported in the supplied CSR: no pharmacoeconomic submission is presented. (CSR pp. 1, 32-36: clinical-trial scope.) <i>State the price per lowest dispensable unit (e.g., per tablet, vial, prefilled syringe) to 2 decimal places for all submitted strengths/forms.</i> • <i>Prices must be aligned with those on the Pricing and Distribution form</i>
Regimen	• Not reported in the supplied CSR: no pharmacoeconomic submission is presented. (CSR pp. 1, 32-36: clinical-trial scope.) <i>Describe the dosage regimen used in the model for DUR</i> • <i>If this differs from the dosage regimen in the product monograph, state any differences and provide source/rationale for alternate dosing regimen.</i> • <i>Note if DUR is used in addition to other treatments (e.g., standard of care) or as part of a regimen (e.g., oncology regimens). Clearly state all components and dosages.</i>

Component	Description
Annual cost, per-cycle cost, or one-time cost of drug under review	- Not reported in the supplied CSR: no pharmacoeconomic submission is presented. (CSR pp. 1, 32-36: clinical-trial scope.)<i>State the acquisition cost used in the model for DUR. For oncology submissions, this will typically be per 28-day treatment cycle. For non-oncology submissions, this will typically be annual treatment cost. If something different, clearly state the duration.</i> <i>Note any modifying assumptions that were made in the calculation of drug costs (e.g., weight, if weight-based dose; relative dose intensity; different costs in first course vs. subsequent course)</i> <i>If DUR is used in addition to standard of care (or another treatment), clearly state the acquisition cost of DUR and the other components</i>
Model information	
Type of economic evaluation	- Not reported in the supplied CSR: no pharmacoeconomic submission is presented. (CSR pp. 1, 32-36: clinical-trial scope.)Cost-utility analysis <i>State the model type: Markov model, PSM, decision tree etc.</i>
Treatment	Not reported in the supplied CSR: no pharmacoeconomic submission is presented. (CSR pp. 1, 32-36: clinical-trial scope.)<i>State the DUR or regimen under review</i>
Included comparator(s)	- Not reported in the supplied CSR: no pharmacoeconomic submission is presented. (CSR pp. 1, 32-36: clinical-trial scope.)<i>State the generic name of each comparator</i> <i>Note if each comparator is used in addition to other treatment(s).</i> <i>If best supportive care, standard of care, etc. is included as a comparator, clearly define the components.</i> <i>If multiple comparators, use an alphabetized, bulleted list.</i> <i>If relevant, note if comparators differ across subgroup analyses</i>
Perspective	- Not reported in the supplied CSR: no pharmacoeconomic submission is presented. (CSR pp. 1, 32-36: clinical-trial scope.)Publicly funded health care payer perspective <i>If this is a Complex Review (Scenario 1), add: Societal perspective</i>
Time horizon	Not reported in the supplied CSR: no pharmacoeconomic submission is presented. (CSR pp. 1, 32-36: clinical-trial scope.)<i>State the model time horizon. If lifetime, state: Lifetime (# years), else state # years</i>
Cycle length	Not reported in the supplied CSR: no pharmacoeconomic submission is presented. (CSR pp. 1, 32-36: clinical-trial scope.)<i>State the model cycle length. If not applicable (e.g., for decision tree), state Not applicable.</i>
Modelled population(s)	- Not reported in the supplied CSR: no pharmacoeconomic submission is presented. (CSR pp. 1, 32-36: clinical-trial scope.)<i>Briefly describe the modelled population</i> <i>If relevant, describe any submitted subgroups</i> <i>Describe any meaningful differences between the modelled population and the Health Canada indication (draft or approved).</i>

Component	Description
Characteristics of modelled population	- Not reported in the supplied CSR: no pharmacoeconomic submission is presented. (CSR pp. 1, 32-36: clinical-trial scope.) <i>State the mean starting age of patients in the population, along with any other relevant characteristics (e.g., sex, weight, BMI, BSA).</i> <i>Specify data for subgroups if relevant.</i>
Model health states	- Not reported in the supplied CSR: no pharmacoeconomic submission is presented. (CSR pp. 1, 32-36: clinical-trial scope.) <i>State the model health states.</i> <i>Detailed information about the health states should be provided in the Model Structure section below.</i>
Duration of treatment	- Not reported in the supplied CSR: no pharmacoeconomic submission is presented. (CSR pp. 1, 32-36: clinical-trial scope.) <i>Describe the duration of treatment in the model for DUR and comparators (if different).</i> <i>Describe any differences between duration of treatment in the economic model versus any proposed reimbursement criteria as well as any differences versus any duration/discontinuation criteria specified in the product monograph.</i>
Data sources	
Comparative efficacy	- Not reported in the supplied CSR: no pharmacoeconomic submission is presented. (CSR pp. 1, 32-36: clinical-trial scope.) <i>Describe the sources, inputs, and assumptions made that inform the comparative efficacy of the drug under review relative to the included comparators.</i> <i>Provide references where appropriate</i>
Natural history and/or clinical pathway	- Not reported in the supplied CSR: no pharmacoeconomic submission is presented. (CSR pp. 1, 32-36: clinical-trial scope.) <i>Briefly describe the sources, inputs, and assumptions made that inform other aspects of the operation and output of the model. This could include:</i> <i>disease natural history, population demographics, epidemiological parameters</i> <i>health state transitions</i> <i>Provide references where appropriate</i>
Health-related utilities and disutilities	- Not reported in the supplied CSR: no pharmacoeconomic submission is presented. (CSR pp. 1, 32-36: clinical-trial scope.) <i>Briefly describe the sources, inputs, and assumptions pertaining to the derivation and application of health state utilities and disutilities</i> <i>Provide references where appropriate</i>
Costs	- Not reported in the supplied CSR: no pharmacoeconomic submission is presented. (CSR pp. 1, 32-36: clinical-trial scope.) <i>Briefly describe the sources, inputs, and assumptions for costs included in the model)</i> <i>Provide references where appropriate</i>
Summary of the submitted results	

