

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

215256Orig1s031

Trade Name: WEGOVY

Generic or Proper Name: semaglutide

Sponsor: Novo Nordisk Inc.

Approval Date: May 5, 2026

Indication: WEGOVY is a glucagon-like peptide-1 (GLP-1) receptor agonist. WEGOVY injection is indicated in combination with a reduced calorie diet and increased physical activity:

- To reduce the risk of major adverse cardiovascular (CV) events (CV death, non-fatal myocardial infarction, or non-fatal stroke) in adults with established CV disease and either obesity or overweight.
- To reduce excess body weight and maintain weight reduction long term in:
 - Adults and pediatric patients aged 12 years and older with obesity.
 - Adults with overweight in the presence of at least one weight related comorbid condition.
- For the treatment of noncirrhotic metabolic dysfunction-associated steatohepatitis (MASH), formerly known as nonalcoholic steatohepatitis (NASH), with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis) in adults.

This indication is approved under accelerated approval based on improvement of MASH and fibrosis [see Clinical Studies (14.4)]. Continued approval for this indication may be contingent upon the verification and description of clinical benefit in a confirmatory trial.

WEGOVY tablets are indicated in combination with a reduced calorie

diet and increased physical activity:

- To reduce the risk of major adverse CV events (CV death, non-fatal myocardial infarction, or non-fatal stroke) in adults with established CV disease and either obesity or overweight.
- To reduce excess body weight and maintain weight reduction long term in adults with obesity, or in adults with overweight in the presence of at least one weight-related comorbid condition.

CENTER FOR DRUG EVALUATION AND RESEARCH

215256Orig1s031

CONTENTS

Reviews / Information Included in this NDA Review.

Approval Letter	X
Other Action Letters	
Labeling	X
REMS	
Summary Review	
Officer/Employee List	
Office Director Memo	
Cross Discipline Team Leader Review	X
Clinical Review(s)	
Product Quality Review(s)	X
Non-Clinical Review(s)	
Statistical Review(s)	
Clinical Microbiology / Virology Review(s)	
Clinical Pharmacology Review(s)	X
Other Reviews	X
Risk Assessment and Risk Mitigation Review(s)	
Proprietary Name Review(s)	
Administrative/Correspondence Document(s)	X

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

215256Orig1s031

APPROVAL LETTER



NDA 215256/S-031
NDA 218316/S-003

SUPPLEMENT APPROVAL

Novo Nordisk Inc.
Attention: Devraj Chakravarty
Director, Regulatory Affairs
800 Scudders Mill Road
P.O. Box 846
Plainsboro, NJ 08536

Dear Devraj Chakravarty:

Please refer to your supplemental new drug applications (sNDAs) dated and received January 5, 2026, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Wegovy (semaglutide) injection and Wegovy (semaglutide) tablets.

NDA 215256/S-031

This Prior Approval sNDA provides for the addition of a new presentation of Wegovy injection in a single dose manual prefilled syringe (mPFS) for the approved doses (0.25 mg, 0.5 mg, 1 mg, 1.7 mg, and 2.4 mg). This supplement provides for updates to the Prescribing Information, as well as a new Instructions for Use and carton and container labeling for the new single dose mPFS presentation.

NDA 218316/S-003

This Prior Approval sNDA provides for alignment of the combined Wegovy injection and Wegovy tablets Prescribing Information based on the addition of a new presentation of Wegovy injection in a single dose mPFS.

APPROVAL & LABELING

We have completed our review of these applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(I)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at

FDA.gov.¹ Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information, Instructions for Use, and Medication Guide), with the addition of any labeling changes in pending “Changes Being Effectuated” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.²

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(I)(1)(i)] in Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling and carton and container labeling submitted on May 5, 2026, as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*. For administrative purposes, designate this submission “**Product Correspondence – Final Printed Carton and Container Labeling for approved NDA 215256/S-031.**” Approval of this submission by FDA is not required before the labeling is used.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format – Promotional Labeling and Advertising in Materials for Human Prescription Drugs*.³

¹ <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

² We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

³ For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/media/128163/download>.

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at FDA.gov.⁴ Information and Instructions for completing the form can be found at FDA.gov.⁵

PATENT LISTING REQUIREMENTS

Pursuant to 21 CFR 314.53(d)(2) and 314.70(f), certain changes to an approved NDA submitted in a supplement require you to submit patent information for listing in the Orange Book upon approval of the supplement. You must submit the patent information required by 21 CFR 314.53(d)(2)(i)(A) through (C) and 314.53(d)(2)(ii)(A) and (C), as applicable, to FDA on Form FDA 3542 within 30 days after the date of approval of the supplement for the patent information to be timely filed (see 21 CFR 314.53(c)(2)(ii)). You also must ensure that any changes to your approved NDA that require the submission of a request to remove patent information from the Orange Book are submitted to FDA at the time of approval of the supplement pursuant to 21 CFR 314.53(d)(2)(ii)(B) and 314.53(f)(2)(iv).

REPORTING REQUIREMENTS

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

Your product, Wegovy injection, is a Part 3 combination product (21 CFR 3.2(e)); therefore, you must also comply with postmarketing safety reporting requirements for an approved combination product (21 CFR 4, Subpart B). Additional information on combination product postmarketing safety reporting is available at FDA.gov.⁶

COMPENDIAL STANDARDS

A drug with a name recognized in the official United States Pharmacopeia or official National Formulary (USP-NF) generally must comply with the compendial standards for strength, quality, and purity, unless the difference in strength, quality, or purity is plainly stated on its label (see FD&C Act § 501(b), 21 USC 351(b)). FDA typically cannot share application-specific information contained in submitted regulatory filings with third parties, which includes USP-NF. To help ensure that a drug continues to comply with compendial standards, application holders may work directly with USP-NF to revise

⁴ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

⁵ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

⁶ <https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products>

official USP monographs. More information on the USP-NF is available on USP's website⁷.

If you have any questions, contact Martin White, Regulatory Project Manager, at 240- 402-6018.

Sincerely,

{See appended electronic signature page}

Raymond E. Soccio, MD, PhD
Supervisory Physician (Acting)
Division of Diabetes, Lipid Disorders, and Obesity
Office of Cardiology, Hematology, Endocrinology,
and Nephrology
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
 - Prescribing Information
 - Medication Guide (version previously approved March 19, 2026)
 - Instructions for Use for Wegovy injection single dose manual prefilled syringe (0.25 mg, 0.5 mg, 1 mg, 1.7 mg, and 2.4 mg)
 - Instructions for Use for Wegovy injection (version previously approved August 24, 2022)
 - Instructions for Use for Wegovy HD injection (version previously approved March 19, 2026)
- Carton and Container Labeling for Wegovy injection single dose manual prefilled syringe (0.25 mg, 0.5 mg, 1 mg, 1.7 mg, and 2.4 mg)

⁷ <https://www.uspnf.com/>

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

215256Orig1s031

LABELING

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use WEGOVY® safely and effectively. See full prescribing information for WEGOVY.

WEGOVY (semaglutide) injection, for subcutaneous use
WEGOVY (semaglutide) tablets, for oral use
Initial U.S. Approval: 2017

WARNING: RISK OF THYROID C-CELL TUMORS See full prescribing information for complete boxed warning.

- In rodents, semaglutide causes thyroid C-cell tumors at clinically relevant exposures. It is unknown whether WEGOVY causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans as the human relevance of semaglutide-induced rodent thyroid C-cell tumors has not been determined. (5.1, 13.1)
- WEGOVY is contraindicated in patients with a personal or family history of MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Counsel patients regarding the potential risk of MTC and symptoms of thyroid tumors. (4, 5.1)

RECENT MAJOR CHANGES

Indications and Usage (1).....08/2025, 12/2025
Dosage and Administration (2).....08/2025, 12/2025, 03/2026
Warnings and Precautions,
Acute Kidney Injury Due to Volume Depletion (5.5).....08/2025
Severe Gastrointestinal Adverse Reactions (5.6).....10/2025
Suicidal Behavior and Ideation (5.10)(Removed) 01/2026

INDICATIONS AND USAGE

WEGOVY is a glucagon-like peptide-1 (GLP-1) receptor agonist. WEGOVY injection is indicated in combination with a reduced calorie diet and increased physical activity:

- To reduce the risk of major adverse cardiovascular (CV) events (CV death, non-fatal myocardial infarction, or non-fatal stroke) in adults with established CV disease and either obesity or overweight. (1)
- To reduce excess body weight and maintain weight reduction long term in:
 - Adults and pediatric patients aged 12 years and older with obesity. (1)
 - Adults with overweight in the presence of at least one weight-related comorbid condition. (1)
- For the treatment of noncirrhotic metabolic dysfunction-associated steatohepatitis (MASH), formerly known as nonalcoholic steatohepatitis (NASH), with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis) in adults. This indication is approved under accelerated approval based on improvement of MASH and fibrosis [see *Clinical Studies* (14.4)]. Continued approval for this indication may be contingent upon the verification and description of clinical benefit in a confirmatory trial. (1)

WEGOVY tablets are indicated in combination with a reduced calorie diet and increased physical activity:

- To reduce the risk of major adverse CV events (CV death, non-fatal myocardial infarction, or non-fatal stroke) in adults with established CV disease and either obesity or overweight. (1)
- To reduce excess body weight and maintain weight reduction long term in adults with obesity, or in adults with overweight in the presence of at least one weight-related comorbid condition. (1)

Limitations of Use:

- Concomitant use of WEGOVY (semaglutide) tablets or WEGOVY (semaglutide) injection with other semaglutide-containing products or with any other GLP-1 receptor agonist is not recommended. (1)

DOSAGE AND ADMINISTRATION

In patients with diabetes, monitor blood glucose prior to starting and during WEGOVY treatment. (2.1)

WEGOVY Injection

- Administer WEGOVY injection once weekly as an adjunct to diet and increased physical activity, on the same day each week, at any time of day, with or without meals. (2.1)
- Inject subcutaneously in the abdomen, thigh, or upper arm. (2.1)
- Initiate at 0.25 mg once weekly for 4 weeks. Then follow the dosage escalation schedule in Table 1, titrating every 4 weeks to achieve the maintenance dosage. (2.2)
- The usual recommended maintenance dosage of WEGOVY injection is 2.4 mg once weekly. Refer to the full PI for maintenance dosages based on the indication. (2.2)

- Initiate WEGOVY tablet with a dosage of 1.5 mg once daily for 30 days. Then follow the dosage escalation schedule, titrating every 30 days to achieve the maintenance dosage. (2.2)
- The recommended maintenance dosage of WEGOVY tablets is 25 mg orally once daily for cardiovascular risk reduction and weight reduction in adults. (2.3)

DOSAGE FORMS AND STRENGTHS

- Injection: prefilled, single-dose pen that delivers doses of 0.25 mg, 0.5 mg, 1 mg, 1.7 mg, 2.4 mg or WEGOVY HD 7.2 mg (3)
- Injection: prefilled, single-dose syringe that delivers doses of 0.25 mg, 0.5 mg, 1 mg, 1.7 mg, 2.4 mg (3)
- Tablets: 1.5 mg, 4 mg, 9 mg and 25 mg (3)

CONTRAINDICATIONS

- Personal or family history of MTC or in patients with MEN 2. (4)
- Known hypersensitivity to semaglutide or any of the excipients in WEGOVY tablets or WEGOVY injection. (4)

WARNINGS AND PRECAUTIONS

- *Acute Pancreatitis*: Has been observed in patients treated with GLP-1 receptor agonists, including WEGOVY. Discontinue if pancreatitis is suspected. (5.2)
- *Acute Gallbladder Disease*: Has occurred in clinical trials. If cholelithiasis is suspected, gallbladder studies and clinical follow-up are indicated. (5.3)
- *Hypoglycemia*: Concomitant use with insulin or an insulin secretagogue may increase the risk of hypoglycemia, including severe hypoglycemia. Reducing the dose of insulin or insulin secretagogue may be necessary. Inform all patients of the risk of hypoglycemia and educate them on the signs and symptoms of hypoglycemia. (5.4)
- *Acute Kidney Injury Due to Volume Depletion*: Monitor renal function in patients reporting adverse reactions that could lead to volume depletion. (5.5)
- *Severe Gastrointestinal Adverse Reactions*: Use has been associated with gastrointestinal adverse reactions, sometimes severe. WEGOVY is not recommended in patients with severe gastroparesis. (5.6)
- *Hypersensitivity Reactions*: Anaphylactic reactions and angioedema have been reported postmarketing. Discontinue WEGOVY if suspected and promptly seek medical advice. (5.7)
- *Diabetic Retinopathy Complications in Patients with Type 2 Diabetes*: Has been reported in trials with semaglutide. Patients with a history of diabetic retinopathy should be monitored. (5.8)
- *Heart Rate Increase*: Monitor heart rate at regular intervals. (5.9)
- *Pulmonary Aspiration During General Anesthesia or Deep Sedation*: Has been reported in patients receiving GLP-1 receptor agonists undergoing elective surgeries or procedures. Instruct patients to inform healthcare providers of any planned surgeries or procedures. (5.10)

ADVERSE REACTIONS

Most common adverse reactions (incidence $\geq 5\%$) in adults or pediatric patients aged 12 years and older are: nausea, diarrhea, vomiting, constipation, abdominal pain, dysesthesia, headache, fatigue, dyspepsia, dizziness, abdominal distension, eructation, hypoglycemia in patients with type 2 diabetes, flatulence, gastroenteritis, gastroesophageal reflux disease, and hair loss. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Novo Nordisk Inc., at 1-833-934-6891 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

WEGOVY delays gastric emptying. May impact absorption of concomitantly administered oral medications. Consider increased clinical or laboratory monitoring when used concomitantly with other oral medications that have a narrow therapeutic index or that require clinical monitoring. (7.2)

USE IN SPECIFIC POPULATIONS

- *Pregnancy*: May cause fetal harm. For patients receiving WEGOVY for CV risk reduction or weight reduction, discontinue WEGOVY when pregnancy is recognized. For patients with MASH, use during pregnancy only if the potential benefit justifies the potential risk to the fetus. (8.1)
- *Lactation*: Breastfeeding not recommended during treatment with WEGOVY tablets. (8.2)
- *Females and Males of Reproductive Potential*: For patients receiving WEGOVY for CV risk reduction or weight reduction, or for MASH where the potential risk outweighs the potential benefit, discontinue WEGOVY at least 2 months before a planned pregnancy because of the long half-life of semaglutide. (8.3)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

- Take WEGOVY tablets orally once-daily on an empty stomach in the morning with water (up to 4 ounces). Do not take with other liquids besides water. (2.1)
- Swallow tablets whole. Do not split, crush, chew or dissolve. (2.1)
- After taking WEGOVY tablet wait at least 30 minutes before eating food, drinking beverages or taking other oral medications. (2.1)

FULL PRESCRIBING INFORMATION: CONTENTS***WARNING: RISK OF THYROID C-CELL TUMORS****1 INDICATIONS AND USAGE****2 DOSAGE AND ADMINISTRATION**

- 2.1 Important Monitoring and Administration Instructions
- 2.2 Recommended Dosage for WEGOVY Injection
- 2.3 Recommended Dosage of WEGOVY Tablets
- 2.4 Recommendations Regarding Missed Dose(s)
- 2.5 Switching Between WEGOVY Injection and WEGOVY Tablets

3 DOSAGE FORMS AND STRENGTHS**4 CONTRAINDICATIONS****5 WARNINGS AND PRECAUTIONS**

- 5.1 Risk of Thyroid C-Cell Tumors
- 5.2 Acute Pancreatitis
- 5.3 Acute Gallbladder Disease
- 5.4 Hypoglycemia
- 5.5 Acute Kidney Injury Due to Volume Depletion
- 5.6 Severe Gastrointestinal Adverse Reactions
- 5.7 Hypersensitivity Reactions
- 5.8 Diabetic Retinopathy Complications in Patients with Type 2 Diabetes
- 5.9 Heart Rate Increase
- 5.10 Pulmonary Aspiration During General Anesthesia or Deep Sedation

6 ADVERSE REACTIONS

- 6.1 Clinical Trials Experience
- 6.2 Postmarketing Experience

7 DRUG INTERACTIONS

- 7.1 Concomitant Use with Insulin or an Insulin Secretagogue (e.g., Sulfonylurea)
- 7.2 Oral Medications

8 USE IN SPECIFIC POPULATIONS

- 8.1 Pregnancy
- 8.2 Lactation
- 8.3 Females and Males of Reproductive Potential
- 8.4 Pediatric Use
- 8.5 Geriatric Use
- 8.6 Type 2 Diabetes Mellitus

10 OVERDOSAGE**11 DESCRIPTION****12 CLINICAL PHARMACOLOGY**

- 12.1 Mechanism of Action
- 12.2 Pharmacodynamics
- 12.3 Pharmacokinetics
- 12.6 Immunogenicity

13 NONCLINICAL TOXICOLOGY

- 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
- 13.2 Animal Toxicology and/or Pharmacology

14 CLINICAL STUDIES

- 14.1 Cardiovascular Outcomes Trial in Adult Patients with Cardiovascular Disease and Either Obesity or Overweight
- 14.2 Weight Reduction and Long-term Maintenance Studies in Adults with Obesity or Overweight
- 14.3 Weight Reduction and Long-term Maintenance Study of WEGOVY Injection in Pediatric Patients Aged 12 Years and Older with Obesity
- 14.4 Noncirrhotic Metabolic Dysfunction-associated Steatohepatitis with Moderate to Advanced Liver Fibrosis in Adults Treated with WEGOVY Injection

16 HOW SUPPLIED/STORAGE AND HANDLING**17 PATIENT COUNSELING INFORMATION**

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

WARNING: RISK OF THYROID C-CELL TUMORS

- In rodents, semaglutide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures. It is unknown whether WEGOVY causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans as human relevance of semaglutide-induced rodent thyroid C-cell tumors has not been determined [see *Warnings and Precautions (5.1)*, *Nonclinical Toxicology (13.1)*].
- WEGOVY is contraindicated in patients with a personal or family history of MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2) [see *Contraindications (4)*]. Counsel patients regarding the potential risk for MTC with the use of WEGOVY and inform them of symptoms of thyroid tumors (e.g., a mass in the neck, dysphagia, dyspnea, persistent hoarseness). Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with WEGOVY [see *Contraindications (4)*, *Warnings and Precautions (5.1)*].

1 INDICATIONS AND USAGE

WEGOVY injection is indicated in combination with a reduced calorie diet and increased physical activity:

- To reduce the risk of major adverse cardiovascular (CV) events (CV death, non-fatal myocardial infarction, or non-fatal stroke) in adults with established CV disease and either obesity or overweight.
- To reduce excess body weight and maintain weight reduction long term in:
 - Adults and pediatric patients aged 12 years and older with obesity.
 - Adults with overweight in the presence of at least one weight-related comorbid condition.
- For the treatment of noncirrhotic metabolic dysfunction-associated steatohepatitis (MASH), formerly known as nonalcoholic steatohepatitis (NASH), with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis) in adults. This indication is approved under accelerated approval based on improvement of MASH and fibrosis [see *Clinical Studies (14.4)*]. Continued approval for this indication may be contingent upon the verification and description of clinical benefit in a confirmatory trial.

WEGOVY tablets are indicated in combination with a reduced calorie diet and increased physical activity:

- To reduce the risk of major adverse CV events (CV death, non-fatal myocardial infarction, or non-fatal stroke) in adults with established CV disease and either obesity or overweight.
- To reduce excess body weight and maintain weight reduction long term in adults with obesity, or in adults with overweight in the presence of at least one weight-related comorbid condition.

Limitations of Use

Concomitant use of WEGOVY (semaglutide) tablets or WEGOVY (semaglutide) injection with other semaglutide-containing products or with any other GLP-1 receptor agonist is not recommended.

2 DOSAGE AND ADMINISTRATION

2.1 Important Monitoring and Administration Instructions

In patients with diabetes mellitus, monitor blood glucose prior to starting WEGOVY and during WEGOVY treatment [see *Warnings and Precautions (5.4)*].

Administer WEGOVY in combination with a reduced-calorie diet and increased physical activity.

WEGOVY Injection

- Prior to initiation of WEGOVY injection, train patients on proper injection technique. Refer to the accompanying Instructions for Use for complete administration instructions with illustrations.
- Visually inspect the WEGOVY injection prior to each administration. Only use if the solution is clear, colorless, and contains no particles.
- Administer WEGOVY injection once weekly, on the same day each week, at any time of day, with or without meals.
- Inject WEGOVY subcutaneously in the abdomen, thigh, or upper arm. The time of day and the injection site can be changed without the need for a dosage modification.

WEGOVY Tablets

- Take one WEGOVY tablet orally once daily on an empty stomach in the morning with water (up to 4 ounces). Do not take WEGOVY tablets with other liquids besides water [see *Clinical Pharmacology* (12.3)].
- Do not take more than one tablet per day.
- Swallow tablets whole. Do not split, crush, chew or dissolve in any solution.
- After taking a WEGOVY tablet, wait at least 30 minutes before eating food, drinking beverages or taking other oral medications [see *Clinical Pharmacology* (12.3)].

2.2 Recommended Dosage for WEGOVY Injection

Recommended Starting Dosage and Dosage Escalation of WEGOVY Injection for All Approved Indications

- The recommended starting dosage of WEGOVY injection is 0.25 mg administered subcutaneously once weekly.
- Follow the dosage escalation in **Table 1** to reduce the risk of gastrointestinal adverse reactions [see *Warnings and Precautions* (5.6), *Adverse Reactions* (6.1)].
- If patients do not tolerate a dose during dosage escalation, consider delaying dosage escalation for 4 weeks.

Table 1. Recommended Starting Dosage and Dosage Escalation of WEGOVY Injection for All Approved Indications in Adults and Pediatric Patients Aged 12 Years and Older

	Weeks	Once-weekly Subcutaneous Injection Dosage
Starting Dosage	1 through 4	0.25 mg
Dosage Escalation	5 through 8	0.5 mg
	9 through 12	1 mg
	13 through 16	1.7 mg
Maintenance Dosage	17 and onward	See the indication below for the recommended maintenance dosage(s)

Recommended Maintenance Dosage of WEGOVY Injection for All Approved Indications

Cardiovascular Risk Reduction in Adults

- The maintenance dosage of WEGOVY injection for cardiovascular risk reduction in adults is either 2.4 mg (recommended) or 1.7 mg once weekly.
- Consider treatment response and tolerability when selecting the maintenance dosage [see *Adverse Reactions* (6.1), *Clinical Studies* (14.1)].