Component	Description
Base case results	- Not reported in the supplied CSR: no pharmacoeconomic submission is presented. (CSR pp. 1, 32-36: clinical-trial scope.) <i>If 1 comparator, state: ICER = \$[to nearest dollar] per QALY gained versus [comparator] (incremental costs = \$X; incremental QALYs = X)</i> <i>If multiple comparators, indicate the ICER for DUR compared to the next drug on the frontier. Include incremental costs and incremental QALYs for the comparator used to calculate the ICER. Do not include comparators not on the frontier</i> <i>If relevant, provide the results by subgroup.</i> <i>If this is a Complex Review (Scenario 1), additionally present the results from the societal perspective</i>
Scenario analysis results	Not reported in the supplied CSR: no pharmacoeconomic submission is presented. (CSR pp. 1, 32-36: clinical-trial scope.) <i>Provide the ICERs for all submitted scenario analyses</i>

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

Model Structure

Not reported in the supplied CSR: no pharmacoeconomic submission is presented. (CSR pp. 1, 32-36: clinical-trial scope.)

- If a PSM has been submitted, this section may be omitted. For all other model structures, provide a narrative description of the submitted model*
- This section should provide a high-level summary of the submitted model structure including the components of the submitted model structure (e.g., health states, events)*

Not reported in the supplied CSR: no pharmacoeconomic submission is presented. (CSR pp. 1, 32-36: clinical-trial scope.)

- Describe how patients move through the model (e.g., cycling, progress and/or improve, tunnel states, time dependencies).*

Not reported in the supplied CSR: no pharmacoeconomic submission is presented. (CSR pp. 1, 32-36: clinical-trial scope.)

Figure 1: Model Structure

Not reported in the supplied CSR: no pharmacoeconomic submission is presented. (CSR pp. 1, 32-36: clinical-trial scope.)

Alt text: *Provide alt-text describing the figure.*

Not reported in the supplied CSR: no pharmacoeconomic submission is presented. (CSR pp. 1, 32-36: clinical-trial scope.)

Abbreviations, add as required (all abbreviations in the figure must be described here).

Not reported in the supplied CSR: no pharmacoeconomic submission is presented. (CSR pp. 1, 32-36: clinical-trial scope.)



Appendix 1: Literature Search Strategy

Example of Literature Search Strategy Reporting

Databases

Not reported in the supplied CSR: no systematic-review methods or results are provided. (CSR pp. 1, 32-36: single-trial scope.)

- Ovid – MEDLINE All (1946-present)

Not reported in the supplied CSR: no systematic-review methods or results are provided. (CSR pp. 1, 32-36: single-trial scope.)

- Ovid – Embase (1974-present)

Not reported in the supplied CSR: no systematic-review methods or results are provided. (CSR pp. 1, 32-36: single-trial scope.)

- Ovid – Cochrane Central Register of Controlled Trials (CCTR)

Not reported in the supplied CSR: no systematic-review methods or results are provided. (CSR pp. 1, 32-36: single-trial scope.)

- EBSCO – CINAHL

Not reported in the supplied CSR: no systematic-review methods or results are provided. (CSR pp. 1, 32-36: single-trial scope.)

- Scopus

Not reported in the supplied CSR: no systematic-review methods or results are provided. (CSR pp. 1, 32-36: single-trial scope.)

- Web of Science

Not reported in the supplied CSR: no systematic-review methods or results are provided. (CSR pp. 1, 32-36: single-trial scope.)

Note: Subject headings and search fields have been customized for each database. Duplicates between databases were removed in Ovid. Other duplicates were removed using bibliographic management software.

Not reported in the supplied CSR: no systematic-review methods or results are provided. (CSR pp. 1, 32-36: single-trial scope.)

Date of searches: [Provide search date. If dates vary, provide search date for each database]

Not reported in the supplied CSR: no systematic-review methods or results are provided. (CSR pp. 1, 32-36: single-trial scope.)