Weight Reduction in Adults

- The maintenance dosage of WEGOVY for weight reduction in adults is either 1.7 mg or 2.4 mg (recommended) injected subcutaneously once weekly.

- For patients who tolerate the 2.4 mg dosage for at least 4 weeks and additional weight reduction is clinically indicated, the dosage may be increased to a maximum dosage of 7.2 mg subcutaneously once weekly.
- Consider treatment response and tolerability when selecting the maintenance dosage [see *Adverse Reactions* (6.1), *Clinical Studies* (14.2)].

Weight Reduction in Pediatric Patients Aged 12 Years and Older

- The maintenance dosage of WEGOVY injection for weight reduction in pediatric patients aged 12 years and older is either 2.4 mg (recommended), 1.7 mg once weekly.
- Consider treatment response and tolerability when selecting the maintenance dosage [see *Adverse Reactions* (6.1), *Clinical Studies* (14.3)].

Noncirrhotic MASH with Moderate to Advanced Liver Fibrosis in Adults

- The recommended maintenance dosage of WEGOVY injection for the treatment of noncirrhotic MASH with moderate to advanced liver fibrosis in adults is 2.4 mg injected subcutaneously once weekly. If patients do not tolerate the maintenance dosage of 2.4 mg once weekly, the dosage can be decreased to 1.7 mg once weekly. Consider reescalation to 2.4 mg once weekly [see *Adverse Reactions* (6.1), *Clinical Studies* (14.4)].

2.3 Recommended Dosage of WEGOVY Tablets

Recommended Dosage of WEGOVY Tablets for Cardiovascular Risk Reduction or Weight Reduction in Adults

- The recommended starting dosage of WEGOVY tablets is 1.5 mg taken orally once daily. Follow the dosage escalation in **Table 2** to reduce the risk of gastrointestinal adverse reactions [see *Warnings and Precautions* (5.6), *Adverse Reactions* (6.1)].
- If patients do not tolerate a dose during dosage escalation, consider delaying dosage escalation.
- The recommended maintenance dosage of WEGOVY tablets is 25 mg orally once daily.
- If patients do not tolerate the 25 mg once daily maintenance dosage, consider switching to WEGOVY injection 1.7 mg once weekly [see *Dosage and Administration* (2.5)].

Table 2. Recommended Dosage of WEGOVY Tablets for Cardiovascular Risk Reduction or Weight Reduction in Adults

	Days	Once Daily Tablet Dosage
Starting Dosage	1 through 30	1.5 mg
Dosage Escalation	31 through 60	4 mg
	61 through 90	9 mg
Maintenance Dosage	91 and onward	25 mg

2.4 Recommendations Regarding Missed Dose(s)

WEGOVY Injection

- If one dose of WEGOVY injection is missed and the next scheduled dose is:
 - More than 2 days away, administer WEGOVY injection as soon as possible.
 - Less than 2 days away do not administer the WEGOVY injection dose. Resume dosing on the regularly scheduled day of the week.
- If 2 or more consecutive doses of WEGOVY injection are missed, resume dosing as scheduled or, if needed, reinstitute WEGOVY injection and follow the dosage escalation schedule, which may reduce the occurrence of gastrointestinal adverse reactions associated with reinitiation of treatment [see *Dosage and Administration* (2.2)].

WEGOVY Tablets

If a dose of WEGOVY tablets is missed, skip the missed dose and take the next dose the following day.

2.5 Switching Between WEGOVY Injection and WEGOVY Tablets

Switching from WEGOVY Injection to WEGOVY Tablets

- Patients taking WEGOVY 2.4 mg injection for cardiovascular risk reduction or weight reduction in adults may switch to WEGOVY 25 mg tablets.
- One week after discontinuing WEGOVY 2.4 mg injection, initiate 25 mg of WEGOVY tablets orally once daily.

Switching from WEGOVY Tablets to WEGOVY Injection

- Patients may switch from WEGOVY 25 mg tablets to WEGOVY injection.
- The day after discontinuing WEGOVY tablets 25 mg once daily, initiate WEGOVY 2.4 mg subcutaneous injection once weekly. For patients who do not tolerate WEGOVY 25 mg tablets, consider switching to WEGOVY 1.7 mg injection.
- If additional weight reduction is needed in patients with type 2 diabetes mellitus treated with WEGOVY 25 mg tablets, consider switching to WEGOVY 1.7 mg injection and follow the recommended dosage escalation for WEGOVY injection. [see Dosage and Administration (2.2), Use in Specific Populations (8.6), Clinical Pharmacology (12.3)].

3 DOSAGE FORMS AND STRENGTHS

Injection: clear, colorless solution available as follows:

Single-Dose Prefilled Pens	
Dose per Injection	Total Strength per Total Volume
0.25 mg	0.25 mg / 0.5 mL
0.5 mg	0.5 mg / 0.5 mL
1 mg	1 mg / 0.5 mL
1.7 mg	1.7 mg/0.75 mL
2.4 mg	2.4 mg/0.75 mL
7.2 mg (WEGOVY HD)	7.2 mg/0.75 mL

Single-Dose Prefilled Syringes	
Dose per Injection	Total Strength per Total Volume
0.25 mg	0.25 mg / 0.5 mL
0.5 mg	0.5 mg / 0.5 mL
1 mg	1 mg / 0.5 mL
1.7 mg	1.7 mg/0.75 mL
2.4 mg	2.4 mg/0.75 mL

Tablets: available as:

Tablet strength	Description
1.5 mg	White to light yellow, round shaped debossed with “1.5” on one side and “novo” on the other side
4 mg	White to light yellow, round shaped debossed with “4” on one side and “novo” on the other side
9 mg	White to light yellow, round shaped debossed with “9” on one side and “novo” on the other side
25 mg	White to light yellow, oval shaped debossed with “25” on one side and “novo” on the other side

4 CONTRAINDICATIONS

WEGOVY is contraindicated in the following conditions:

- A personal or family history of MTC or in patients with MEN 2 [see *Warnings and Precautions* (5.1)].
- A prior serious hypersensitivity reaction to semaglutide or to any of the excipients in WEGOVY injection or WEGOVY tablet. Serious hypersensitivity reactions, including anaphylaxis and angioedema, have been reported with WEGOVY [see *Warnings and Precautions* (5.7)].

5 WARNINGS AND PRECAUTIONS

5.1 Risk of Thyroid C-Cell Tumors

In mice and rats, semaglutide caused a dose-dependent and treatment-duration-dependent increase in the incidence of thyroid C-cell tumors (adenomas and carcinomas) after lifetime exposure at clinically relevant plasma exposures [see *Nonclinical Toxicology* (13.1)]. It is unknown whether WEGOVY causes thyroid C-cell tumors, including MTC, in humans, as human relevance of semaglutide-induced rodent thyroid C-cell tumors has not been determined.

Cases of MTC in patients treated with liraglutide, another GLP-1 receptor agonist, have been reported in the postmarketing period; the data in these reports are insufficient to establish or exclude a causal relationship between MTC and GLP-1 receptor agonist use in humans.

WEGOVY is contraindicated in patients with a personal or family history of MTC or in patients with MEN 2. Counsel patients regarding the potential risk for MTC with the use of WEGOVY and inform them of symptoms of thyroid tumors (e.g., a mass in the neck, dysphagia, dyspnea, persistent hoarseness).

Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with WEGOVY. Such monitoring may increase the risk of unnecessary procedures, due to the low-test specificity for serum calcitonin and a high background incidence of thyroid disease. Significantly elevated serum calcitonin value may indicate MTC and patients with MTC usually have calcitonin values greater than 50 ng/L. If serum calcitonin is measured and found to be elevated, the patient should be further evaluated. Patients with thyroid nodules noted on physical examination or neck imaging should also be further evaluated.

5.2 Acute Pancreatitis

Acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis, has been observed in patients treated with GLP-1 receptor agonists, including WEGOVY [see *Adverse Reactions* (6)]. After initiation of WEGOVY, observe patients carefully for signs and symptoms of acute pancreatitis, which may include persistent or severe abdominal pain (sometimes radiating to the back), and which may or may not be accompanied by nausea or vomiting. If pancreatitis is suspected, discontinue WEGOVY and initiate appropriate management.

5.3 Acute Gallbladder Disease

Treatment with WEGOVY is associated with an increased occurrence of cholelithiasis and cholecystitis. The incidence of cholelithiasis and cholecystitis was higher in WEGOVY injection-treated pediatric patients aged 12 years and older than in WEGOVY injection-treated adults. In randomized clinical trials in adults for weight reduction, cholelithiasis was reported by 1.6% of WEGOVY injection-treated patients and 0.7% of placebo injection-treated patients, and by 2.5% of WEGOVY tablet-treated patients and 1% of placebo tablet-treated patients. Cholecystitis was reported by 0.6% of WEGOVY injection-treated adult patients and 0.2% of placebo-treated patients. In a clinical trial in pediatric patients aged 12 years and older for weight reduction, cholelithiasis was reported by 3.8% of WEGOVY injection-treated patients and 0% placebo-treated patients. Cholecystitis was reported by 0.8% of WEGOVY injection-treated pediatric patients and 0% placebo-treated patients [see *Adverse Reactions* (6.1)].

Substantial or rapid weight loss can increase the risk of cholelithiasis; however, the incidence of acute gallbladder disease was greater in WEGOVY-treated patients than in placebo-treated patients, even after accounting for the degree of weight loss. If cholelithiasis is suspected, gallbladder studies and appropriate clinical follow-up are indicated.

5.4 Hypoglycemia

WEGOVY lowers blood glucose and can cause hypoglycemia.

In a trial of WEGOVY injection in adult patients with type 2 diabetes and body mass index (BMI) greater than or equal to 27 kg/m² for weight reduction (Study 3), hypoglycemia (defined as a plasma glucose less than 54 mg/dL) was reported in more patients treated with WEGOVY versus placebo [see *Adverse Reactions* (6.1)]. One episode of severe hypoglycemia (requiring the assistance of another person) was reported in one WEGOVY treated patient versus no placebo-treated patients [see *Clinical Studies* (14.2)].

In glycemic control clinical trials, the risk of hypoglycemia was increased when semaglutide injection or tablet was used concomitantly with insulin or an insulin secretagogue (e.g., sulfonylurea). Patients with diabetes mellitus taking WEGOVY in combination with insulin or an insulin secretagogue may have an increased risk of hypoglycemia, including severe hypoglycemia. The use of WEGOVY in patients with type 1 diabetes mellitus or in combination with insulin has not been evaluated.

Inform patients of the risk of hypoglycemia and educate them on the signs and symptoms of hypoglycemia. In patients with diabetes, monitor blood glucose prior to starting WEGOVY and during WEGOVY treatment. When initiating WEGOVY, consider reducing the dose of concomitantly administered insulin or insulin secretagogue to reduce the risk of hypoglycemia [see *Drug Interactions* (7.1)].

5.5 Acute Kidney Injury Due to Volume Depletion

There have been postmarketing reports of acute kidney injury, in some cases requiring hemodialysis, in patients treated with semaglutide [see *Adverse Reactions* (6)]. The majority of the reported events occurred in patients who experienced gastrointestinal adverse reactions leading to dehydration such as nausea, vomiting, or diarrhea [see *Adverse Reactions* (6)].

Monitor renal function in patients reporting adverse reactions to WEGOVY that could lead to volume depletion, especially during dosage initiation and escalation of WEGOVY.

5.6 Severe Gastrointestinal Adverse Reactions

Use of WEGOVY has been associated with gastrointestinal adverse reactions, sometimes severe [see *Adverse Reactions* (6)]. In clinical trials for adults for weight reduction, severe gastrointestinal adverse reactions were reported more frequently among patients receiving WEGOVY than placebo. Severe gastrointestinal adverse reactions were reported in 4.1% and 0.9% of WEGOVY injection and placebo-treated patients, respectively, and in 2% of WEGOVY tablet-treated and 0% of placebo-treated patients, respectively. Severe gastrointestinal adverse reactions have also been reported postmarketing with GLP-1 receptor agonists.

WEGOVY is not recommended in patients with severe gastroparesis.

5.7 Hypersensitivity Reactions

Serious hypersensitivity reactions (e.g., anaphylaxis, angioedema) have been reported with WEGOVY. If hypersensitivity reactions occur, discontinue use of WEGOVY, treat promptly per standard of care, and monitor until signs and symptoms resolve. WEGOVY is contraindicated in patients with a prior serious hypersensitivity reaction to semaglutide or to any of the excipients in WEGOVY [see *Adverse Reactions* (6.2)].

Anaphylaxis and angioedema have been reported with other GLP-1 receptor agonists. Use caution in a patient with a history of anaphylaxis or angioedema with another GLP-1 receptor agonist because it is unknown whether such patients will be predisposed to these reactions with WEGOVY.

5.8 Diabetic Retinopathy Complications in Patients with Type 2 Diabetes

In a 2-year trial with semaglutide 0.5 mg and 1 mg once-weekly injection in adult patients with type 2 diabetes and high CV risk, diabetic retinopathy complications (which was a 4-component adjudicated endpoint) occurred in patients treated with semaglutide injection (3%) compared to placebo (1.8%). The absolute risk increase for diabetic retinopathy complications was larger among patients with a history of diabetic retinopathy at baseline (semaglutide injection 8.2%, placebo 5.2%) than among patients without a known history of diabetic retinopathy (semaglutide injection 0.7%, placebo 0.4%).

In a trial of adult patients with type 2 diabetes and BMI greater than or equal to 27 kg/m² for weight reduction (Study 3), diabetic retinopathy was reported by 4% of WEGOVY injection-treated patients and 2.7% placebo-treated patients [*see Clinical Studies (14.2)*].

In a glycemic control trial evaluating a dose comparable to the 9 mg dose and the 25 mg semaglutide tablet dose in patients with type 2 diabetes, a similar proportion of patients in each dose group reported diabetic retinopathy related adverse reactions during the trial; 1.3% and 1.9% of patients in the 9 mg and 25 mg semaglutide group, respectively, reported moderate-severe non-proliferative diabetic retinopathy events, and 0% and 0.4% reported proliferative retinopathy events, respectively.

Rapid improvement in glucose control has been associated with a temporary worsening of diabetic retinopathy. The effect of long-term glycemic control with semaglutide on diabetic retinopathy complications has not been studied. Patients with a history of diabetic retinopathy should be monitored for progression of diabetic retinopathy.

5.9 Heart Rate Increase

Treatment with WEGOVY was associated with increases in resting heart rate. Mean increases in resting heart rate of 1 to 4 beats per minute (bpm) were observed in WEGOVY injection-treated adult patients compared to placebo in clinical trials for weight reduction. More adult patients treated with WEGOVY injection compared to placebo had maximum changes from baseline at any visit of 10 to 19 bpm (41% versus 34%, respectively) and 20 bpm or more (26% versus 16%, respectively). In a clinical trial in pediatric patients aged 12 years and older with normal baseline heart rate, more patients treated with WEGOVY injection compared to placebo had maximum changes in heart rate of 20 bpm or more (54% versus 39%) [*see Adverse Reactions (6.1)*]. Findings were similar in a trial with the WEGOVY tablets.

Monitor heart rate at regular intervals consistent with usual clinical practice. Instruct patients to inform their healthcare providers of palpitations or feelings of a racing heartbeat while at rest during WEGOVY treatment. If patients experience a sustained increase in resting heart rate, discontinue WEGOVY.

5.10 Pulmonary Aspiration During General Anesthesia or Deep Sedation

WEGOVY delays gastric emptying [*see Clinical Pharmacology (12.2)*]. There have been rare postmarketing reports of pulmonary aspiration in patients receiving GLP-1 receptor agonists undergoing elective surgeries or procedures requiring general anesthesia or deep sedation who had residual gastric contents despite reported adherence to preoperative fasting recommendations.

Available data are insufficient to inform recommendations to mitigate the risk of pulmonary aspiration during general anesthesia or deep sedation in patients taking WEGOVY, including whether modifying preoperative fasting recommendations or temporarily discontinuing WEGOVY could reduce the incidence of retained gastric contents. Instruct patients to inform healthcare providers prior to any planned surgeries or procedures if they are taking WEGOVY.

6 ADVERSE REACTIONS

The following serious adverse reactions are described below or elsewhere in the prescribing information:

- Risk of Thyroid C-Cell Tumors [see *Warnings and Precautions* (5.1)]
- Acute Pancreatitis [see *Warnings and Precautions* (5.2)]
- Acute Gallbladder Disease [see *Warnings and Precautions* (5.3)]
- Hypoglycemia [see *Warnings and Precautions* (5.4)]
- Acute Kidney Injury Due to Volume Depletion [see *Warnings and Precautions* (5.5)]
- Severe Gastrointestinal Adverse Reactions [see *Warnings and Precautions* (5.6)]
- Hypersensitivity Reactions [see *Warnings and Precautions* (5.7)]
- Diabetic Retinopathy Complications in Patients with Type 2 Diabetes [see *Warnings and Precautions* (5.8)]
- Heart Rate Increase [see *Warnings and Precautions* (5.9)]
- Pulmonary Aspiration During General Anesthesia or Deep Sedation [see *Warnings and Precautions* (5.10)]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice.

Adverse Reactions in Clinical Trials in Adults with Obesity or Overweight for Weight Reduction

WEGOVY 2.4 mg Subcutaneous Injection Weekly Dosage

WEGOVY was evaluated for safety in 3 randomized, double-blind, placebo-controlled trials that included 2,116 adult patients with obesity or overweight treated with 2.4 mg WEGOVY injection for up to 68 weeks and a 7-week off-drug follow-up period [see *Clinical Studies* (14.2)]. Baseline characteristics included a mean age of 48 years, 71% female, 72% White, 14% Asian, 9% Black or African American, and 5% reported as other or unknown; and 85% were not Hispanic or Latino ethnicity, 13% were Hispanic or Latino ethnicity, and 2% reported as unknown. The baseline characteristics were 42% with hypertension, 19% with type 2 diabetes, 43% with dyslipidemia, 28% with a BMI greater than 40 kg/m² and 4% with CV disease.

In these clinical trials, 6.8% of patients treated with 2.4 mg WEGOVY injection and 3.2% of patients treated with placebo permanently discontinued treatment as a result of adverse reactions. The most common adverse reactions leading to discontinuation were nausea (1.8% versus 0.2%), vomiting (1.2% versus 0%), and diarrhea (0.7% versus 0.1%) for WEGOVY and placebo, respectively.

Table 3 shows adverse reactions reported in greater than or equal to 2% of WEGOVY 2.4 mg injection-treated adult patients and more frequently than in the placebo group from these trials.

Table 3. Adverse Reactions (≥2% and Greater Than Placebo) in WEGOVY 2.4 mg Injection-treated Adults with Obesity or Overweight for Weight Reduction

	Placebo N=1,261 %	WEGOVY Injection (2.4 mg Once Weekly) N=2,116 %
Nausea	16	44
Diarrhea	16	30
Vomiting	6	24
Constipation	11	24
Abdominal Pain ^a	10	20
Headache	10	14

	Placebo N=1,261 %	WEGOVY Injection (2.4 mg Once Weekly) N=2,116 %
Fatigue ^b	5	11
Dyspepsia	3	9
Dizziness	4	8
Abdominal Distension	5	7
Eructation	<1	7
Hypoglycemia in T2DM ^c	2	6
Flatulence	4	6
Gastroenteritis	4	6
Gastroesophageal Reflux Disease	3	5
Gastritis ^d	1	4
Gastroenteritis Viral	3	4
Hair Loss	1	3
Dysesthesia ^e	1	2

^a Includes abdominal pain, abdominal pain upper, abdominal pain lower, gastrointestinal pain, abdominal tenderness, abdominal discomfort and epigastric discomfort.

^b Includes fatigue and asthenia.

^c Defined as blood glucose <54 mg/dL with or without symptoms of hypoglycemia or severe hypoglycemia (requiring the assistance of another person) in patients with type 2 diabetes not on concomitant insulin (Study 3, WEGOVY N=403, Placebo N=402). See text below for further information regarding hypoglycemia in patients with and without type 2 diabetes. T2DM = type 2 diabetes mellitus.

^d Includes chronic gastritis, gastritis, gastritis erosive, and reflux gastritis.

^e Includes paresthesia, hyperesthesia, burning sensation, allodynia, dysesthesia, skin burning sensation, pain of skin, and sensitive skin.

CV Outcomes Trial

In a CV outcomes trial, 8,803 patients were exposed to WEGOVY injection for a median of 37.3 months and 8,801 patients were exposed to placebo for a median of 38.6 months [see *Clinical Studies (14.1)*]. Safety data collection was limited to serious adverse events (including death), adverse events leading to discontinuation, and adverse events of special interest. Sixteen percent (16%) of WEGOVY injection-treated patients and 8% of placebo-treated patients, respectively, discontinued study drug due to an adverse event. Additional information from this trial is included in subsequent sections below when relevant.

WEGOVY 7.2 mg Subcutaneous Injection Weekly Dosage

The safety of WEGOVY 7.2 mg injection was evaluated in two 72-week double-blinded randomized placebo-controlled 3-armed trials (Study 8 and Study 9), including 1,311 patients with obesity (BMI ≥ 30 kg/m²) exposed in the treatment arm with WEGOVY 7.2 mg injection, 304 patients exposed in the treatment arm with WEGOVY 2.4 mg injection, and 303 patients exposed to placebo [see *Clinical Studies (14.2)*]. After dosage escalation, 1,149 patients received at least one dose of WEGOVY 7.2 mg injection, and 578 patients received 7.2 mg for at least 1 year. Baseline characteristics in the WEGOVY 7.2 mg injection arm included a mean age of 49 years, 70% female, 85% White, 5% Asian, 8% Black or African American, and 2% reported as other or unknown; and 5% were Hispanic or Latino ethnicity. At baseline, mean BMI was 39.5 kg/m², 52% with hypertension, 38% with dyslipidemia, 40% with a BMI greater than 40 kg/m², and 14% with CV disease.