Search filters applied: Systematic reviews; meta-analyses; network meta-analyses; health technology assessments; guidelines; overview of reviews; randomized controlled trials; controlled clinical trials; qualitative studies; observational studies; economic evaluations; costs and cost analysis studies, and quality of life studies.

Not reported in the supplied CSR: no systematic-review methods or results are provided. (CSR pp. 1, 32-36: single-trial scope.)

Limits

Not reported in the supplied CSR: no systematic-review methods or results are provided. (CSR pp. 1, 32-36: single-trial scope.)

- Publication date limit: none

Not reported in the supplied CSR: no systematic-review methods or results are provided. (CSR pp. 1, 32-36: single-trial scope.)

- Language limit: none

Not reported in the supplied CSR: no systematic-review methods or results are provided. (CSR pp. 1, 32-36: single-trial scope.)

- Humans

Not reported in the supplied CSR: no systematic-review methods or results are provided. (CSR pp. 1, 32-36: single-trial scope.)

Database Search Strategies

Provide search strategies

Not reported in the supplied CSR: no systematic-review methods or results are provided. (CSR pp. 1, 32-36: single-trial scope.)

Clinical Trials Registries

ClinicalTrials.gov

Not reported in the supplied CSR: no systematic-review methods or results are provided. (CSR pp. 1, 32-36: single-trial scope.)

Produced by the U.S. National Library of Medicine. Targeted search used to capture registered clinical trials. [Search terms – List search terms]

Not reported in the supplied CSR: no systematic-review methods or results are provided. (CSR pp. 1, 32-36: single-trial scope.)

WHO ICTRP

Not reported in the supplied CSR: no systematic-review methods or results are provided. (CSR pp. 1, 32-36: single-trial scope.)

International Clinical Trials Registry Platform, produced by the World Health Organization. Targeted search used to capture registered clinical trials. [Search terms – List search terms]

Not reported in the supplied CSR: no systematic-review methods or results are provided. (CSR pp. 1, 32-36: single-trial scope.)

Health Canada's Clinical Trials Database

Not reported in the supplied CSR: no systematic-review methods or results are provided. (CSR pp. 1, 32-36: single-trial scope.)

Produced by Health Canada. Targeted search used to capture registered clinical trials. [Search terms – List search terms]

Not reported in the supplied CSR: no systematic-review methods or results are provided. (CSR pp. 1, 32-36: single-trial scope.)

EU Clinical Trials Register

Not reported in the supplied CSR: no systematic-review methods or results are provided. (CSR pp. 1, 32-36: single-trial scope.)

European Union Clinical Trials Register, produced by the European Union. Targeted search used to capture registered clinical trials. [Search terms – List search terms]

Appendix 2: List of Excluded Studies

Table 31: Excluded Studies

Reference	Reason for Exclusion
Not reported in the supplied CSR: no systematic-review methods or results are provided. (CSR pp. 1, 32-36: single-trial scope.) Add reference	Not reported in the supplied CSR: no systematic-review methods or results are provided. (CSR pp. 1, 32-36: single-trial scope.) When identifying the reason for exclusion, please use a similar format as the following examples: • Study design • Intervention (if the intervention in the study does not meet that identified in the systematic review protocol, for example, different dose, formulation, etc.) • Comparator • Study population • Duplicate study
As above Not reported in the supplied CSR: no systematic-review methods or results are provided. (CSR pp. 1, 32-36: single-trial scope.)	As above Not reported in the supplied CSR: no systematic-review methods or results are provided. (CSR pp. 1, 32-36: single-trial scope.)
Add rows as necessary Not reported in the supplied CSR: no systematic-review methods or results are provided. (CSR pp. 1, 32-36: single-trial scope.)	Not reported in the supplied CSR: no systematic-review methods or results are provided. (CSR pp. 1, 32-36: single-trial scope.)

References

1. Novo Nordisk. Clinical trial report: NN9536-4373 (STEP 1). Effect and safety of semaglutide 2.4 mg once-weekly in subjects with overweight or obesity. Version 1.0, final; 17 August 2020. Supplied file: Phase3a-STEP1-report(1).pdf. Report covers the main trial phase. (CSR pp. 1-2, 32.) The example references retained below are template text, not evidence used for this completion.

References must be provided in this section and should adhere to standard citation practices for publication, as per the following examples:

1. Murray CJL. Maximizing antiretroviral therapy in developing countries: the dual challenge of efficiency and quality [published online December 1, 2014]. *JAMA*. doi:10.1001/jama.2014.16376
2. Centers for Medicare & Medicaid Services. CMS proposals to implement certain disclosure provisions of the Affordable Care Act. <http://www.cms.gov/apps/media/press/factsheet.asp?Counter=4221>. Accessed January 30, 2012.
3. McPhee SJ, Winker MA, Rabow MW, Pantilat SZ, Markowitz AJ, eds. *Care at the Close of Life: Evidence and Experience*. New York, NY: McGraw Hill Medical; 2011.