In these clinical trials, 5% of patients treated with 7.2 mg WEGOVY injection, 5% of patients treated with 2.4 mg of WEGOVY injection and 2% of patients treated with placebo permanently discontinued treatment as a result of adverse reactions. The most common adverse reactions leading to discontinuation were gastrointestinal disorders: 3%, 3%, and 0.3%, for WEGOVY 7.2 mg injection, WEGOVY 2.4 mg injection, and placebo, respectively.

Table 4 shows adverse reactions reported in greater than or equal to 2% of WEGOVY 7.2 mg injection and more frequently than 2.4 mg injection-treated and placebo-treated patients from these studies.

Table 4. Adverse Reactions (2% and Greater Than WEGOVY 2.4 mg and Placebo) in WEGOVY 7.2 mg Injection-treated Adults with Obesity for Weight Reduction

	Placebo N=303 %	WEGOVY Injection (2.4 mg Once Weekly) N=304 %	WEGOVY Injection (7.2 mg Once Weekly) N=1,311 %
Nausea	13	35	39
Vomiting	6	16	22
Dysesthesia ^a	0	6	22
Constipation	8	19	20
Abdominal pain ^b	7	9	12
Fatigue ^c	5	9	11
Headache	7	8	9
Dizziness ^d	1	5	6
Hair loss	1	3	6
Flatulence	2	2	4

^a Includes allodynia, burning sensation, dysesthesia, hyperesthesia, hyperpathia, pain of skin, paresthesia, sensitive skin, skin burning sensation, skin discomfort, and skin sensitization.

^b Includes abdominal pain, abdominal pain upper, abdominal pain lower, gastrointestinal pain, abdominal tenderness, abdominal discomfort and epigastric discomfort.

^c Includes fatigue and asthenia.

^d Includes dizziness and dizziness postural.

WEGOVY Tablet 25 mg Oral Daily Dosage

WEGOVY tablet was evaluated for safety in a randomized, double-blind, placebo-controlled trial that included 204 adult patients with obesity or overweight and at least one weight-related comorbidity, treated with WEGOVY 25 mg tablets for up to 64 weeks and a 7-week off drug follow-up period (Study 7) [see *Clinical Studies (14.2)*]. Patients with type 2 diabetes mellitus were excluded. Baseline characteristics included a mean age of 48 years, 76% were female, 93% were White, 0.5% were Asian, 6% were Black or African American, and 8% were Hispanic or Latino ethnicity. Mean baseline body weight was 106.4 kg and mean BMI was 37.5 kg/m². The baseline characteristics were 44% with hypertension, 31% with dyslipidemia, 27% with a BMI greater than 40 kg/m² and 1.5% with coronary artery disease.

In the clinical trial, 6.9% of patients treated with WEGOVY 25 mg tablets and 5.9% patients treated with placebo permanently discontinued treatment as a result of adverse reactions. The most common event type leading to discontinuation was gastrointestinal adverse reactions reported in 3.4% with WEGOVY tablets and 2% with placebo.

In the clinical trial with WEGOVY 25 mg tablets, the types and frequency of common adverse reactions were similar to those listed in **Table 3**.

Adverse Reactions in a Clinical Trial of Pediatric Patients Aged 12 Years and Older with Obesity Treated with WEGOVY 2.4 mg Injection for Weight Reduction

WEGOVY injection was evaluated in a 68-week, double-blind, randomized, parallel group, placebo-controlled, multi-center trial in 201 pediatric patients aged 12 years and older with obesity [see *Clinical Studies (14.3)*]. Baseline characteristics included a mean age of 15.4 years; 38% of patients were male; 79% were White, 8%

were Black or African American, 2% were Asian, and 11% were of other or unknown race; and 11% were of Hispanic or Latino ethnicity. The mean baseline body weight was 107.5 kg, and mean BMI was 37 kg/m².

Table 5 shows adverse reactions reported in greater than or equal to 3% of WEGOVY injection-treated pediatric patients and more frequently than in the placebo group from a trial in pediatric patients aged 12 years and older.

Table 5. Adverse Reactions (≥3% and Greater than Placebo) in WEGOVY 2.4 mg Injection-treated Pediatric Patients Aged 12 Years and Older with Obesity for Weight Reduction

	Placebo N=67 %	WEGOVY Injection (2.4 mg Once Weekly) N=133 %
Nausea	18	42
Vomiting	10	36
Diarrhea	19	22
Headache	16	17
Abdominal Pain	6	15
Nasopharyngitis	10	12
Dizziness	3	8
Gastroenteritis	3	7
Constipation	2	6
Gastroesophageal Reflux Disease	2	4
Sinusitis	2	4
Urinary tract infection	2	4
Ligament sprain	2	4
Anxiety	2	4
Hair Loss	0	4
Cholelithiasis	0	4
Eructation	0	4
Influenza	0	3
Rash	0	3
Urticaria	0	3

Adverse Reactions in Clinical Trials in Adults with MASH Treated with WEGOVY Injection

The safety of WEGOVY injection was evaluated in a randomized, double-blind, placebo-controlled trial (Study 9) that included 1,195 adult patients with MASH, including 800 patients who were exposed to WEGOVY for a median of 95.3 weeks and 395 patients who were exposed to placebo for a median of 83.1 weeks [see *Clinical Studies (14.4)*].

The most commonly reported adverse reactions were consistent with the other approved WEGOVY indications (see **Table 3**). There is limited information in patients with MASH and a BMI <25 kg/m². Additional information from the MASH trial is included in subsequent sections when notable. Unless indicated, the incidence of the adverse reactions in MASH patients was similar to other approved indications.

Other Adverse Reactions in Adults and/or Pediatric Patients Treated with WEGOVY Injection or WEGOVY Tablets

The safety of WEGOVY tablets and WEGOVY 7.2 mg injection have not been established in pediatric patients or patients with MASH.

Acute Gallbladder Disease

In WEGOVY clinical trials in adults for weight reduction, cholelithiasis was reported by 1.6% of WEGOVY injection-treated patients and 0.7% of placebo-treated patients and by 2.5% of WEGOVY tablet-treated patients and 1% of placebo tablet-treated patients. Cholecystitis was reported by 0.6% of WEGOVY injection-treated adult patients and 0.2% of placebo-treated patients. In a clinical trial in pediatric patients aged 12 years and older for weight reduction [see *Clinical Studies (14.3)*], cholelithiasis was reported by 3.8% of WEGOVY injection-treated patients and 0% placebo-treated patients. Cholecystitis was reported by 0.8% of WEGOVY injection-treated pediatric patients and 0% placebo-treated patients.

Hypoglycemia

Patients with Type 2 Diabetes

In a trial of adult patients with type 2 diabetes and BMI greater than or equal to 27 kg/m² for weight reduction, clinically significant hypoglycemia (defined as a plasma glucose less than 54 mg/dL) was reported in 6.2% of WEGOVY injection-treated patients versus 2.5% of placebo-treated patients. A higher rate of clinically significant hypoglycemic episodes was reported with WEGOVY injection (semaglutide 2.4 mg) versus semaglutide 1 mg injection (10.7 vs. 7.2 episodes per 100 patient years of exposure, respectively); the rate in the placebo-treated group was 3.2 episodes per 100 patient years of exposure. In addition, one episode of severe hypoglycemia requiring intravenous glucose was reported in a WEGOVY injection-treated patient versus none in placebo-treated patients. The risk of hypoglycemia was increased when WEGOVY was used with a sulfonylurea.

In a glycemic control trial evaluating a dose comparable to the 9 mg and 25 mg semaglutide tablet dose in patients with type 2 diabetes not on insulin, clinically significant hypoglycemia was reported in similar proportions of subjects in both treatment groups.

Patients without Type 2 Diabetes

Episodes of hypoglycemia have been reported with GLP-1 receptor agonists in adult patients without type 2 diabetes mellitus. In WEGOVY clinical trials in adult patients without type 2 diabetes mellitus for weight reduction, there was no systematic capturing or reporting of hypoglycemia.

In a CV outcomes trial in adult patients without type 2 diabetes, 3 episodes of serious hypoglycemia were reported in WEGOVY injection-treated patients versus 1 episode in placebo. Patients with a history of bariatric surgery (a risk factor for hypoglycemia) had more events of serious hypoglycemia while taking WEGOVY injection (2.3%, 2/87) than placebo (0%, 0/97).

Retinal Disorders in Patients with Type 2 Diabetes

In a trial of adult patients with type 2 diabetes and BMI greater than or equal to 27 kg/m² for weight reduction, retinal disorders were reported by 6.9% of patients treated with WEGOVY injection (semaglutide 2.4 mg), 6.2% of patients treated with semaglutide 1 mg, and 4.2% of patients treated with placebo. The majority of events were reported as diabetic retinopathy (4%, 2.7%, and 2.7%, respectively) and non-proliferative retinopathy (0.7%, 0%, and 0%, respectively).

In a glycemic control trial evaluating the 9 mg and 25 mg semaglutide tablet doses in patients with type 2 diabetes, a similar proportion of patients in each dose group reported diabetic retinopathy related adverse reactions during the trial; 1.3% and 1.9% of patients in the 9 mg and 25 mg semaglutide group, respectively, reported moderate-severe non-proliferative diabetic retinopathy events, and 0% and 0.4% reported proliferative retinopathy events, respectively.

In a 2-year trial with semaglutide 0.5 mg and 1 mg once-weekly injection in adult patients with type 2 diabetes and high cardiovascular risk, diabetic retinopathy complications (which was a 4-component adjudicated endpoint) occurred in patients treated with semaglutide injection (3%) compared to placebo (1.8%). The absolute risk increase for diabetic retinopathy complications was larger among patients with a history of

diabetic retinopathy at baseline (semaglutide injection 8.2%, placebo 5.2%) than among patients without a known history of diabetic retinopathy (semaglutide injection 0.7%, placebo 0.4%).

Gastrointestinal Adverse Reactions

In clinical trials in adults for weight reduction, 73% of WEGOVY injection-treated patients and 47% of patients receiving placebo reported gastrointestinal adverse reactions, including severe reactions that were reported more frequently among patients receiving WEGOVY injection (4.1%) than placebo (0.9%). The most frequently reported reactions were nausea (44% vs. 16%), vomiting (25% vs. 6%), and diarrhea (30% vs. 16%). Other reactions that occurred at a higher incidence among WEGOVY injection-treated adult patients included dyspepsia, abdominal pain, abdominal distension, eructation, flatulence, gastroesophageal reflux disease, gastritis, hemorrhoids, and hiccups. These reactions were most frequently reported during dosage escalation.

Severe gastrointestinal adverse reactions were reported in 2% of WEGOVY tablet-treated and 0% of placebo-treated patients, respectively.

In the pediatric clinical trial for weight reduction, 62% of WEGOVY injection-treated patients and 42% of placebo-treated patients reported gastrointestinal adverse reactions. The most frequently reported reactions were nausea (42% vs. 18%), vomiting (36% vs. 10%), and diarrhea (22% vs. 19%). Other gastrointestinal-related reactions that occurred at a higher incidence than placebo among WEGOVY injection-treated pediatric patients included abdominal pain, constipation, eructation, gastroesophageal reflux disease, dyspepsia, and flatulence.

Permanent discontinuation of treatment as a result of a gastrointestinal adverse reaction occurred in 4.3% of WEGOVY injection-treated adult patients versus 0.7% of placebo-treated patients. In a pediatric clinical trial for weight reduction, 2.3% of patients treated with WEGOVY injection versus 1.5% of patients who received placebo discontinued treatment as a result of gastrointestinal adverse reactions.

Dysesthesia

Dysesthesia, and related events of altered skin sensations including paresthesia, pain of skin, sensitive skin, and burning skin sensation, occurred in clinical trials with WEGOVY injection and tablet. The incidence of dysesthesia with WEGOVY increased with increasing dosage and drug levels in the blood.

In clinical trials evaluating patients with and without type 2 diabetes mellitus, WEGOVY 7.2 mg injection dysesthesia was reported at a higher rate in the WEGOVY 7.2 mg injection group (22%), compared to WEGOVY 2.4 mg injection (6%) and placebo (0.3%). Among 288 patients who experienced dysesthesia with WEGOVY 7.2 mg injection, 2% permanently discontinued treatment, 8% had temporary interruption, and 23% had dose reduction; most subjects with these actions taken to WEGOVY 7.2 mg injection (permanent discontinuation, temporary interruption, or dose reduction) recovered from the event. When an action was taken with WEGOVY, events resolved faster than the events where no action was taken with WEGOVY. Among patients who experienced dysesthesia with WEGOVY 7.2 mg injection, 18% did not report recovering during the trial duration; in most of the patients who did not recover, the WEGOVY dosage was unchanged and not discontinued. Of the patients who recovered after action taken with WEGOVY, 38 patients were re-escalated to 7.2 mg. Of these 38 patients, 17 (45%) subsequently reported recurrence of dysesthesia.

In a clinical trial with WEGOVY 25 mg tablets, 5% of WEGOVY-treated patients and no placebo-treated patients reported dysesthesia adverse reactions.

Other Adverse Reactions in Adults and/or Pediatric Patients

The below adverse reactions were reported in WEGOVY injection clinical trials and are applicable to both WEGOVY injection and WEGOVY tablets. The safety of WEGOVY tablets have not been established in pediatric patients or patients with MASH.

Acute Pancreatitis

In WEGOVY clinical trials in adults for weight reduction, acute pancreatitis was confirmed by adjudication in 4 WEGOVY-treated patients (0.2 cases per 100 patient years) and 1 in placebo-treated patients (less than 0.1 cases per 100 patient years). One additional case of acute pancreatitis was confirmed in a patient treated with WEGOVY in another clinical trial.

Acute Kidney Injury

Acute kidney injury occurred in clinical trials for weight reduction in 7 adult patients (0.4 cases per 100 patient years) receiving WEGOVY versus 4 patients (0.2 cases per 100 patient years of exposure) receiving placebo. Some of these adverse reactions occurred in association with gastrointestinal adverse reactions or dehydration. In addition, 2 patients treated with WEGOVY had acute kidney injury with dehydration in other clinical trials. The risk of renal adverse reactions with WEGOVY was increased in adult patients with a history of renal impairment (trials included 65 patients with a history of moderate or severe renal impairment at baseline), and occurred more frequently during dose titration.

Increase in Heart Rate

Mean increases in resting heart rate of 1 to 4 beats per minute (bpm) were observed with routine clinical monitoring in WEGOVY-treated adult patients compared to placebo in clinical trials for weight reduction. In weight reduction trials in which adult patients were randomized prior to dose-escalation, more patients treated with WEGOVY, compared with placebo, had maximum changes from baseline at any visit of 10 to 19 bpm (41% versus 34%, respectively) and 20 bpm or more (26% versus 16%, respectively). In a clinical trial for weight reduction in pediatric patients aged 12 years and older with normal baseline heart rate, more patients treated with WEGOVY compared to placebo had maximum changes in heart rate of 20 bpm or more (54% versus 39%).

Hypotension and Syncope

Adverse reactions related to hypotension (hypotension, orthostatic hypotension, and decreased blood pressure) were reported in 1.3% of WEGOVY-treated adult patients versus 0.4% of placebo-treated patients and syncope was reported in 0.8% of WEGOVY-treated patients versus 0.2% of placebo-treated patients in clinical trials for weight reduction. Some reactions were related to gastrointestinal adverse reactions and volume loss associated with WEGOVY. Hypotension and orthostatic hypotension were more frequently seen in patients on concomitant antihypertensive therapy. In a clinical trial in pediatric patients aged 12 years and older for weight reduction, hypotension was reported in 2.3% of WEGOVY-treated patients versus 0% in placebo-treated patients.

Appendicitis

Appendicitis (including perforated appendicitis) occurred in 10 (0.5%) WEGOVY-treated adult patients and 2 (0.2%) patients receiving placebo in clinical trials for weight reduction.

Injection Site Reactions

In clinical trials in adults for weight reduction, 1.4% of WEGOVY-treated patients and 1% of patients receiving placebo experienced injection site reactions (including injection site pruritus, erythema, inflammation, induration, and irritation).

Hypersensitivity Reactions

Serious hypersensitivity reactions (e.g., anaphylaxis, angioedema) have been reported with WEGOVY.

In a pediatric clinical trial for weight reduction, rash was reported in 3% of WEGOVY-treated patients and 0% of placebo-treated patients, and urticaria was reported in 3% of WEGOVY-treated patients and 0% of placebo-treated patients.

In adult clinical trials for weight reduction, allergic reactions occurred in 16% (8/50) of WEGOVY-treated patients with anti-semaglutide antibodies and in 7% (114/1659) of WEGOVY-treated patients who did not develop anti-semaglutide antibodies [see *Clinical Pharmacology* (12.6)].

Fractures

In the CV outcomes trial in adults, more fractures of the hip and pelvis were reported on WEGOVY than on placebo in female patients: 1% (24/2,448) vs. 0.2% (5/2,424), and in patients ages 75 years and older: 2.4% (17/703) vs. 0.6% (4/663), respectively.

In a clinical trial in adults with MASH, fractures occurred in 4.4% of WEGOVY-treated patients (2.6 cases per 100 patient years) compared to 3.3% of placebo-treated patients (2 cases per 100 patient years). Fractures were reported in both males and females with a median age of 61 years (range, 44 to 75).

Urolithiasis

In a CV outcomes trial, 1.2% of WEGOVY-treated patients and 0.8% of patients receiving placebo reported urolithiasis, including serious reactions that were reported more frequently among patients receiving WEGOVY (0.6%) than placebo (0.4%).

Dysgeusia

In clinical trials in adults for weight reduction, 1.7% of WEGOVY-treated patients and 0.5% of placebo-treated patients reported dysgeusia.

Hair Loss

Hair loss adverse reactions in WEGOVY injection-treated patients were associated with weight reduction. In a pool of studies 2, 3, and 4, hair loss was reported in 3.3% of patients treated with WEGOVY 2.4 mg (4% female, 0.9% male) and in 1% of patients treated with placebo (2% female, 0 male). In a pediatric trial, hair loss was reported in 4% of patients treated with 2.4 mg of WEGOVY and no placebo-treated patients.

In clinical trials with WEGOVY 7.2 mg injection, hair loss was reported in 5.8% of patients treated with WEGOVY 7.2 mg (8.4% female, 0.2% male), 3.3% of patients treated with WEGOVY 2.4 mg (5.4% female, 0 male), and 1.0% of patients on placebo (1.5% female, 0 male). In the WEGOVY 7.2 mg group, 1 event led to permanent treatment discontinuation, 1 event led to temporary interruption, and 5 events led to dose reduction, versus none of these actions in the WEGOVY 2.4 mg or placebo groups.

Laboratory Abnormalities in Adults and/or Pediatric Patients Treated with WEGOVY Injection

The below laboratory abnormalities are applicable for both WEGOVY injection and WEGOVY tablets and include descriptions of WEGOVY injection clinical trial data, where relevant. The safety and effectiveness of WEGOVY tablets have not been established in pediatric patients or patients with MASH.

Amylase and Lipase

Adult and pediatric patients treated with WEGOVY had a mean increase from baseline in amylase of 15% to 16% and lipase of 39% in clinical trials for weight reduction. These changes were not observed in the placebo group.

In a clinical trial in adults with MASH, increases in lipase greater than 3 times the upper limit of normal (ULN) occurred in 4.7% (35/750) of WEGOVY-treated patients compared with 1.3% (5/374) of placebo-treated patients. The clinical significance of elevations in lipase or amylase with WEGOVY is unknown in the absence of other signs and symptoms of pancreatitis.

Liver Tests

In a pediatric clinical trial for weight reduction, increases in alanine aminotransferase (ALT) greater than or equal to 5 times the ULN were observed in 4 (3%) WEGOVY-treated patients compared with 0% of placebo-treated patients. In some patients, increases in ALT and AST were associated with other confounding factors (such as gallstones). In the CV outcomes trial in adults, increases in total bilirubin greater than or equal to 3 times the ULN were observed in 0.3% (30/8,585) of WEGOVY-treated patients versus 0.2% (14/8,579) of placebo-treated patients.

6.2 Postmarketing Experience

The following adverse reactions have been reported during post-approval use of semaglutide, the active ingredient of WEGOVY. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Gastrointestinal Disorders: acute pancreatitis and necrotizing pancreatitis, sometimes resulting in death; ileus, intestinal obstruction, severe constipation including fecal impaction

Hypersensitivity: anaphylaxis, angioedema, rash, urticaria

Pulmonary: Pulmonary aspiration has occurred in patients receiving GLP-1 receptor agonists undergoing elective surgeries or procedures requiring general anesthesia or deep sedation

Renal and Urinary Disorders: acute kidney injury

7 DRUG INTERACTIONS

7.1 Concomitant Use with Insulin or an Insulin Secretagogue (e.g., Sulfonylurea)

WEGOVY lowers blood glucose and can cause hypoglycemia. The risk of hypoglycemia is increased when WEGOVY is used concomitantly with insulin or insulin secretagogues (e.g., sulfonylureas). The addition of WEGOVY in patients treated with insulin has not been evaluated.

When initiating WEGOVY, consider reducing the dose of concomitantly administered insulin secretagogue or insulin to reduce the risk of hypoglycemia [*see Warnings and Precautions (5.4), Adverse Reactions (6.1)*].

7.2 Oral Medications

WEGOVY causes a delay of gastric emptying and thereby has the potential to impact the absorption of concomitantly administered oral medications. In clinical pharmacology trials with semaglutide 1 mg once weekly injection, semaglutide did not affect the absorption of orally administered medications [*see Clinical Pharmacology (12.3)*]. In a drug interaction study with the semaglutide tablet, levothyroxine exposure was increased 33% (90% CI: 1.25-1.42). Monitor the effects of oral medications concomitantly administered with WEGOVY. Consider increased clinical or laboratory monitoring for medications that have a narrow therapeutic index or that require clinical monitoring.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to WEGOVY during pregnancy. Pregnant women exposed to WEGOVY and healthcare providers are encouraged to contact Novo Nordisk at 1-877-390-2760 or www.wegovypregnancyregistry.com.

Risk Summary

Based on animal reproduction studies, there may be potential risks to the fetus from exposure to semaglutide during pregnancy. Available pharmacovigilance data and data from clinical trials with WEGOVY use in pregnant patients are insufficient to establish a drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes.

Weight loss offers no benefit to a pregnant patient and may cause fetal harm. When a pregnancy is recognized, advise the pregnant patient of the risk to a fetus. Discontinue WEGOVY in pregnant patients who are using it for weight reduction (see *Clinical Considerations*).

There may be risks to the mother and fetus related to underlying MASH with advanced liver fibrosis (see *Clinical Considerations*). Whether WEGOVY treatment during pregnancy reduces these risks is unknown. WEGOVY for the treatment of MASH with advanced liver fibrosis should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

In pregnant rats administered semaglutide during organogenesis, embryofetal mortality, structural abnormalities and alterations to growth occurred at clinically relevant maternal exposures at the maximum recommended human dose (MRHD) of WEGOVY subcutaneous injection 7.2 mg/week, based on AUC. In pregnant rabbits and cynomolgus monkeys administered semaglutide during organogenesis, early pregnancy losses and structural abnormalities were observed in rabbits and monkeys at clinically relevant exposures. These findings coincided with a marked maternal body weight loss in both animal species (see *Data*).

The background risk of major birth defects and miscarriage for the indicated populations are unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations

Disease-Associated Maternal and/or Embryo/fetal Risk: Appropriate weight gain based on pre-pregnancy weight is currently recommended for all pregnant patients, including those who already have overweight or obesity, because of the obligatory weight gain that occurs in maternal tissues during pregnancy.

There may be risks to the mother and fetus related to MASH with advanced liver fibrosis, such as increased risks of gestational diabetes, hypertensive complications, preterm birth, and postpartum hemorrhage. The effect of WEGOVY on these risks is unknown.

Data

Animal Data: In a combined fertility and embryofetal development study in male and female rats, subcutaneous semaglutide doses of 0.01, 0.03, and 0.09 mg/kg/day (up to 0.1-fold the MRHD, based on AUC) were administered to male rats for 4 weeks prior to and throughout mating and to female rats for 2 weeks prior to mating, and throughout organogenesis to Gestation Day 17. In parental rats, pharmacologically mediated reductions in body weight gain and food consumption were observed at all dose levels. In the offspring, reduced growth and fetuses with visceral (heart blood vessels) and skeletal (cranial bones, vertebra, ribs) abnormalities were observed at clinically relevant exposures at the MRHD.

In an embryofetal development study in pregnant rabbits, subcutaneous semaglutide doses of 0.001, 0.0025, or 0.0075 mg/kg/day (up to 0.3-fold the MRHD) were administered throughout organogenesis from Gestation Day 6 to 19. Pharmacologically mediated reductions in maternal body weight gain and food consumption were observed at all dose levels. Early pregnancy losses and increased incidences of minor visceral (kidney, liver) and skeletal (sternbra) fetal abnormalities were observed at greater than or equal to 0.0025 mg/kg/day, at clinically relevant exposures at the MRHD.

In an embryofetal development study in pregnant cynomolgus monkeys, subcutaneous semaglutide doses of 0.015, 0.075, and 0.15 mg/kg twice weekly (up to 2-fold the MRHD) were administered throughout organogenesis, from Gestation Day 16 to 50. Pharmacologically mediated, marked initial maternal body weight loss and reductions in body weight gain and food consumption coincided with the occurrence of sporadic abnormalities (vertebra, sternbra, ribs) at greater than or equal to 0.075 mg/kg twice weekly, at clinically relevant exposures at the MRHD.

In a pre- and postnatal development study in pregnant cynomolgus monkeys, subcutaneous semaglutide doses of 0.015, 0.075, and 0.15 mg/kg twice weekly (up to 0.8-fold the MRHD) were administered from Gestation Day 16 to 140. Pharmacologically mediated marked initial maternal body weight loss and reductions in body weight gain and food consumption coincided with an increase in early pregnancy losses and led to delivery of slightly smaller offspring at greater than or equal to 0.075 mg/kg twice weekly, at clinically relevant exposures at the MRHD.

Salcaprozate sodium (SNAC), an absorption enhancer in WEGOVY tablets, crosses the placenta and reaches fetal tissues in rats. In a pre- and postnatal development study in pregnant Sprague Dawley rats, SNAC was administered orally at 1,000 mg/kg/day (exposure levels were not measured) on Gestation Day 7 through lactation Day 20. An increase in gestation length, an increase in the number of stillbirths and a decrease in pup viability were observed.

8.2 Lactation

Risk Summary

WEGOVY Oral Tablets

Data from a clinical lactation study with semaglutide oral tablet formulation reported semaglutide concentrations below the lower limit of quantification in human milk. However, SNAC and/or its metabolites are present in human milk. Since the activity of enzymes involved in SNAC clearance may be lower in infants compared to adults, higher SNAC plasma levels may occur in neonates and infants. Because of the unknown potential for serious adverse reactions in the breastfed infant due to the possible accumulation of SNAC, and because there are alternative formulations of semaglutide that do not contain SNAC that can be used during lactation, advise patients that breastfeeding is not recommended during treatment with WEGOVY tablets.

WEGOVY Subcutaneous Injection

There are no data on the presence of subcutaneously administered semaglutide or its metabolites in human milk, the effects on the breastfed infant, or the effects on milk production. WEGOVY subcutaneous injection does not contain the SNAC metabolites.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for WEGOVY and any potential adverse effects on the breastfed infant from WEGOVY or from the underlying maternal condition.

8.3 Females and Males of Reproductive Potential

Because of the potential for fetal harm, discontinue WEGOVY in patients at least 2 months before they plan to become pregnant to account for the long half-life of semaglutide [*see Use in Specific Populations (8.1)*].

8.4 Pediatric Use

The safety and effectiveness of WEGOVY injection in combination with a reduced-calorie diet and increased physical activity to reduce excess body weight and maintain weight reduction long term in pediatric patients aged 12 years and older with obesity have been established. Use of WEGOVY injection for this indication is supported by a 68-week, double-blind, placebo-controlled clinical trial in 201 pediatric patients aged 12 years and older with a BMI corresponding to ≥ 95 th percentile for age and sex [*see Clinical Studies (14.3)*] and from trials in adult patients with obesity [*see Clinical Studies (14.2)*]. Use of the 1.7 mg once weekly maintenance dosage of WEGOVY injection in pediatric patients is also supported by additional exposure-efficacy and safety analyses in pooled adult and pediatric patients.

Adverse reactions with WEGOVY injection treatment in pediatric patients aged 12 years and older were generally similar to those reported in adults. Pediatric patients aged 12 years and older treated with WEGOVY injection had greater incidences of cholelithiasis, cholecystitis, hypotension, rash, and urticaria compared to adults treated with WEGOVY [*see Adverse Reactions (6.1)*].

Although there was an increased frequency of hypoglycemia in adults with type 2 diabetes with obesity or overweight treated with WEGOVY injection, there are insufficient data to determine if the risk of hypoglycemia is higher in WEGOVY-treated pediatric patients with type 2 diabetes with obesity. Inform pediatric patients of the risk of hypoglycemia and educate them on the signs and symptoms of hypoglycemia. In pediatric patients aged 12 years and older with type 2 diabetes, monitor blood glucose prior to starting WEGOVY injection and during treatment. When initiating WEGOVY injection in pediatric patients aged 12 years and older with type 2 diabetes, consider reducing the dosage of concomitantly administered insulin secretagogue (such as sulfonylureas) or insulin to reduce the risk of hypoglycemia [see *Warnings and Precautions* (5.4)].

The safety and effectiveness of WEGOVY injection have not been established in pediatric patients:

- to reduce the risk of major adverse CV events. Clinical trials for this indication are highly impracticable because of the low prevalence of the condition in pediatric patients.
- to reduce excess body weight and maintain weight reduction long term with the 7.2 mg once weekly dosage.
- to reduce excess body weight and maintain weight reduction long term in those less than 12 years of age.
- for the treatment of noncirrhotic MASH.

The safety and effectiveness of WEGOVY tablets have not been established in pediatric patients.

8.5 Geriatric Use

In the WEGOVY injection clinical trials for weight reduction and long-term maintenance, 233 (9%) WEGOVY injection-treated patients were aged 65 to less than 75 years and 23 (1%) WEGOVY injection-treated patients were aged 75 years and older [see *Clinical Studies* (14.2)]. In a WEGOVY 25 mg tablets clinical trial for weight reduction and long-term maintenance, 16 (8%) WEGOVY tablets-treated patients were aged 65 to less than 75 years and 5 (2%) WEGOVY tablet-treated patients were aged 75 years and older [see *Clinical Studies* (14.2)].

In a CV outcomes trial, 2,656 (30%) WEGOVY injection-treated patients were aged 65 to 75 years and 703 (8%) WEGOVY injection-treated patients were aged 75 years and older [see *Clinical Studies* (14.1)]. No overall difference in the effectiveness was observed between patients aged 65 years and older and younger adult patients. In the CV outcomes trial, patients aged 75 years and older reported more hip and pelvis fractures in the WEGOVY injection-treated patients than placebo-treated patients. Patients aged 75 years and older (WEGOVY injection-treated and placebo-treated) reported more serious adverse reactions overall compared to younger adult patients [see *Adverse Reactions* (6.1)].

In the clinical trial in patients with MASH, of the 534 patients randomized to WEGOVY injection, 138 (26%) were aged 65 years and older and 13 (2%) were aged 75 years and older [see *Clinical Studies* (14.4)]. No overall differences in safety or effectiveness of WEGOVY injection have been observed between patients 65 years of age and older and younger adult patients with MASH.

8.6 Type 2 Diabetes Mellitus

WEGOVY tablets have not been studied for weight reduction in adults with type 2 diabetes and obesity or overweight [see *Clinical Studies* (14.2)].

Administration of WEGOVY injection resulted in less weight reduction in patients with type 2 diabetes and obesity or overweight compared to those without type 2 diabetes and obesity or overweight [see *Clinical Studies* (14.2)].

In patients without type 2 diabetes, the average semaglutide blood concentrations following administration of WEGOVY 25 mg tablets once daily or WEGOVY 2.4 mg injection once weekly were similar. In patients with

type 2 diabetes, the average semaglutide blood concentrations following administration of WEGOVY 25 mg tablets once daily were lower than the average semaglutide blood concentrations following use of WEGOVY 2.4 mg injection once weekly [see *Clinical Pharmacology* (12.3)]. The lower semaglutide blood concentrations after administration of WEGOVY tablets in patients with type 2 diabetes may be associated with reductions in absolute bioavailability.

Given the differences in average semaglutide blood concentrations after administration of WEGOVY tablets and WEGOVY injection, and the higher variability in semaglutide blood concentrations after administration of WEGOVY tablets in all patient populations, some patients with type 2 diabetes taking WEGOVY tablets may experience subtherapeutic semaglutide blood concentrations. In patients with type 2 diabetes with an inadequate response to WEGOVY tablets, consider alternative therapies, including switching to WEGOVY injection [see *Dosage and Administration* (2.5)].

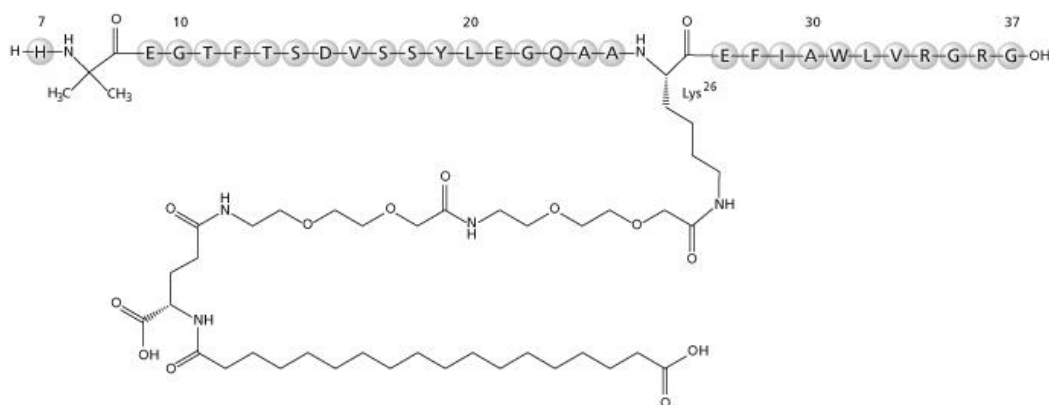
10 OVERDOSAGE

Overdoses have been reported with other GLP-1 receptor agonists. Effects have included severe nausea, severe vomiting, and severe hypoglycemia. In the event of overdose, appropriate supportive treatment should be initiated according to the patient's clinical signs and symptoms. In the event of an overdose of WEGOVY, consider contacting the Poison Help line (1-800-222-1222) or a medical toxicologist for additional overdose management recommendations. A prolonged period of observation and treatment for these symptoms may be necessary, taking into account the long half-life of WEGOVY of approximately 1 week.

11 DESCRIPTION

WEGOVY contains semaglutide, a human GLP-1 receptor agonist (or GLP-1 analog). The peptide backbone is produced by yeast fermentation. The main protraction mechanism of semaglutide is albumin binding, facilitated by modification of position 26 lysine with a hydrophilic spacer and a C18 fatty di-acid. Furthermore, semaglutide is modified in position 8 to provide stabilization against degradation by the enzyme dipeptidyl-peptidase 4 (DPP-4). A minor modification was made in position 34 to ensure the attachment of only one fatty di-acid. The molecular formula is $C_{187}H_{291}N_{45}O_{59}$ and the molecular weight is 4113.58 g/mol.

Figure 1. Structural Formula of Semaglutide



WEGOVY injection is a sterile, aqueous, clear, colorless solution. Each 0.5 mL single-dose pen contains a solution of WEGOVY containing 0.25 mg, 0.5 mg or 1 mg of semaglutide; and each 0.75 mL single-dose pen contains a solution of WEGOVY containing 1.7, 2.4 mg or 7.2 mg of semaglutide. Each 0.5 mL single-dose prefilled syringe contains a solution of WEGOVY containing 0.25 mg, 0.5 mg or 1 mg of semaglutide; and each 0.75 mL single-dose prefilled syringe contains a solution of WEGOVY containing 1.7, 2.4 mg of semaglutide. Each 1 mL of WEGOVY contains the following inactive ingredients: disodium phosphate dihydrate, 1.42 mg; sodium chloride, 8.25 mg; and water for injection. WEGOVY has a pH of approximately 7.4. Hydrochloric acid or sodium hydroxide may be added to adjust pH.

WEGOVY tablets include semaglutide as a white to almost white hygroscopic powder. Each tablet of WEGOVY contains 1.5 mg, 4 mg, 9 mg or 25 mg of semaglutide and the following inactive ingredients: magnesium stearate and salcaprozate sodium (SNAC).

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Semaglutide is a GLP-1 analogue with 94% sequence homology to human GLP-1. Semaglutide acts as a GLP-1 receptor agonist that selectively binds to and activates the GLP-1 receptor, the target for native GLP-1.

GLP-1 is a physiological regulator of appetite and caloric intake, and the GLP-1 receptor is present in several areas of the brain involved in appetite regulation. Animal studies show that semaglutide distributed to and activated neurons in brain regions involved in regulation of food intake.

The exact mechanism of semaglutide in CV risk reduction in adults has not been established.

For treatment of MASH in humans, the precise mechanism of action of semaglutide is not fully understood and may involve multiple pathways mediated by weight loss and other factors. In a mouse model of diet-induced MASH, treatment with semaglutide resulted in histological improvements in steatosis, inflammation, and fibrosis in liver compared to baseline, which was associated with body weight loss, intermittent periods of reduced food intake, and improvements in relevant biomarkers. The relationship between the pathophysiology of MASH in animal models and humans has not been fully established.

12.2 Pharmacodynamics

Semaglutide lowers body weight with greater fat mass loss than lean mass loss. Semaglutide decreases caloric intake. The effects are likely mediated by affecting appetite.

Semaglutide stimulates insulin secretion and reduces glucagon secretion in a glucose-dependent manner. These effects can lead to a reduction of blood glucose.

Gastric Emptying

Semaglutide delays gastric emptying.

Cardiac Electrophysiology (QTc)

The effect of semaglutide on cardiac repolarization was tested in a thorough QTc trial. Semaglutide did not prolong QTc intervals at subcutaneous doses up to 1.5 mg at steady state.

Noninvasive Liver Disease Markers

Semaglutide decreases liver fat content measured by Magnetic Resonance Imaging Proton Density Fat Fraction (MRI-PDFF), liver stiffness assessed by transient elastography (TE), Enhanced Liver Fibrosis (ELF) score, and the levels of the pro-peptide of type III collagen biomarker (Pro-C3). The clinical relevance of these changes is yet to be confirmed.

12.3 Pharmacokinetics

Absorption

WEGOVY Injection

Absolute bioavailability of semaglutide is 89% following subcutaneous administration. Maximum concentration of semaglutide is reached 1 to 3 days post dose.

Similar exposure was achieved with subcutaneous administration of semaglutide in the abdomen, thigh, or upper arm.

The average semaglutide steady state concentration following subcutaneous administration of WEGOVY 2.4 mg once weekly was approximately 75 nmol/L in patients with obesity or overweight (BMI greater than or equal to 27 kg/m²). The average semaglutide steady state concentration following subcutaneous administration of WEGOVY 7.2 mg once weekly injection was approximately 230 nmol/L in patients with obesity (BMI greater than or equal to 30 kg/m²). The steady state exposure concentrations increased proportionally with doses up to 7.2 mg once weekly.

WEGOVY Tablets

WEGOVY tablets are co-formulated with SNAC which facilitates the absorption of semaglutide after oral WEGOVY tablet administration. The absorption of semaglutide predominantly occurs in the stomach.

Absolute bioavailability of semaglutide is estimated to be approximately 1% to 2% following oral tablet administration. Maximum concentration of semaglutide is reached 1 hour post dose.

The average semaglutide steady state concentration following 25 mg tablet oral administration was approximately 77 nmol/L in patients with obesity or overweight (BMI greater than or equal to 27 kg/m²). The steady-state concentrations increased approximately proportionally with doses up to 25 mg once daily.

In patients with overweight or obesity without type 2 diabetes, semaglutide concentrations following once-daily administration of oral WEGOVY 25 mg tablet are predicted to be comparable to WEGOVY 2.4 mg once-weekly injection, with higher variability in semaglutide concentrations compared to subcutaneous administration (90% of patients had average concentrations between 27 and 186 nmol/L with WEGOVY 25 mg tablet versus 51 and 110 nmol/L with WEGOVY 2.4 mg once-weekly injection).

Effect of Volume and Timing of Water Consumption: Single doses of oral semaglutide tablet were administered with 50 mL or 240 mL of water after an 8-hour overnight fast and a continued fast of 4 hours post-dose in healthy subjects. Semaglutide absorption [i.e., area under the curve (AUC) and peak concentrations (C_{max})] was higher following dosing with 50 mL water compared to that of 240 mL water.

For 10 days, healthy subjects received once daily doses of oral semaglutide with 50 mL or 120 mL of water under fasting conditions with post-dose fasting period of 15, 30, 60, or 120 minutes. In this study, semaglutide absorption (i.e., AUC and C_{max}) was higher after a longer post-dose fasting period. There were no clinically significant differences in semaglutide absorption with administration of 50 mL or 120 mL of water.

Distribution

The mean volume of distribution of semaglutide following subcutaneous administration in patients with obesity or overweight is approximately 12.5 L. Semaglutide is extensively bound to plasma albumin (greater than 99%) which results in decreased renal clearance and protection from degradation.

Elimination

The apparent clearance of semaglutide in patients with overweight or obesity is approximately 0.05 L/h. With an elimination half-life of approximately 1 week, semaglutide will be present in the circulation for about 5 to 7 weeks after the last injectable dose of 2.4 mg or 7.2 mg or oral dose of 25 mg.

Metabolism: The primary route of elimination for semaglutide is metabolism following proteolytic cleavage of the peptide backbone and sequential beta-oxidation of the fatty acid sidechain.

Excretion: The primary excretion routes of semaglutide-related material are via the urine and feces. Approximately 3% of the dose is excreted in the urine as intact semaglutide.

Specific Populations

Age, Sex, Race, Ethnicity, Body Weight, and Other Intrinsic Factors: No clinically significant differences in semaglutide pharmacokinetics were observed based on age (<65 years, 65 to 74, ≥75 years old), sex, race (White, Asian, or Black or African American), ethnicity, body weight, upper GI disease (i.e. chronic gastritis and/or gastroesophageal reflux disease), renal impairment [estimated glomerular filtration rate (eGFR) ≥30 to <90 mL/minute], or mild, moderate, and severe hepatic impairment (Child-Pugh Class A-C) or fibrosis stage (F2 or F3 in patients with MASH).

There is no difference observed in the exposure of semaglutide following subcutaneous administration of WEGOVY between patients with MASH and patients with overweight or obesity.

Patients with Type 2 Diabetes: The average semaglutide steady state concentration following subcutaneous administration of WEGOVY 2.4 mg once weekly was approximately 68 nmol/L in patients with type 2 diabetes and obesity or overweight (BMI greater than or equal to 27 kg/m²). The average semaglutide steady state concentration following 25 mg oral administration was approximately 44 nmol/L in patients with type 2 diabetes and obesity or overweight (BMI greater than or equal to 25 kg/m²) with higher variability in semaglutide concentrations compared to subcutaneous administration (90% of patients had average concentrations between 11 nmol/L and 134 nmol/L with WEGOVY 25 mg tablet versus 47 nmol/L and 99 nmol/L with WEGOVY 2.4 mg once-weekly injection) [see *Use in Specific Populations* (8.6)].

Drug Interactions Studies

Subcutaneous Injection

The delay of gastric emptying with semaglutide may influence the absorption of concomitantly administered oral medications [see *Drug Interactions* (7.2)].

Oral Tablets

Clinical Studies and Model-Informed Approaches: The delay of gastric emptying with semaglutide may influence the absorption of concomitantly administered oral drugs [see *Drug Interactions* (7.2)]. Trials were conducted to study the potential effect of semaglutide on the absorption of oral drugs taken with semaglutide tablets administered orally at steady-state exposure.

- *Levothyroxine:* Total thyroxine (i.e., adjusted for endogenous levels) AUC of was increased by 33% following administration of a single dose of levothyroxine 600 mcg concomitantly administered with oral semaglutide. Maximum exposure (C_{max}) was unchanged.
- *Other Drugs:* No clinically significant differences in semaglutide pharmacokinetics were observed when used concomitantly with omeprazole. No clinically significant differences in the pharmacokinetics of the following drugs were observed when used concomitantly with semaglutide: lisinopril, S-warfarin, R-warfarin, metformin, digoxin, ethinyl estradiol, levonorgestrel, furosemide or rosuvastatin.

In Vitro Studies: Semaglutide has very low potential to inhibit or induce CYP enzymes, and to inhibit drug transporters.

12.6 Immunogenicity

The observed incidence of anti-drug antibodies is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of anti-drug antibodies in the studies described below with the incidence of anti-drug antibodies in other studies, including those of semaglutide or of other semaglutide products.

During the 68-week treatment periods in Studies 2 and 3 in adults [see *Clinical Studies* (14.2)], 50/1709 (3%) of patients treated with WEGOVY 2.4 mg injection developed anti-semaglutide antibodies (referred to as anti-drug-antibodies or ADA). A total of 28 (56% of the 50 patients treated with WEGOVY 2.4 mg injection who tested ADA positive) patients developed antibodies that cross-reacted with native GLP-1 in Studies 2 and 3.

Using a new assay, 202/1311 (15.4%) of patients treated with WEGOVY 7.2 mg injection and 34/304 (11.2%) of patients treated with WEGOVY 2.4 mg injection developed anti-semaglutide antibodies during 72-week treatment periods in Studies 8 and 9. A total of 36 (17.8% of 202 patients treated with WEGOVY 7.2 mg injection who tested ADA positive) and 3 (8.8% of 34 patients treated with WEGOVY 2.4 mg injection who tested ADA positive) patients developed antibodies that cross reacted with native GLP-1 in Studies 8 and 9. The clinical consequences of antibodies that cross react with native GLP-1 are unknown.

In adults with MASH treated with WEGOVY injection for 72 weeks in Study 11 [*see Clinical Studies (14.4)*], 3/763 (0.4%) of patients developed ADA which were also cross-reactive to native GLP-1. No identified clinically significant effect of ADA on pharmacokinetics for WEGOVY injection was observed.

There is insufficient evidence to characterize the effects of ADA on pharmacodynamics, safety, or effectiveness of WEGOVY.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

In a 2-year carcinogenicity study in CD-1 mice, subcutaneous semaglutide doses of 0.3, 1 and 3 mg/kg/day (up to 7-fold the MRHD of WEGOVY subcutaneous injection 7.2 mg/week, based on AUC) were administered to the males, and 0.1, 0.3 and 1 mg/kg/day (up to 2-fold MRHD) were administered to the females. A statistically significant increase in thyroid C-cell adenomas and a numerical increase in C-cell carcinomas were observed in males and females at all dose levels, at clinically relevant exposures.

In a 2-year carcinogenicity study in Sprague Dawley rats, subcutaneous semaglutide doses of 0.0025, 0.01, 0.025 and 0.1 mg/kg/day were administered (up to 0.7-fold the exposure at the MRHD). A statistically significant increase in thyroid C-cell adenomas was observed in males and females at all dose levels, and a statistically significant increase in thyroid C-cell carcinomas was observed in males at greater than or equal to 0.01 mg/kg/day, at clinically relevant exposures.

Human relevance of thyroid C-cell tumors in rats is unknown and could not be determined by clinical studies or nonclinical studies [*see Warnings and Precautions (5.1)*].

Semaglutide was not mutagenic or clastogenic in a standard battery of genotoxicity tests (i.e., bacterial mutagenicity [Ames], human lymphocyte chromosome aberration, rat bone marrow micronucleus).

In a combined fertility and embryo-fetal development study in rats, subcutaneous semaglutide doses of 0.01, 0.03 and 0.09 mg/kg/day (up to 0.1-fold the MRHD) were administered to male and female rats. Males were dosed for 4 weeks prior to mating, and females were dosed for 2 weeks prior to mating and throughout organogenesis until Gestation Day 17. No effects were observed on male fertility. In females, an increase in estrus-cycle length was observed at all dose levels, together with a small reduction in numbers of corpora lutea at greater than or equal to 0.03 mg/kg/day, at clinically relevant exposures. These effects were likely an adaptive response secondary to the pharmacological effect of semaglutide on food consumption and body weight.

13.2 Animal Toxicology and/or Pharmacology

WEGOVY tablets contain SNAC as an absorption enhancer. An increase in lactate levels and a decrease in glucose levels in plasma and cerebrospinal fluid (CSF) were observed in mechanistic rat studies with SNAC. Small but statistically significant increases in lactate levels (up to 2-fold) were observed in a few rats at approximately the clinical exposure. At higher exposures these findings were associated with moderate to marked adverse clinical signs (lethargy, abnormal respiration, ataxia, and reduced activity, body tone and reflexes) and marked decreases in plasma and CSF glucose levels. These findings are consistent with inhibition of cellular respiration and lead to mortality at SNAC concentrations >100-times the clinical C_{max}.

14 CLINICAL STUDIES

14.1 Cardiovascular Outcomes Trial in Adult Patients with Cardiovascular Disease and Either Obesity or Overweight

Overview of Clinical Trial

Study 1 (NCT03574597) was a multi-national, multi-center, placebo-controlled, double-blind trial to determine the effect of WEGOVY injection relative to placebo on major adverse CV events (MACE) when added to current standard of care, which included management of CV risk factors and individualized healthy lifestyle counseling (including diet and physical activity) in adults with established CV disease and either obesity or overweight. The primary endpoint, MACE, was the time to first occurrence of a three-part composite outcome which included CV death, non-fatal myocardial infarction, and non-fatal stroke. During the 16-week dose escalation period, patients were titrated to WEGOVY 2.4 mg injected subcutaneously once weekly or placebo. Patients who could not tolerate the recommended escalation dosage, could stay at a lower dose level.

All patients were 45 years or older, with an initial BMI of 27 kg/m² or greater and established CV disease (prior myocardial infarction, prior stroke, or peripheral arterial disease). Patients with a history of type 1 or type 2 diabetes were excluded. Concomitant CV therapies could be adjusted, at the discretion of the investigator, to ensure participants were treated according to the current standard of care for patients with established CV disease.

In this trial, 17,604 patients were randomized to WEGOVY injection or placebo. At baseline, the mean age was 62 years (range 45 to 93), 72% were male, 84% were White, 4% were Black or African American, and 8% were Asian, and 10% were Hispanic or Latino. Mean baseline body weight was 97 kg and mean BMI was 33 kg/m². At baseline, prior myocardial infarction was reported in 76% of randomized individuals, prior stroke in 23%, and peripheral arterial disease in 9%. Heart failure was reported in 24% of patients. At baseline, CV disease and risk factors were managed with lipid-lowering therapy (90%), platelet aggregation inhibitors (86%), angiotensin converting enzyme inhibitors or angiotensin II receptor blockers (74%), and beta blockers (70%). A total of 10% had moderate renal impairment (eGFR 30 to <60 mL/min/1.73m²) and 0.4% had severe renal impairment eGFR <30 mL/min/1.73m².

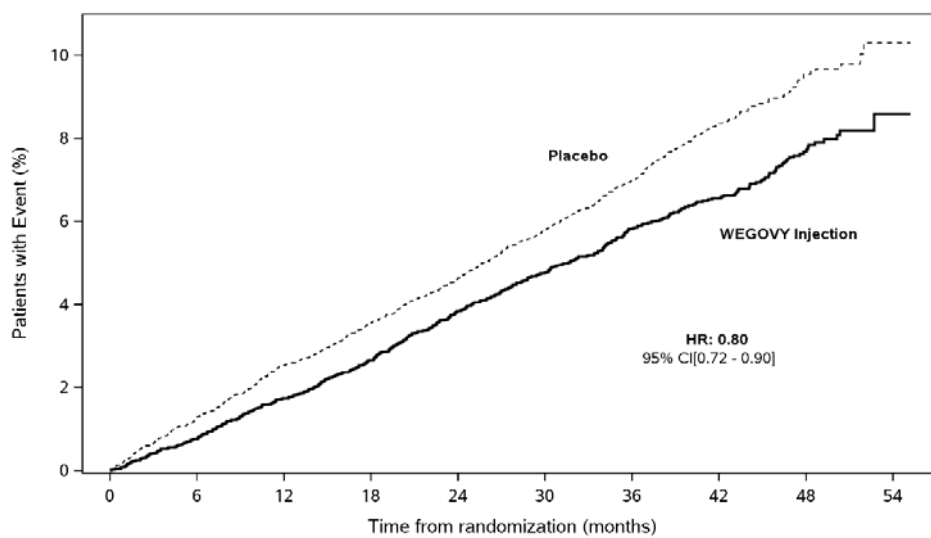
Results

In total, 96.9% of patients completed the trial, and vital status was available for 99.4% of patients. The median follow-up duration was 41.8 months. A total of 31% of WEGOVY injection-treated patients and 27% of placebo-treated patients permanently discontinued study drug. Of those patients on treatment at 1 year, 76% were on the 2.4 mg dose, 8% were on the 1.7 mg dose, and 16% were on lower doses. Of those patients on treatment at 2 years, 77% were on the 2.4 mg dose, 7% were on the 1.7 mg dose, and 17% were on lower doses.

For the primary analysis, a Cox proportional hazards model was used to test for superiority. Type 1 error was controlled across multiple tests.

WEGOVY injection significantly reduced the risk for first occurrence of MACE. The estimated hazard ratio (95% CI) was 0.80 (0.72, 0.90) (see **Figure 2** and **Table 6**).

Figure 2. Cumulative Incidence Function: Time to First Occurrence of MACE in Study 1 with WEGOVY Injection



Patients at risk										
	8803	8695	8561	8427	8254	7229	5777	4126	1734	71
WEGOVY Injection	8803	8695	8561	8427	8254	7229	5777	4126	1734	71
Placebo	8801	8652	8487	8326	8164	7101	5660	4015	1672	59

Data from the in-trial period. Cumulative incidence estimates are based on time from randomization to first EAC-confirmed cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke with non-CV death modeled as competing risk using the Aalen-Johansen estimator. Patients without events of interest were censored at the end of their in-trial observation period. Time from randomization to first cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke was analyzed using a Cox proportional hazards model with treatment as categorical fixed factor. The hazard ratio and confidence interval are adjusted for the group sequential design using the likelihood ratio ordering. HR: Hazard ratio; CI: confidence interval; CV: cardiovascular

The treatment effect for the primary composite endpoint, its components, and other relevant endpoints in Study 1 are shown in **Table 6**.

Table 6. Treatment Effect for MACE and Other Events in Study 1 with WEGOVY Injection

	Patients with events n (%)		Hazard Ratio (95% CI)
	Placebo N=8,801	WEGOVY Injection N=8,803	
Primary composite endpoint			
Composite of CV death, non-fatal myocardial infarction, or non-fatal stroke ¹	701 (8%)	569 (6.5%)	0.8 (0.72; 0.9)* ²
Key secondary endpoints			
CV death ³	262 (3%)	223 (2.5%)	0.85 (0.71; 1.01)
All-cause death ⁴	458 (5.2%)	375 (4.3%)	0.81 (0.71; 0.93)
Other endpoints			
Fatal or non-fatal myocardial infarction ⁵	334 (3.8%)	243 (2.8%)	0.72 (0.61; 0.85)
Fatal or non-fatal stroke ⁵	178 (2%)	160 (1.8%)	0.89 (0.72; 1.11)
Hospitalization for heart failure or urgent heart failure visits ^{5,6}	122 (1.4%)	97 (1.1%)	0.79 (0.6; 1.03)

* p-value <0.001, one-sided p-value

¹ Primary endpoint

² Adjusted for group sequential design using the likelihood ratio ordering.

³ CV death was the first confirmatory secondary endpoint in the testing hierarchy and superiority was not confirmed.

⁴ Confirmatory secondary endpoint. Not statistically significant based on the prespecified testing hierarchy.

⁵ Not included in the prespecified testing hierarchy for controlling type-I error.

⁶ Effect on heart failure has not been established.

NOTE: Time to first event was analyzed in a Cox proportional hazards model with treatment as factor. For patients with multiple events, only the first event contributed to the composite endpoint.

Table 7. Mean Changes in Anthropometry and Cardiometabolic Parameters at Week 104 in Study 1^{1,2}

	PLACEBO		WEGOVY Injection		Difference from Placebo (LSMean)
	Baseline	Change from Baseline (LSMean)	Baseline	Change from Baseline (LSMean)	
Body Weight (kg)	96.8	-0.9 ³	96.5	-9.4 ³	-8.5 ³
Waist Circumference (cm)	111.4	-1	111.3	-7.6	-6.5
Systolic Blood Pressure (mmHg)	131	-0.5	131	-3.8	-3.3
Diastolic Blood Pressure (mmHg)	79	-0.5	79	-1	-0.5
Heart Rate	69	0.7	69	3.8	3.1
HbA _{1c} (%)	5.8	0	5.8	-0.3	-0.3
	Baseline	% Change from Baseline (LSMean)	Baseline	% Change from Baseline (LSMean)	Relative difference from placebo (%) (LSMean)
Total Cholesterol (mg/dL) ⁴	156	-1.9	155.5	-4.6	-2.8
LDL Cholesterol (mg/dL) ⁴	78.5	-3.1	78.5	-5.3	-2.2
HDL Cholesterol (mg/dL) ⁴	44.2	0.6	44.1	4.9	4.2
Triglycerides (mg/dL) ⁴	139.5	-3.2	138.6	-18.3	-15.6

¹ Parameters listed in the table were not included in the pre-specified hierarchical testing.

² Responses were analyzed using an ANCOVA with treatment as fixed factor and baseline value as covariate. Before analysis, missing data were multiple imputed. The imputation model (linear regression) was done separately for each treatment arm and included baseline value as a covariate and was fitted to all subjects with a measurement regardless of treatment status at Week 104.

³ For body weight the 'change from baseline' and 'difference to placebo' the unit is percentage change from baseline.

⁴ Baseline value is the geometric mean.

The reduction of MACE with WEGOVY injection was not impacted by age, sex, race, ethnicity, BMI at baseline, or level of renal function impairment.

14.2 Weight Reduction and Long-term Maintenance Studies in Adults with Obesity or Overweight

Overview of Clinical Trials in Adults

The efficacy of WEGOVY once weekly subcutaneous injection for weight reduction and long-term maintenance of body weight in conjunction with a reduced-calorie diet and increased physical activity were studied in three 68-week, randomized, double-blind, placebo-controlled trials; one 68-week, randomized, double-blind, placebo withdrawal trial; one 68-week, randomized, double-blind trial that investigated two different doses of WEGOVY injection versus placebo and two 72-week randomized, double-blind trials that investigated two different doses of WEGOVY injection versus placebo. In Studies 2 (NCT#03548935), 3 (NCT#03552757), and 4 (NCT#03611582), WEGOVY or matching placebo was escalated to 2.4 mg subcutaneous injection weekly during a 16-week period followed by 52 weeks on maintenance dose. In Study 5 (NCT#03548987), WEGOVY injection was escalated during a 20-week run-in period, and patients who reached a WEGOVY 2.4 mg subcutaneous injection weekly dosage after the run-in period were randomized to either continued treatment with WEGOVY injection or placebo for 48 weeks. In Study 6 (NCT#03811574), WEGOVY injection was escalated to 1.7 mg or 2.4 mg subcutaneous weekly dosages or placebo over 12 to 16 weeks followed by 52 weeks on either maintenance dose. In Study 8 (NCT#05646706) and Study 9 (NCT#05649137) WEGOVY injection was escalated to 2.4 mg or 7.2 mg subcutaneous weekly dosages or placebo over 20 weeks followed by 52 weeks on maintenance dose.

The efficacy of WEGOVY 25 mg oral once daily tablet for weight reduction and long-term maintenance of body weight in conjunction with a reduced-calorie diet and increased physical activity was evaluated in a 64-week randomized, double-blind, placebo-controlled trial [Study 7 (NCT#05564117)]. WEGOVY tablet or matching placebo was escalated to a 25 mg tablet once daily during a 12-week period followed by 52-week maintenance period.

In Studies 2, 3, 5, 7, 8 and 9, all patients received instruction for a reduced-calorie diet (approximately 500 kcal/day deficit) and increased physical activity counseling (recommended to a minimum of 150 min/week) that began with the first dose of study medication or placebo and continued throughout the trial. In Study 4, patients received an initial 8-week low-calorie diet (total energy intake 1,000 to 1,200 kcal/day) followed by 60 weeks of a reduced-calorie diet (1200 to 1800 kcal/day) and increased physical activity (100 mins/week with gradual increase to 200 mins/week).

Study 2 was a 68-week trial that enrolled 1,961 patients with obesity (BMI greater than or equal to 30 kg/m²) or with overweight (BMI 27 to 29.9 kg/m²) and at least one weight-related comorbid condition, such as treated or untreated dyslipidemia or hypertension; patients with type 2 diabetes mellitus were excluded. Patients were randomized in a 2:1 ratio to either WEGOVY injection or placebo. At baseline, mean age was 46 years (range 18 to 86), 74% were female, 75% were White, 13% were Asian and 6% were Black or African American. A total of 12% were Hispanic or Latino ethnicity. Mean baseline body weight was 105.3 kg and mean BMI was 37.9 kg/m².

Study 3 was a 68-week trial that enrolled 807 patients with type 2 diabetes and BMI greater than or equal to 27 kg/m². Patients included in the trial had HbA_{1c} 7-10% and were treated with either: diet and exercise alone or 1 to 3 oral anti-diabetic drugs (metformin, sulfonylurea, glitazone or sodium-glucose co-transporter 2 inhibitor). Patients were randomized in a 1:1 ratio to receive either WEGOVY injection or placebo. At baseline, the mean age was 55 years (range 19 to 84), 51% were female, 62% were White, 26% were Asian and 8% were Black or African American. A total of 13% were Hispanic or Latino ethnicity. Mean baseline body weight was 99.8 kg and mean BMI was 35.7 kg/m².

Study 4 was a 68-week trial that enrolled 611 patients with obesity (BMI greater than or equal to 30 kg/m²) or with overweight (BMI 27 to 29.9 kg/m²) and at least one weight-related comorbid condition such as treated or untreated dyslipidemia or hypertension; patients with type 2 diabetes mellitus were excluded. The patients were randomized in a 2:1 ratio to receive either WEGOVY injection or placebo. At baseline, the mean age was 46 years, 81% were female, 76% were White, 19% were Black or African American and 2% were Asian. A total of 20% were Hispanic or Latino ethnicity. Mean baseline body weight was 105.8 kg and mean BMI was 38 kg/m².

Study 5 was a 68-week trial that enrolled 902 patients with obesity (BMI greater than or equal to 30 kg/m²) or with overweight (BMI 27 to 29.9 kg/m²) and at least one weight-related comorbid condition such as treated or untreated dyslipidemia or hypertension; patients with type 2 diabetes mellitus were excluded. Mean body weight at baseline for the 902 patients was 106.8 kg and mean BMI was 38.3 kg/m². All patients received WEGOVY injection during the run-in period of 20 weeks that included 16 weeks of dose escalation. Trial product was permanently discontinued before randomization in 99 of 902 patients (11%); the most common reason was adverse reactions (n=48, 5.3%); 803 patients reached WEGOVY 2.4 mg injection and were then randomized in a 2:1 ratio to either continue on WEGOVY injection or receive placebo. Among the 803 randomized patients, the mean age was 46 years, 79% were female, 84% were White, 13% were Black or African American, and 2% Asian. A total of 8% were Hispanic or Latino ethnicity. Mean body weight at randomization (Week 20) was 96.1 kg and mean BMI at randomization (Week 20) was 34.4 kg/m².

Study 6 was a 68-week trial that enrolled 401 East-Asian patients (Japan and South Korea) with BMI greater than or equal to 35 kg/m² and at least one weight-related comorbid condition or with BMI 27 to 34.9 kg/m² and at least two weight-related comorbid conditions. The patients were randomized 2:1:1 to receive subcutaneous injection of WEGOVY 2.4 mg, WEGOVY 1.7 mg, or placebo. At baseline, the mean age was 51 years, 63% were male, and all patients were Asian. Mean baseline body weight was 87.5 kg and mean BMI was 31.9 kg/m². At baseline, 24.7% of patients had type 2 diabetes mellitus.

Study 7 was a 64-week trial that enrolled 307 patients with obesity (BMI greater than or equal to 30 kg/m²) or with overweight (BMI 27-29.9 kg/m²) and at least one weight-related comorbid condition, such as treated or

untreated dyslipidemia or hypertension; patients with type 2 diabetes mellitus were excluded. Patients were randomized in a 2:1 ratio to either WEGOVY 25 mg tablet or placebo. At baseline, mean age was 48 years, 79% were women, 92% were White, 1% were Asian and 7% were Black or African American. A total of 7.8% were Hispanic or Latino ethnicity. Mean baseline body weight was 106 kg and mean BMI was 38 kg/m².

Study 8 was a 72-week trial that enrolled 1,407 patients with obesity (BMI greater than or equal to 30 kg/m²), patients with type 2 diabetes mellitus were excluded. Patients were randomized in a 5:1:1 ratio to either WEGOVY 7.2 mg, WEGOVY 2.4 mg or placebo once weekly. At baseline, mean age was 47 years (range 18 to 80), 74% were female, 86% were White, 4% were Asian and 9% were Black or African American. A total of 5% were Hispanic or Latino ethnicity. Mean baseline body weight was 113 kg and mean BMI was 39.9 kg/m².

Study 9 was a 72-week trial that enrolled 512 patients with obesity and type 2 diabetes. Patients included in the trial had HbA_{1c} 7 to 10% and were treated with either: diet and exercise alone or 1 to 3 oral antidiabetic drugs (metformin, sulfonylurea, glitazone or sodium-glucose co-transporter 2 inhibitor). Patients were randomized in a 3:1:1 ratio to receive either WEGOVY 7.2 mg, WEGOVY 2.4 mg or placebo once weekly. At baseline, the mean age was 56 years (range 19 to 79), 52% were female, 84% were White, 6% were Asian and 9% were Black or African American. A total of 6% were Hispanic or Latino ethnicity. Mean baseline body weight was 110.1 kg and mean BMI was 38.6 kg/m².

Results

In Studies 2, 3, and 4, 16% of WEGOVY injection-treated patients and 19% of the placebo-treated patients discontinued therapy. In these studies, 6.8% of WEGOVY injection-treated patients and 3.2% of placebo-treated patients discontinued their treatment due to an adverse reaction [see *Adverse Reactions (6.1)*]. In Study 5, the proportions of patients who discontinued study drug were 5.8% and 11.6% for WEGOVY injection and placebo, respectively. In Study 6, the proportions of patients who discontinued study drug were 7.9%, 6.5%, and 3% for WEGOVY 1.7 mg injection, WEGOVY 2.4 mg injection, and placebo, respectively. In Study 7, the proportions of patients who discontinued study drug were 18% and 25.5% for WEGOVY 25 mg tablet and placebo, respectively. Adverse reactions led to treatment discontinuation in 6.8% of patients treated with WEGOVY 25 mg tablet and 5.9% patients receiving placebo. In Study 8, 5.4% of patients treated with WEGOVY 7.2 mg and 1% patients treated with placebo permanently discontinued treatment as a result of adverse reactions. In Study 9, 5.5% of patients treated with WEGOVY 7.2 mg and 2% patients treated with placebo permanently discontinued treatment as a result of adverse reactions.

For Studies 2, 3 and 4, the primary efficacy parameters were mean percent change in body weight and the percentages of patients achieving greater than or equal to 5% weight loss from baseline to Week 68.

After 68 weeks, treatment with WEGOVY injection resulted in a statistically significant reduction in body weight compared with placebo. Greater proportions of patients treated with WEGOVY injection achieved 5%, 10% and 15% weight loss than those treated with placebo as shown in **Table 8**.

Table 8. Changes in Body Weight at Week 68 in Studies 2, 3, and 4 with WEGOVY 2.4 mg Injection

	Study 2 (Obesity or Overweight with Comorbidity)		Study 3 (Type 2 Diabetes with Obesity or Overweight)		Study 4 (Obesity or Overweight with Comorbidity Undergoing Intensive Lifestyle Therapy)	
Intention-to-Treat ¹	PLACEBO N=655	WEGOVY Injection N=1,306	PLACEBO N=403	WEGOVY Injection N=404	PLACEBO N=204	WEGOVY Injection N=407
Body Weight						
Baseline mean (kg)	105.2	105.4	100.5	99.9	103.7	106.9
% change from baseline (LSMean)	-2.4	-14.9	-3.4	-9.6	-5.7	-16

	Study 2 (Obesity or Overweight with Comorbidity)		Study 3 (Type 2 Diabetes with Obesity or Overweight)		Study 4 (Obesity or Overweight with Comorbidity Undergoing Intensive Lifestyle Therapy)	
Intention-to-Treat ¹	PLACEBO N=655	WEGOVY Injection N=1,306	PLACEBO N=403	WEGOVY Injection N=404	PLACEBO N=204	WEGOVY Injection N=407
% difference from placebo (LSMean) (95% CI)		-12.4 (-13.3; -11.6)*		-6.2 (-7.3; -5.2)*		-10.3 (-11.8; -8.7)*
% of Patients losing greater than or equal to 5% body weight	31.1	83.5	30.2	67.4	47.8	84.8
% difference from placebo (LSMean) (95% CI)		52.4 (48.1; 56.7)*		37.2 (30.7; 43.8)*		37 (28.9; 45.2)*
% of Patients losing greater than or equal to 10% body weight	12	66.1	10.2	44.5	27.1	73
% difference from placebo (LSMean) (95% CI)		54.1 (50.4; 57.9)*		34.3 (28.4; 40.2)*		45.9 (38; 53.7)*
% of Patients losing greater than or equal to 15% body weight	4.8	47.9	4.3	25.1	13.2	53.4
% difference from placebo (LSMean) (95% CI)		43.1 (39.8; 46.3)*		20.7 (15.7; 25.8)*		40.2 (33.1; 47.3)*
% of Patients losing greater than or equal to 20% body weight ²	1.7	30.2	2.3	12.8	3.5	33.9
% difference from placebo (LSMean) (95% CI) ²		28.6 (25.8; 31.3)		10.6 (6.4; 14.7)		30.4 (24.8; 36.1)

LSMean = least squares mean; CI = confidence interval

¹ The intent-to-treat population includes all randomized patients. In Study 2, at Week 68, the body weight was missing for 7.2% and 11.9% of patients randomized to WEGOVY injection and placebo, respectively. In Study 3, at Week 68, the body weight was missing for 4% and 6.7% of patients randomized to WEGOVY injection and placebo, respectively. In Study 4, at Week 68, the body weight was missing for 8.4% and 7.4% of patients randomized to WEGOVY injection and placebo, respectively. Missing data were imputed from retrieved subjects of the same randomized treatment arm (RD-MI).

² Not included in the pre-specified hierarchical testing.

* p<0.0001 (unadjusted 2-sided) for superiority.

For Study 5, the primary efficacy parameter was mean percent change in body weight from randomization (Week 20) to Week 68.

From randomization (week 20) to Week 68, treatment with WEGOVY injection resulted in a statistically significant reduction in body weight compared with placebo (**Table 9**). Because patients who discontinued WEGOVY injection during titration and those who did not reach the 2.4 mg weekly dose were not eligible for the randomized-treatment period, the results may not reflect the experience of patients in the general population who are first starting WEGOVY injection.

Table 9. Changes in Body Weight at Week 68 in Study 5 (Obesity or Overweight with Comorbidity After 20-week Run-in) with WEGOVY 2.4 mg Injection

	WEGOVY Injection N=803 ¹	
Body Weight (only randomized patients)		
Mean at Week 0 (kg)	107.2	
	PLACEBO N=268	WEGOVY Injection N=535
Body Weight		
Mean at Week 20 (SD) (kg)	95.4 (22.7)	96.5 (22.5)
% change from Week 20 at Week 68 (LSMean)	6.9	-7.9
% difference from placebo (LSMean) (95% CI)		-14.8 (-16; -13.5)*

LSMean = least squares mean; CI = confidence interval

¹ 902 patients were enrolled at Week 0 with a mean baseline body weight of 106.8 kg. The intent-to-treat population includes all randomized patients. At Week 68, the body weight was missing for 2.8% and 6.7% of patients randomized to WEGOVY injection and placebo, respectively. Missing data were imputed from retrieved subjects of the same randomized treatment arm (RD-MI).

* p<0.001 (unadjusted 2-sided) for superiority, controlled for multiplicity.

For Study 6, the primary efficacy parameters were mean percent change in body weight and the percentage of patients achieving greater than or equal to 5% weight loss from baseline to Week 68.

After 68 weeks, treatment with WEGOVY 1.7 mg and 2.4 mg injection resulted in a statistically significant reduction in body weight compared with placebo. Greater proportions of patients treated with WEGOVY injection achieved 5%, 10%, and 15% weight loss than those treated with placebo as shown in **Table 10**.

Table 10. Changes in Body Weight at Week 68 in Study 6 in East-Asian Patients with WEGOVY 1.7 and 2.4 mg Injection

	Study 6 (BMI ≥35 kg/m ² with at least one Comorbidity or BMI 27-34.9 kg/m ² with at least two Comorbidities)		
Intention-to-treat ¹	PLACEBO N=101	WEGOVY 1.7 mg Injection N=101	WEGOVY 2.4 mg Injection N=199
Body Weight			
Baseline mean (kg)	90.2	86.1	86.9
% change from baseline (LSMean)	-2.1	-9.6	-13.2
% difference from placebo (LSMean) (95% CI)		-7.5 (-9.6; -5.4)*	-11.1 (-12.9; -9.2)*
% of Patients losing greater than or equal to 5% body weight	19.4	72.8	84
% difference from placebo (LSMean) (95% CI)		53.3 (41; 65.6)*	64.5 (54.8; 74.3)*
% of Patients losing greater than or equal to 10% body weight	4.5	39.1	59.9
% difference from placebo (LSMean) (95% CI)		34.5 (23.9; 45.1)*	55.4 (47.3; 63.6)*
% of Patients losing greater than or equal to 15% body weight	2.6	20.8	38.2
% difference from placebo (LSMean) (95% CI)		18.2 (9.8; 26.7)*	35.6 (27.9; 43.3)*

LSMean = least squares mean; CI = confidence interval

¹ The intent-to-treat population includes all randomized patients. At baseline, 24.7% of patients had type 2 diabetes mellitus. At Week 68, the body weight was missing for 3%, 3%, and 1% of patients randomized to WEGOVY 1.7 mg injection, WEGOVY 2.4 mg injection, and placebo, respectively. Missing data were imputed from retrieved subjects of the same randomized treatment arm (RD-MI).

* p<0.0001 (unadjusted 2-sided) for superiority.

For Study 7, the primary efficacy parameters were mean percent change in body weight and the percentages of patients achieving greater than or equal to 5% weight loss from baseline to Week 64.

After 64 weeks, treatment with WEGOVY 25 mg tablets resulted in a statistically significant reduction in body weight compared with placebo. Greater proportions of patients treated with WEGOVY 25 mg tablets achieved 5%, 10%, 15% and 20% weight loss than those treated with placebo as shown in **Table 11**.

Table 11. Changes in Body Weight at Week 64 in Study 7 with WEGOVY 25 mg Tablets

	Study 7 (Obesity or overweight with Comorbidity)	
Intention-to-Treat ¹	PLACEBO N=102	WEGOVY 25 mg Tablet N=205
Body Weight		
Baseline mean (kg)	104.8	106.4
% change from baseline (LSMean) ³	-2.4	-13.6
% difference from placebo (LSMean) (95% CI) ³		-11.2 [-13.6; -8.8] ²

Intention-to-Treat ¹	Study 7 (Obesity or overweight with Comorbidity)	
	PLACEBO N=102	WEGOVY 25 mg Tablet N=205
% of Patients losing greater than or equal to 5% body weight ³	31.3	76.3
% difference from placebo (LSMean) (95% CI) ³		45.1 [33.8; 56.3] ²
% of Patients losing greater than or equal to 10% body weight	14.4	59.8
% difference from placebo (LSMean) (95% CI) ³		45.3 [35.5; 55.2] ²
% of Patients losing greater than or equal to 15% body weight ³	5.5	47
% difference from placebo (LSMean) (95% CI) ³		41.5 [33.2; 49.8] ²
% of Patients losing greater than or equal to 20% body weight ³	3.1	27.9
% difference from placebo (LSMean) (95% CI) ³		24.8 [17.7; 31.9] ²

LSMean=least squares mean; CI=confidence interval

¹ The intent-to-treat population includes all randomized patients. In Study 7, at Week 64, the body weight was missing for 6.3% and 11.8% of patients randomized to WEGOVY tablets and placebo, respectively.

² p<0.0001 (unadjusted 2-sided) for superiority.

³ Model based estimates are based on an analysis of covariance (or logistic regression for the 5%, 10%, 15% or 20% achievement endpoints) including treatment as a factor and baseline value as a covariate. Missing data were multiple imputed from retrieved subjects of the same randomized treatment arm (RD-MI). The imputation model was a linear regression of the endpoint with gender as factor and baseline value of the endpoint, timing and the value of last available observation – on study (LAO-OS) of the endpoint as covariates, imputed by treatment status. For the 5%, 10%, 15% or 20% achievement endpoints, the missing body weight measurements were imputed before performing the logistic regression analyses.

RD-MI: Retrieved Drop-outs Multiple Imputation

For Studies 8 and 9, the primary efficacy parameters were mean percent change in body weight and the percentages of patients achieving greater than or equal to 5% weight loss from baseline to Week 72.

After 72 weeks of treatment, WEGOVY 7.2 mg injection resulted in a statistically significant reduction in body weight compared with placebo in Studies 8 and 9 (see **Table 12** and **Figure 6** and **10**).

Table 12. Changes in Body Weight at Week 72 in Studies 8 and 9 with WEGOVY 7.2 mg Injection

Intention-to-Treat ¹	Study 8 (Patients with obesity)			Study 9 (Type 2 diabetes with obesity)		
	PLACEBO N=201	WEGOVY 2.4 mg Injection N=201	WEGOVY 7.2 mg Injection N=1005	PLACEBO N=102	WEGOVY 2.4 mg Injection N=103	WEGOVY 7.2 mg Injection N=307
Body Weight						
Baseline mean (kg)	112.4	116.5	112.4	112.1	107	110.5
% change from baseline (LSMean) ^a	-3.9	-15.5	-18.8	-3.8	-10.4**	-13.2
% difference from placebo (LSMean) (95% CI)			-14.9 [-16.2; -13.6]*			-9.4 [-11.0; -7.8]*
Difference (%) from 2.4 mg [95% CI]			-3.3 [-4.9; -1.6]*			
% of Patients losing greater than or equal to 5% body weight	38.3	86.6**	88.7	34	74**	83.7
% difference from placebo (LSMean) (95% CI)			50.4 [42.5; 58.3]*			49.8 [39.6; 59.9]*
% of Patients losing greater than or equal to 10% body weight	20.3	72**	79.8	11.2	49.5**	60.7
% difference from placebo (LSMean) (95% CI)			59.5 [53.0; 66.0]*			49.5 [41.2; 57.7]*
% of Patients losing greater than or equal to 15% body weight	7.5	52.3**	63.8	6.9	27**	39.8
% difference from placebo (LSMean) (95% CI)			56.4 [51.5; 61.2]*			32.9 [25.5; 40.3]*
% of Patients losing greater than or equal to 20% body weight	2.8	32.3	45.5	2	13.5**	20.6
% difference from placebo (LSMean) (95% CI)			42.7 [38.8; 46.6]*			18.7 [13.4; 24.1]*

^a p<0.0001 (unadjusted 2-sided) for superiority.

** This endpoint was not included in the hierarchy testing and is only for informative purposes.

¹ The intent-to-treat population includes all randomized patients. In Study 8, at Week 72, the body weight was missing for 5.5%, 6.0% and 15.0% of patients randomized to WEGOVY 7.2 mg, WEGOVY 2.4 mg and placebo, respectively. In Study 9, at week 72, the body weight was missing for 5.2% and 6.9% of patients randomized to WEGOVY 7.2 mg and placebo, respectively.

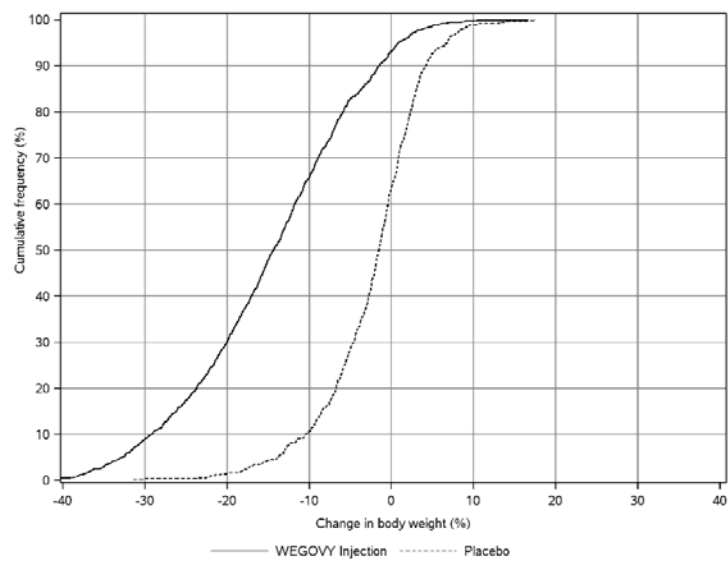
^a Model based estimates are based on an analysis of covariance (or logistic regression for the 5%, 10%, 15% or 20% achievement endpoints) including treatment as a factor and baseline value as a covariate. Missing data were multiple imputed from retrieved subjects of the same randomized treatment arm (RD-MI) in Study 8 or all retrieved subjects regardless of treatment arm assignment in Study 9. The imputation model was a linear regression of the endpoint with gender as factor and baseline value of the endpoint, timing and the value of last available observation – on study (LAO-OS) of the endpoint as covariates, imputed by treatment status. For the 5%, 10%, 15% or 20% achievement endpoints, the missing body weight measurements were imputed before performing the logistic regression analyses.

RD-MI: Retrieved Drop-outs Multiple Imputation

A reduction in body weight was observed with WEGOVY irrespective of age, sex, race, ethnicity, BMI at baseline, body weight (kg) at baseline, and level of renal function impairment.

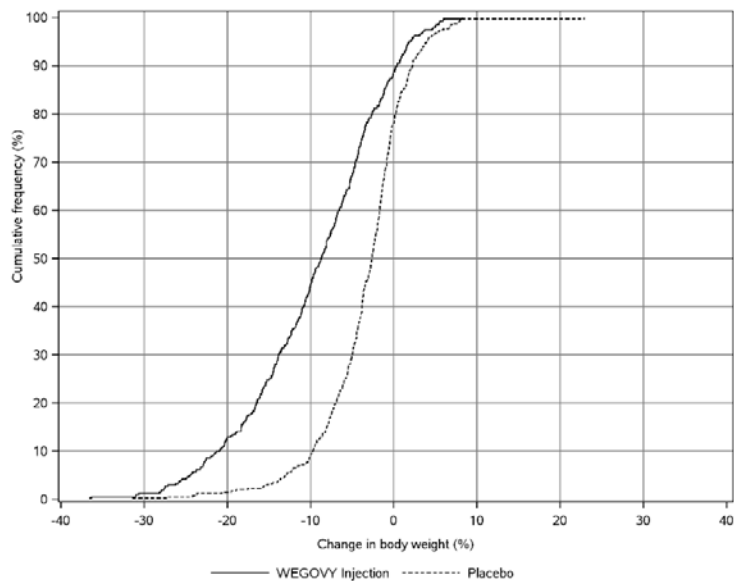
The cumulative frequency distributions of change in body weight are shown in **Figure 3**, **Figure 4**, **Figure 5** and **Figure 6** for Studies 2, 3, 7 and 8. One way to interpret this figure is to select a change in body weight of interest on the horizontal axis and note the corresponding proportions of patients (vertical axis) in each treatment group who achieved at least that degree of weight loss. For example, note that the vertical line arising from -10% in Study 2 intersects the WEGOVY injection and placebo curves at approximately 66%, and 12%, respectively, which correspond to the values shown in **Table 8**.

Figure 3. Change in Body Weight (%) from Baseline to Week 68 (Study 2) with WEGOVY Injection



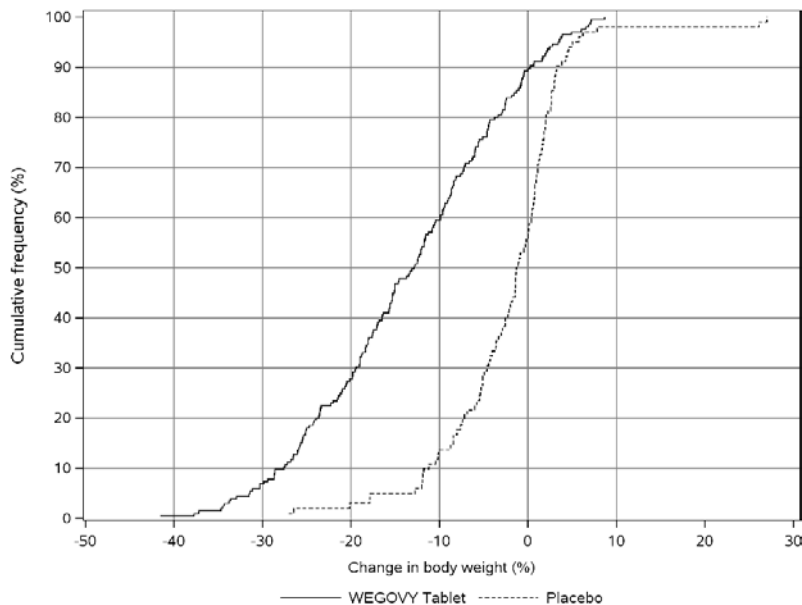
Observed data from in-trial period including imputed data for missing observations (RD-MI).

Figure 4. Change in Body Weight (%) from Baseline to Week 68 (Study 3) with WEGOVY Injection



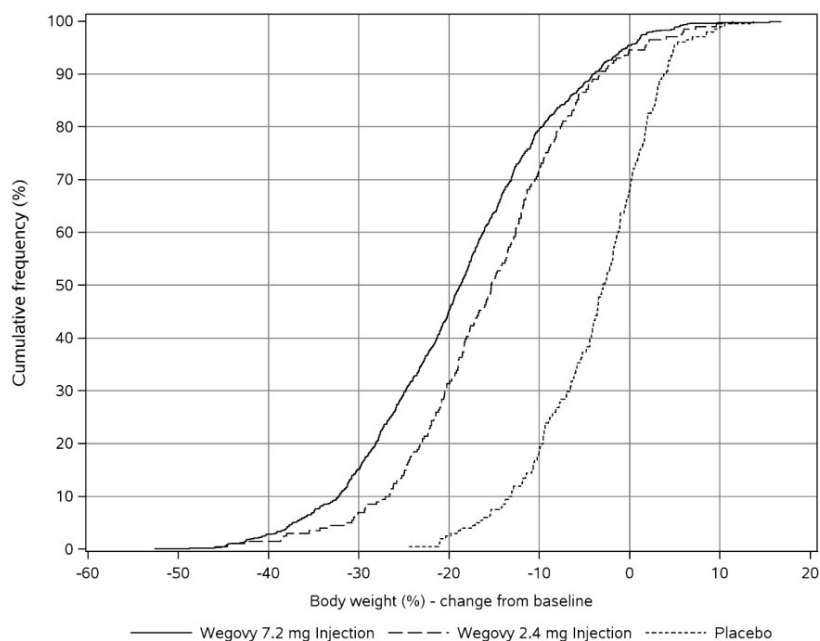
Observed data from in-trial period including imputed data for missing observations (RD-MI).

Figure 5. Change in Body Weight (%) from Baseline to Week 64 (Study 7) with WEGOVY 25 mg Tablets



Observed data from in-trial period including imputed data for missing observations (RD-MI). The missing observation was the patient-level average from the 1,000 imputed datasets.

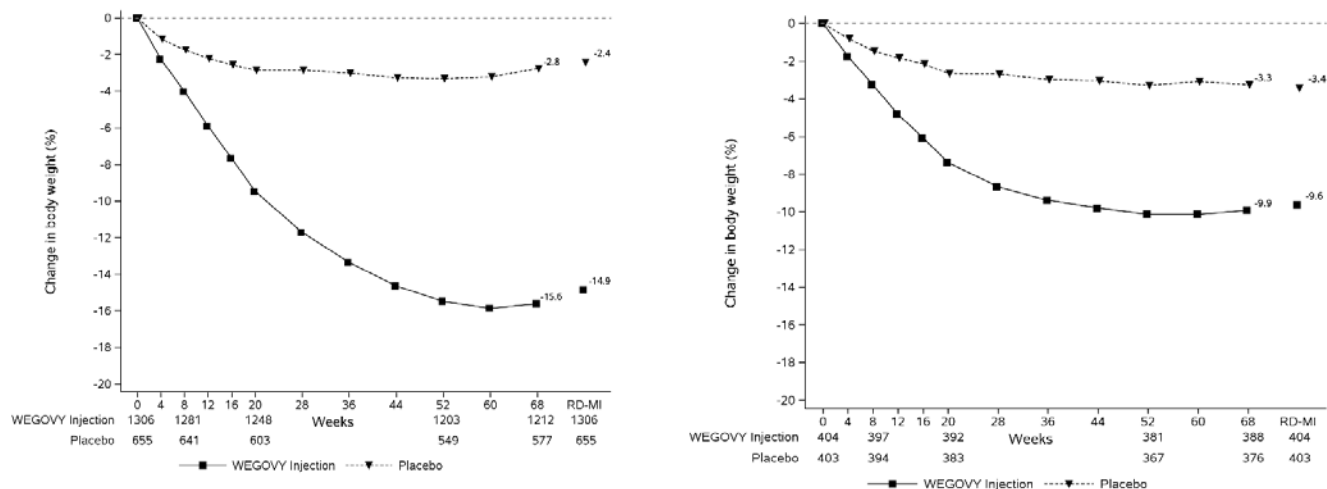
Figure 6. Change in Body Weight (%) from Baseline to Week 72 (Study 8) with WEGOVY 7.2 mg Injection



Observed data from in-trial period including imputed data for missing observations (RD-MI). Missing observations were multiply (x1000) imputed from retrieved participants of the same randomized treatment arm and missing value was replaced by the average across imputations.

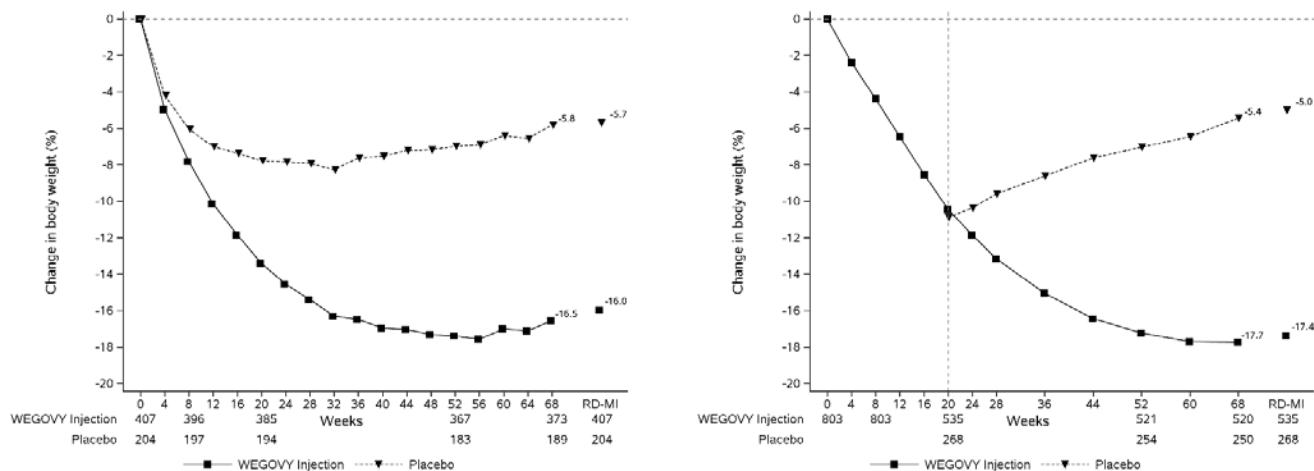
The time courses of weight loss with WEGOVY injection and placebo from baseline through Week 68 are depicted in **Figures 7, 8, and 9**, and through week 72 in **Figure 10**.

Figure 7. Change from Baseline (%) in Body Weight (Study 2 on Left and Study 3 on Right) with WEGOVY Injection



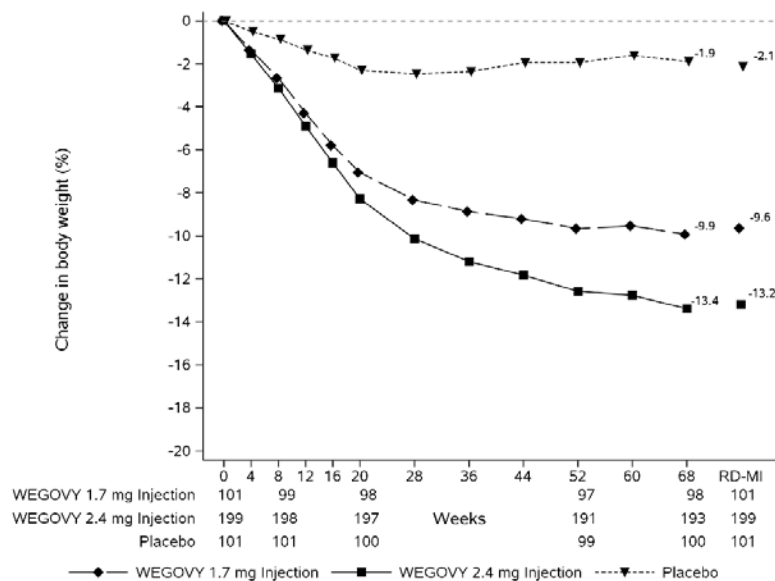
Observed values for patients completing each scheduled visit, and estimates with multiple imputations from retrieved dropouts (RD-MI).

Figure 8. Change from Baseline (%) in Body Weight (Study 4 on Left and Study 5^a on Right) with WEGOVY Injection



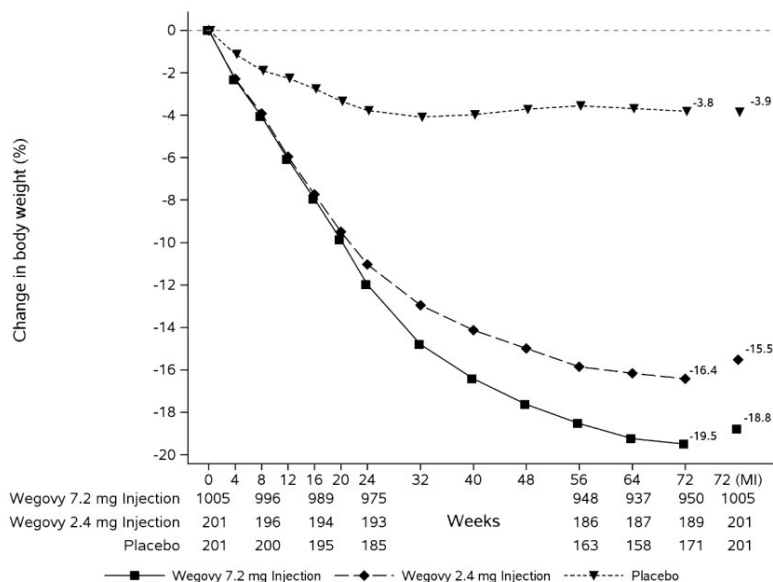
Observed values for patients completing each scheduled visit, and estimates with multiple imputations from retrieved dropouts (RD-MI).
^a Change from Week 0 was not a primary endpoint in Study 5. Dotted line indicates time of randomization. Randomized patients (shown) do not include 99 patients that discontinued during the 20-week run-in period.

Figure 9. Change in Body Weight (%) from Baseline to Week 68 (Study 6 in East-Asian Patients) with WEGOVY Injection



Observed values for patients completing each scheduled visit and estimates with multiple imputations from retrieved dropouts (RD-MI). At baseline, 24.7% of patients had type 2 diabetes mellitus.

Figure 10. Mean Change in Body Weight (%) from Baseline to Week 72 (WEGOVY 7.2 mg Injection–Study 8)



Observed values for patients completing each scheduled visit, and estimates with multiple imputations from retrieved dropouts (RD-MI).

Effect of WEGOVY Injection on Anthropometry and Cardiometabolic Parameters in Adults

Changes in waist circumference and cardiometabolic parameters with WEGOVY injection are shown in **Table 13** for Studies 2, 3, and 4; in **Table 14** for Study 5; in **Table 15** for Study 6; **Table 16** for study 7, and in **Table 17** for Studies 8 and 9.

Table 13. Changes in Anthropometry and Cardiometabolic Parameters at Week 68 in Studies 2, 3 and 4 with WEGOVY Injection

	Study 2 (Obesity or overweight with comorbidity)		Study 3 (Type 2 diabetes with obesity or overweight)		Study 4 (Obesity or overweight with comorbidity undergoing intensive lifestyle therapy)	
Intention-to-Treat	PLACEBO N=655	WEGOVY Injection N=1,306	PLACEBO N=403	WEGOVY Injection N=404	PLACEBO N=204	WEGOVY Injection N=407
Waist Circumference (cm)						
Baseline	114.8	114.6	115.5	114.5	111.8	113.6
Changes from baseline (LSMean ¹)	-4.1	-13.5	-4.5	-9.4	-6.3	-14.6
Difference from placebo (LSMean)		-9.4		-4.9		-8.3
Systolic Blood Pressure (mmHg)						
Baseline	127	126	130	130	124	124
Changes from baseline (LSMean ¹)	-1.1	-6.2	-0.5	-3.9	-1.6	-5.6
Difference from placebo (LSMean)		-5.1		-3.4		-3.9
Diastolic Blood Pressure (mmHg) ²						
Baseline	80	80	80	80	81	80
Changes from baseline (LSMean ¹)	-0.4	-2.8	-0.9	-1.6	-0.8	-3
Difference from placebo (LSMean)		-2.4		-0.7		-2.2

	Study 2 (Obesity or overweight with comorbidity)		Study 3 (Type 2 diabetes with obesity or overweight)		Study 4 (Obesity or overweight with comorbidity undergoing intensive lifestyle therapy)	
Intention-to-Treat	PLACEBO N=655	WEGOVY Injection N=1,306	PLACEBO N=403	WEGOVY Injection N=404	PLACEBO N=204	WEGOVY Injection N=407
Heart Rate ^{2,3}						
Baseline	72	72	76	75	71	71
Changes from baseline (LSMean ¹)	-0.7	3.5	-0.2	2.5	2.1	3.1
Difference from placebo (LSMean)		4.3		2.7		1
HbA _{1c} (%) ²						
Baseline	5.7	5.7	8.1	8.1	5.8	5.7
Changes from baseline (LSMean ¹)	-0.2	-0.4	-0.4	-1.6	-0.3	-0.5
Difference from placebo (LSMean)		-0.3		-1.2		-0.2
Total Cholesterol (mg/dL) ^{2,4}						
Baseline	192.1	189.6	170.8	170.8	188.7	185.4
Percent Change from baseline (LSMean ¹)	0.1	-3.3	-0.5	-1.4	2.1	-3.9
Relative difference from placebo (LSMean)		-3.3		-0.9		-5.8
LDL Cholesterol (mg/dL) ^{2,4}						
Baseline	112.5	110.3	90.1	90.1	111.8	107.7
Percent Change from baseline (LSMean ¹)	1.3	-2.5	0.1	0.5	2.6	-4.7
Relative difference from placebo (LSMean)		-3.8		0.4		-7.1
HDL (mg/dL) ^{2,4}						
Baseline	49.5	49.4	43.8	44.7	50.9	51.6
Percent Change from baseline (LSMean ¹)	1.4	5.2	4.1	6.9	5	6.5
Relative difference from placebo (LSMean)		3.8		2.7		1.5
Triglycerides (mg/dL) ^{2,4}						
Baseline	127.9	126.2	159.5	154.9	110.9	107.9
Percent Change from baseline (LSMean ¹)	-7.3	-21.9	-9.4	-22	-6.5	-22.5
Relative difference from placebo (LSMean)		-15.8		-13.9		-17

Missing data were imputed from retrieved subjects of the same randomized treatment arm (RD-MI).

¹ Model based estimates based on an analysis of covariance model including treatment (and stratification factors for Study 3 only) as a factor and baseline value as a covariate.

² Not included in the pre-specified hierarchical testing (except HbA_{1c} for Study 3).

³ Model based estimates based on a mixed model for repeated measures including treatment (and stratification factors for Study 3 only) as a factor and baseline values as a covariate.

⁴ Baseline value is the geometric mean.

Table 14. Mean Changes in Anthropometry and Cardiometabolic Parameters in Study 5 (Obesity or Overweight with Comorbidity After 20-week Run-in)¹ with WEGOVY Injection

	PLACEBO N=268		WEGOVY Injection N=535		
	Randomization (Week 20)	Change from Randomization (Week 20) to Week 68 (LSMean ¹)	Randomization (Week 20)	Change from Randomization (Week 20) to Week 68 (LSMean ¹)	Difference from placebo (LSMean)
Waist Circumference (cm)	104.7	3.3	105.5	-6.4	-9.7
Systolic Blood Pressure (mmHg)	121	4.4	121	0.5	-3.9
Diastolic Blood Pressure (mmHg) ²	78	0.9	78	0.3	-0.5
Heart Rate ^{2,3}	76	-5.3	76	-2	3.3
HbA _{1c} (%) ²	5.4	0.1	5.4	-0.1	-0.2
	Randomization (Week 20)	% Change from Randomization (Week 20) (LSMean ¹)	Randomization (Week 20)	% Change from Randomization (Week 20) (LSMean ¹)	Relative difference from placebo (LSMean)
Total Cholesterol (mg/dL) ^{2,4}	175.1	11.4	175.9	4.9	-5.8
LDL Cholesterol (mg/dL) ^{2,4}	109.1	7.6	108.7	1.1	-6.1
HDL Cholesterol (mg/dL) ^{2,4}	43.6	17.8	44.5	18.2	0.3
Triglycerides (mg/dL) ^{2,4}	95.3	14.8	98.1	-5.6	-17.8

Missing data were imputed from retrieved subjects of the same randomized treatment arm (RD-MI).

¹ Model based estimates based on an analysis of covariance model including treatment as a factor and baseline value as a covariate.

² Not included in the pre-specified hierarchical testing.

³ Model based estimates based on a mixed model for repeated measures including treatment as a factor and baseline values as a covariate.

⁴ Baseline value is the geometric mean.

Table 15. Mean Changes in Anthropometry and Cardiometabolic Parameters at Week 68 in Study 6 in East-Asian Patients with WEGOVY Injection

	Study 6 (BMI ≥35 kg/m ² with at least one comorbidity or BMI 27 to 34.9 kg/m ² with at least two comorbidities)		
Intention-to-treat	PLACEBO N=101	WEGOVY 1.7 mg Injection N=101	WEGOVY 2.4 mg Injection N=199
Waist circumference (cm)			
Baseline	103.8	101.4	103.8
Change from baseline (LSMean ¹)	-1.8	-7.7	-11
Difference from placebo (LSMean)		-5.9	-9.3
Systolic blood pressure (mmHg) ²			
Baseline	133	135	133
Change from baseline (LSMean ¹)	-5.3	-10.8	-10.8
Difference from placebo (LSMean)		-5.4	-5.5
Diastolic blood pressure (mmHg) ²			
Baseline	86	85	83
Change from baseline (LSMean ¹)	-2.2	-4.6	-5.3
Difference from placebo (LSMean)		-2.4	-3.1
Heart Rate ^{2,3}			
Baseline	73	73	73
Change from baseline (LSMean ¹)	2.4	4.4	6.3
Difference from placebo (LSMean)		2	3.9
HbA _{1c} (%) ²			
Baseline	6.4	6.4	6.4
Change from baseline (LSMean ¹)	0	-0.9	-0.9
Difference from placebo (LSMean)		-0.9	-0.9
Total Cholesterol (mg/dL) ^{2,4}			
Baseline	203.1	203.3	197.2
Percent change from baseline (LSMean ¹)	0.8	-6.6	-8.7
Relative difference from placebo (LSMean)		-7.3	-9.4

LDL Cholesterol (mg/dL) ^{2,4}			
Baseline	123.3	120.1	116.5
Percent change from baseline (LSMean ¹)	-3.8	-10.1	-14.6
Relative difference from placebo (LSMean)		-6.5	-11.2
HDL Cholesterol (mg/dL) ^{2,4}			
Baseline	48.7	50.2	50.8
Percent change from baseline (LSMean ¹)	5.9	6.7	9.2
Relative difference from placebo (LSMean)		0.7	3.1
Triglyceride (mg/dL) ^{2,4}			
Baseline	134.2	138.8	127.1
Percent change from baseline (LSMean ¹)	5.5	-19.5	-21.2
Relative difference from placebo (LSMean)		-23.7	-25.3

Missing data were imputed from retrieved subjects of the same randomized treatment arm (RD-MI). At baseline, 24.7% of patients had type 2 diabetes mellitus.

¹ Model based estimates based on an analysis of covariance model including treatment and type 2 diabetes status as factors and baseline value as a covariate.

² Not included in the pre-specified hierarchical testing.

³ Model based estimates based on a mixed model for repeated measures including treatment and type 2 diabetes status as factors and baseline values as a covariate.

⁴ Baseline value is the geometric mean.

Table 16. Mean Changes in Anthropometry and Cardiometabolic Parameters in Study 7 with WEGOVY 25 mg Tablets (Obesity or Overweight with Comorbidity)

Intention-to-treat	Study 7 (Obesity or overweight with comorbidity)	
	PLACEBO N=102	WEGOVY Tablets 25 mg N=205
Waist circumference (cm) ²		
Baseline	113.6	114
Change from baseline (LSMean ¹)	-2.8	-12.2
Difference from placebo (LSMean)		-9.4
Systolic blood pressure (mmHg) ²		
Baseline	131	131
Change from baseline (LSMean ¹)	-5.4	-7
Difference from placebo (LSMean)		-1.6
Diastolic blood pressure (mmHg) ²		
Baseline	83	83
Change from baseline (LSMean ¹)	-1.8	-2.8
Difference from placebo (LSMean)		-1
Heart Rate ²		
Baseline	74	72
Change from baseline (LSMean ¹)	2.4	2.7
Difference from placebo (LSMean)		0.4
HbA _{1c} (%) ²		
Baseline	5.7	5.7
Change from baseline (LSMean ¹)	-0.1	-0.3
Difference from placebo (LSMean)		-0.2
Total Cholesterol (mg/dL) ^{2,3}		
Baseline	190.5	191.4
Percent change from baseline (LSMean ¹)	-2.2	-3.3
Relative difference from placebo (LSMean)		-1.2
LDL Cholesterol (mg/dL) ^{2,3}		
Baseline	114.2	111.1
Percent change from baseline (LSMean ¹)	0.2	-2.9
Relative difference from placebo (LSMean)		-3.1
HDL Cholesterol (mg/dL) ^{2,3}		
Baseline	50.1	49.6
Percent change from baseline (LSMean ¹)	-1.1	3.3
Relative difference from placebo (LSMean)		4.5
Triglyceride (mg/dL) ^{2,3}		
Baseline	117.5	115.9
Percent change from baseline (LSMean ¹)	-9.1	-18.1
Relative difference from placebo (LSMean)		-9.9

¹ Model based estimates are based on an analysis of covariance including treatment as a factor and baseline value as a covariate. Missing data were multiple imputed from retrieved subjects of the same randomized treatment arm (RD-MI). The imputation model was a linear regression of the endpoint with gender as factor and baseline value of the endpoint, timing and the value of last available observation – on study (LAO-OS) of the endpoint as covariates, imputed by treatment status.

RD-MI: Retrieved Drop-outs Multiple Imputation

² Not included in the pre-specified hierarchical testing.

³ Baseline value is the geometric mean.

Table 17. Changes in Anthropometry and Cardiometabolic Parameters at Week 72 in Studies 8 and 9 (WEGOVY 7.2 mg Injection)

Intention-to-Treat	Study 8 (Patients with obesity)			Study 9 (Type 2 diabetes with obesity)		
	PLACEBO N=201	WEGOVY 2.4 mg Injection N=201	WEGOVY 7.2 mg Injection N=1,005	PLACEBO N=102	WEGOVY 2.4 mg Injection N=103	WEGOVY 7.2 mg Injection N=307
Waist Circumference (cm)						
Baseline	118.6	120.3	118.4	123.9	119.1	121.8
Changes from baseline (LSMean ¹)	-5.6	-14.2	-17.5	-5.8	-10.7	-12.3
Difference from placebo (LSMean [95% CI])	-		-11.9 [-13.2; -10.6]*	-		-6.6 [-9; -4.1]*
Systolic Blood Pressure (mmHg) ²						
Baseline	130	129	131	132	134	134
Changes from baseline (LSMean ¹)	-4.8	-8.5	-10.1	-3.5	-5.6	-7.5
Difference from placebo (LSMean)	-		-5.3	-		-4
Diastolic Blood Pressure (mmHg) ²						
Baseline	83	83	84	82	83	82
Changes from baseline (LSMean ¹)	-1.8	-3	-4.5	-2.9	-2.3	-3.1
Difference from placebo (LSMean)	-		-2.7			-0.2
Heart Rate (beats/min) ²						
Baseline	75	76	75	77	76	77
Changes from baseline (LSMean ¹)	-0.6	0.3	0.5	-2.7	1	1.1
Difference from placebo (LSMean)			1			3.9
HbA _{1c} (%) ²						
Baseline	5.7	5.6	5.7	8.2	8.1	8
Changes from baseline (LSMean ¹)	0.0	-0.3	-0.3	-0.2	-1.6	-1.7
Difference from placebo (LSMean [95% CI])			-0.3			-1.5 [-1.8; -1.2]*
Total Cholesterol (mg/dL) ^{2,3}						
Baseline	193.4	190.4	193.6	176.8	172.6	175.2
Percent change from baseline (LSMean ¹)	-4.0	-3.6	-3.4	3.5	-1.4	0.1
Relative difference from placebo (LSMean)	-		0.6	-		-3.4
LDL Cholesterol (mg/dL) ^{2,3}						
Baseline	116.4	114.4	115.8	93.5	93.8	91.5
Percent change from baseline (LSMean ¹)	-4.8	-4.8	-3.5	6.7	2.7	10.5
Relative difference from placebo (LSMean)	-		1.3	-		3.8
HDL (mg/dL) ^{2,3}						
Baseline	48.9	48.2	48.8	42.5	41.9	42.6
Percent change from baseline (LSMean ¹)	-0.5	7.0	9.5	7.4	6	11.4
Relative difference from placebo (LSMean)	-		10.1			4.0
Triglycerides (mg/dL) ^{2,3}						
Baseline	121.9	121.6	124.2	180.5	161.1	175.5
Percent change from baseline (LSMean ¹)	-0.9	-9.8	-16.4	17.2	-14.8	-7.8
Relative difference from placebo (LSMean)	-		-15.4			-25.0

* p<0.0001 (unadjusted 2-sided) for superiority.

The difference or relative difference from placebo was comparison between Wegovy 7.2 mg and the placebo arms.

¹ Model based estimates based on an analysis of covariance model including randomized treatment as factor and baseline value as a covariate

Missing data were multiple imputed from retrieved subjects of the same randomized treatment arm (RD-MI) in Study 8 or all retrieved subjects regardless of treatment arm assignment in Study 9. The imputation model was a linear regression of the endpoint with gender as factor and baseline value of the endpoint, timing and the value of last available observation – on study (LAO-OS) of the endpoint as covariates, imputed by treatment status.

RD-MI: Retrieved Drop-outs Multiple Imputation

² Not included in the pre-specified hierarchical testing (except the comparison between placebo and Wegovy 7.2 mg in Study 8 and Study 9 for waist circumference and HbA_{1c} for Study 9).

³ Baseline value is the geometric mean.

14.3 Weight Reduction and Long-term Maintenance Study of WEGOVY Injection in Pediatric Patients Aged 12 Years and Older with Obesity

Overview of Clinical Trial in Pediatric Patients

WEGOVY injection was evaluated to reduce excess body weight in pediatric patients aged 12 years of age and older with obesity in a 68-week, double-blind, randomized, parallel group, placebo-controlled, multi-center trial in 201 pubertal pediatric patients aged 12 years and older with BMI corresponding to ≥ 95 th percentile standardized for age and sex (Study 10) (NCT#04102189). After a 12-week lifestyle run-in period (including dietary recommendations and physical activity counseling), patients were randomized 2:1 to WEGOVY injection once weekly or placebo once weekly. WEGOVY injection or matching placebo was escalated to 2.4 mg or maximally tolerated dose during a 16-week period followed by 52 weeks on maintenance dose. Of WEGOVY injection-treated patients who completed the trial, 86.7% were on the 2.4 mg dosage at the end of the trial; for 5% of patients, 1.7 mg was the maximum tolerated dosage.

The mean age was 15 years; 38% of patients were male; 79% were White, 8% were Black or African American, 2% were Asian, and 11% were of other or unknown race; and 11% were of Hispanic or Latino ethnicity. The mean baseline body weight was 108 kg, and mean BMI was 37 kg/m².

Results

The proportions of patients who discontinued study drug were 10% for the WEGOVY injection-treated group and 10% for the placebo-treated group.

The primary endpoint was percent change in BMI from baseline to Week 68. After 68 weeks, treatment with WEGOVY injection resulted in a statistically significant reduction in percent BMI compared with placebo. Greater proportions of patients treated with WEGOVY injection achieved $\geq 5\%$ reduction in baseline BMI than those treated with placebo as shown in **Table 18**.

Table 18. Changes in Weight and BMI at Week 68 in Pediatric Patients with Obesity Aged 12 Years and Older in Study 10 with WEGOVY 2.4 mg Injection in Study 10

Intention-to-Treat ^a	PLACEBO N=67	WEGOVY 2.4 mg Injection N=134
BMI		
Baseline mean (kg/m ²)	35.7	37.7
% change from baseline in BMI (LSMean)	0.6	-16.1
% difference from placebo (LSMean) (95% CI)		-16.7 (-20.3; -13.2)*
% of Patients with greater than or equal to 5% reduction in baseline BMI ^b	19.7	77.1
% difference from placebo (LSMean)		57.4
% of Patients with greater than or equal to 10% reduction in baseline BMI ^b	7.7	65.1
% difference from placebo (LSMean)		57.5
% of Patients with greater than or equal to 15% reduction in baseline BMI ^b	4	57.8
% difference from placebo (LSMean)		53.9
Body Weight ^b		

Intention-to-Treat ^a	PLACEBO N=67	WEGOVY 2.4 mg Injection N=134
Baseline mean (kg)	102.6	109.9
% change from baseline (LSMean) ^a	2.7	-14.7
% difference from placebo (LSMean)		-17.4

LSMean=least squares mean; CI=confidence interval

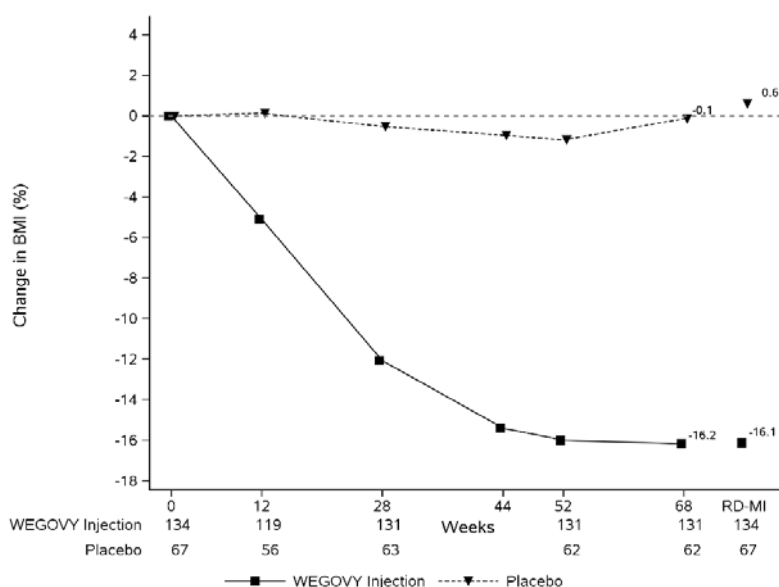
^a The intention-to-treat population includes all randomized patients. Missing data were imputed using available data according to value and timing of last available observation on treatment and endpoint's baseline value from retrieved subjects (RD-MI). At Week 68, the BMI was missing for 2.2% and 7.5% of patients randomized to WEGOVY injection and placebo, respectively.

^b Parameters not included in the pre-specified hierarchical testing.

* p<0.0001 (unadjusted 2-sided) for superiority.

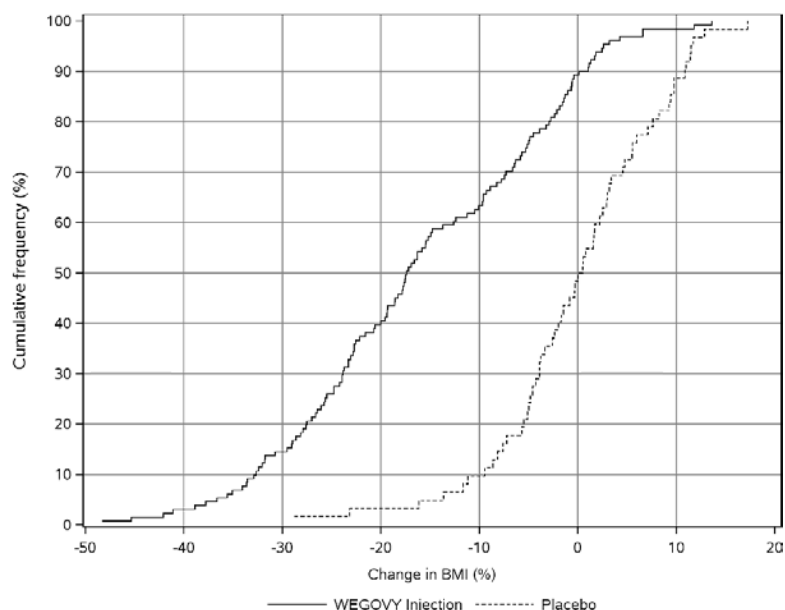
The time course of change in BMI with WEGOVY injection and placebo from baseline through Week 68 is depicted in **Figure 11**. The cumulative frequency distribution of change in BMI is shown in **Figure 10**.

Figure 11. Change from Baseline (%) in BMI in Pediatric Patients with Obesity Aged 12 Years and Older in Study 10 with WEGOVY Injection



Observed values for patients completing each scheduled visit, and estimates with multiple imputations from retrieved dropouts (RD-MI).

Figure 12. Change in BMI (%) from Baseline to Week 68 in Pediatric Patients with Obesity Aged 12 Years and Older in Study 10 with WEGOVY Injection



Observed data from in-trial period including imputed data for missing observations (RD-MI).

Effect of WEGOVY Injection on Anthropometry and Cardiometabolic Parameters in Pediatric Patients with Obesity Aged 12 Years and Older

Changes in waist circumference and cardiometabolic parameters with WEGOVY injection are shown in **Table 19** for the study in pediatric patients aged 12 years and older.

Table 19. Mean Changes in Anthropometry and Cardiometabolic Parameters in Pediatric Patients with Obesity Aged 12 Years and Older in Study 10 with WEGOVY Injection

	PLACEBO N=67		WEGOVY Injection N=134		Difference from placebo (LSMean)
	Baseline	Change from Baseline (LSMean)	Baseline	Change from Baseline (LSMean)	
Waist Circumference (cm) ²	107.3	-0.6	111.9	-12.7	-12.1
Systolic Blood Pressure (mmHg) ²	120	-0.8	120	-2.7	-1.9
Diastolic Blood Pressure (mmHg) ²	73	-0.8	73	-1.4	-0.6
Heart Rate ³	76	-2.3	79	1.2	3.5
HbA _{1c} (%) ^{2,4}	5.4	-0.1	5.5	-0.4	-0.2
	Baseline	% Change from Baseline (LSMean)	Baseline	% Change from Baseline (LSMean)	Relative difference from placebo (LSMean)
Total Cholesterol (mg/dL) ^{2,5}	160.1	-1.3	159.4	-8.3	-7.1
LDL Cholesterol (mg/dL) ^{2,5}	91.7	-3.6	89.8	-9.9	-6.6
HDL Cholesterol (mg/dL) ^{2,5}	43.3	3.2	43.7	8	4.7
Triglycerides (mg/dL) ^{2,5}	108	2.6	111.3	-28.4	-30.2

¹ Parameters listed in the table were not included in the pre-specified hierarchical testing.

² Missing data were imputed using available data according to value and timing of last available observation on treatment and endpoint's baseline value from retrieved subjects (RD-MI). Model based estimates based on an analysis of covariance model including treatment and stratification groups (gender, Tanner stage group) and the interaction between stratification groups as factors and baseline value as a covariate.

³ Model based estimates based on a mixed model for repeated measures including treatment as a factor and baseline value as a covariate all nested within visit.

⁴ For patients without type 2 diabetes at randomization (N=129 for WEGOVY injection-treated patients and N=64 for placebo-treated patients).

⁵ Baseline value is the geometric mean.

14.4 Noncirrhotic Metabolic Dysfunction-associated Steatohepatitis with Moderate to Advanced Liver Fibrosis in Adults Treated with WEGOVY Injection

Overview of Clinical Trial

The efficacy of WEGOVY injection was evaluated based on an efficacy analysis at Week 72 in Study 11 (NCT#04822181), a 240-week, randomized, double-blind, placebo-controlled trial. Enrolled patients had a baseline or recent liver biopsy showing clinically significant MASLD (metabolic dysfunction-associated steatotic liver disease), defined as MASH with fibrosis stage 2 or 3 and a non-alcoholic fatty liver disease (NAFLD) Activity Score (NAS) ≥ 4 with a score of 1 or more in steatosis, lobular inflammation, and hepatocyte ballooning. Efficacy determination was based on the effect of WEGOVY injection on resolution of steatohepatitis without worsening of liver fibrosis and on at least one stage improvement in liver fibrosis without worsening of steatohepatitis, on post-baseline liver biopsies collected at 72 weeks.

The Week 72 analysis included 800 F2 and F3 (at eligibility) patients randomized 1:2 to receive placebo (n=266) or WEGOVY once weekly (n=534), in addition to standard of care for cardiometabolic comorbidities and healthy lifestyle counseling. WEGOVY injection or matching placebo was escalated to 2.4 mg once weekly during the initial 16 weeks of the treatment period. Dose escalation could be prolonged or patients could remain at a lower dose if 2.4 mg once weekly was not tolerable.

Demographic and baseline characteristics were balanced between treatment and placebo groups. Overall, the median (Q1 to Q3) age of patients at baseline was 57 (49 to 65) years, 57% were female, 18% were Hispanic, 68% were White, 27% were Asian, and 0.6% were Black or African American. Median (Q1 to Q3) body mass index (BMI) was 34 (30 to 38) kg/m² and median (Q1 to Q3) body weight was 93 (79 to 110) kg. Baseline characteristics are presented in **Table 20**.

Table 20. Baseline Characteristics in Adults Patients with Noncirrhotic MASH with Stage 2 to Stage 3 Fibrosis in Study 11

Characteristic	Overall (N=800)
Fibrosis stage, n (%)	
F2	250 (31)
F3	550 (69)
Body Mass Index (BMI, kg/m ²), n (%) ^a	
<25	53 (7)
25-30	164 (21)
30-35	252 (32)
≥ 35	330 (41)
Lean MASH, n (%) ^b	22 (3)
Type 2 Diabetes, n (%)	447 (56)
Hypertension, n (%)	503 (63)
Dyslipidemia, n (%)	198 (25)
Statin use, n (%)	300 (38)
Fibrosis Index Based on 4 Factors (FIB-4), Median (Q1, Q3) ^a	1.6 (1.1, 2.3)
Enhanced Liver Fibrosis (ELF), Median (Q1, Q3)	9.9 (9.3, 10.5)

^a Less than 5% missingness in the variable is omitted.

^b Lean MASH defined as BMI <25 kg/m² for non-Asian patients and BMI <23 kg/m² for Asian patients.

Among the 79% of the patients with vibration-controlled transient elastography (VCTE) at baseline, median (Q1 to Q3) VCTE was 10.9 (8.6 to 15.5) kPa, which may not be representative of the entire study population. The 21% of patients with missing VCTE at baseline had higher percentages of being female and having baseline diabetes, hypertension, and dyslipidemia.

Results

Table 21 presents the Week 72 histopathology primary endpoint results comparing WEGOVY injection with placebo on:

- 1) the estimated percentage of patients with resolution of steatohepatitis and no worsening of liver fibrosis and
- 2) the estimated percentage of patients with at least one stage improvement in liver fibrosis and no worsening of steatohepatitis. The secondary endpoint results of the estimated percentage of patients with resolution of steatohepatitis and improvement in liver fibrosis at Week 72 are also presented. Two pathologists independently read the liver biopsies for each patient; a third pathologist performed adjudication if consensus could not be reached between the two pathologists. WEGOVY injection demonstrated improvement on these histopathology endpoints at Week 72 compared to placebo.

Table 21. Efficacy Results at Week 72 in Adult Patients with Noncirrhotic MASH with Stage 2 or Stage 3 Fibrosis in Study 11 of WEGOVY Injection

	Placebo N=266	WEGOVY Injection N=534
Resolution of steatohepatitis and no worsening of liver fibrosis		
Response Rate (%)	34	63
Difference in response rate vs. placebo (95% CI)		29 (21, 36)*
Improvement in liver fibrosis and no worsening of steatohepatitis		
Response Rate (%)	22	37
Difference in response rate vs. placebo (95% CI)		14 (8, 21)*
Resolution of steatohepatitis and improvement in liver fibrosis		
Response Rate (%)	16	33
Difference in response rate vs. placebo (95% CI)		17 (10, 23)*

* Results were statistically significant.

Endpoints were evaluated according to the MASH Clinical Research Network (CRN). Resolution of steatohepatitis is defined as a score of 0 to 1 for lobular inflammation, 0 for ballooning, and any value for steatosis. No worsening of steatohepatitis is defined as no increase from baseline in score for ballooning, lobular inflammation, or steatosis.

Estimated using pooled Mantel-Haenszel (MH) estimates stratified by baseline type 2 diabetes status (presence or absence) and baseline fibrosis stage (F2 or F3) with missing data handled by reference-based multiple imputation and 95% confidence intervals (CIs) calculated using Rubin's rule to pool Sato's estimate of standard errors across the imputed datasets.

Another secondary endpoint was the percent change in body weight from baseline to Week 72. Patients treated with WEGOVY injection (mean baseline body weight 95.4 kg) achieved an average of 10.5% weight loss from baseline at Week 72, and patients treated with placebo (mean baseline weight 97.6 kg) achieved an average of 2% weight loss from baseline at Week 72; treatment with WEGOVY injection resulted in an average of 8.5% greater weight loss from baseline compared to placebo (95% CI: 7.4% to 9.5%).

Starting at Week 12 and through Week 72, there was a trend of greater reductions from baseline in average ALT and AST in the WEGOVY injection group as compared to the placebo group.

16 HOW SUPPLIED/STORAGE AND HANDLING

WEGOVY Injection

How Supplied

WEGOVY injection is a clear, colorless solution in a prefilled, disposable, single-dose pen or single dose syringe with an integrated needle. It is supplied in cartons containing 4 pens or 4 syringes in the following packaging configurations:

Device Type	Name	Total Strength per Total Volume	NDC
Pen	WEGOVY	0.25 mg/0.5 mL	0169-4525-14
Pen		0.5 mg/0.5 mL	0169-4505-14
Pen		1 mg/0.5 mL	0169-4501-14
Pen		1.7 mg/0.75 mL	0169-4517-14
Pen		2.4 mg/0.75 mL	0169-4524-14
Pen	WEGOVY HD	7.2 mg/0.75 mL	0169-4572-14
Syringe	WEGOVY	0.25 mg/0.5 mL	XXXX-XXXX-XX
Syringe		0.5 mg/0.5 mL	XXXX-XXXX-XX
Syringe		1 mg/0.5 mL	XXXX-XXXX-XX
Syringe		1.7 mg/0.75 mL	XXXX-XXXX-XX
Syringe		2.4 mg/0.75 mL	XXXX-XXXX-XX

Recommended Storage

Store the WEGOVY prefilled single-dose pen or single-dose syringe in the refrigerator from 2°C to 8°C (36°F to 46°F). If needed, prior to the pen or syringe cap removal, the pen can be kept from 8°C to 30°C (46°F to

86°F) up to 28 days. Do not store WEGOVY injection in the freezer or directly adjacent to the refrigerator cooling element. Do not freeze WEGOVY injection and do not use if it has been frozen. Protect WEGOVY injection from light. WEGOVY injection must be kept in the original carton until time of administration. Discard the WEGOVY pen or syringe after use.

WEGOVY Tablets

How Supplied

WEGOVY tablets are available as:

Tablet strength	Description	Package Configuration	NDC Number
1.5 mg	White to light yellow, round shaped debossed with “1.5” on one side and “novo” on the other side	Bottle of 30 tablets	0169-4415-31
4 mg	White to light yellow, round shaped debossed with “4” on one side and “novo” on the other side	Bottle of 30 tablets	0169-4404-31
9 mg	White to light yellow, round shaped debossed with “9” on one side and “novo” on the other side	Bottle of 30 tablets	0169-4409-31
25 mg	White to light yellow, oval shaped debossed with “25” on one side and “novo” on the other side	Bottle of 30 tablets	0169-4425-31

Recommended Storage

Store at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature]. Store and dispense WEGOVY tablets in the original bottle. Store WEGOVY tablet in the original bottle until use to protect tablets from moisture. Store WEGOVY tablets in a dry place away from moisture.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide and Instructions for Use).

Risk of Thyroid C-cell Tumors

Inform patients that semaglutide causes thyroid C-cell tumors in rodents and that the human relevance of this finding has not been determined. Counsel patients to report symptoms of thyroid tumors (e.g., a lump in the neck, hoarseness, dysphagia, or dyspnea) to their physician [see *Boxed Warning, Warnings and Precautions (5.1)*].

Acute Pancreatitis

Inform patients of the potential risk for acute pancreatitis and its symptoms: severe abdominal pain that sometimes radiates to the back, and which may or may not be accompanied by nausea or vomiting. Instruct patients to discontinue WEGOVY promptly and contact their physician if pancreatitis is suspected [see *Warnings and Precautions (5.2)*].

Acute Gallbladder Disease

Inform patients of the risk of acute gallbladder disease. Advise patients that substantial or rapid weight loss can increase the risk of gallbladder disease, but that gallbladder disease may also occur in the absence of substantial or rapid weight loss. Instruct patients to contact their healthcare provider for appropriate clinical follow-up if gallbladder disease is suspected [see *Warnings and Precautions (5.3)*].

Hypoglycemia

Inform patients of the risk of hypoglycemia and educate patients on the signs and symptoms of hypoglycemia. Advise patients with diabetes mellitus on glycemic lowering therapy that they may have an increased risk of

hypoglycemia when using WEGOVY and to report signs and/or symptoms of hypoglycemia to their healthcare provider [see *Warnings and Precautions* (5.4)].

Acute Kidney Injury Due to Volume Depletion

Inform patients of the potential risk of acute kidney injury due to dehydration associated with gastrointestinal adverse reactions. Advise patients to take precautions to avoid fluid depletion. Inform patients of the signs and symptoms of acute kidney injury and instruct them to promptly report any of these signs or symptoms or persistent (or extended) nausea, vomiting, and diarrhea to their healthcare provider [see *Warnings and Precautions* (5.5)].

Severe Gastrointestinal Adverse Reactions

Inform patients of the potential risk of severe gastrointestinal adverse reactions. Instruct patients to contact their healthcare provider if they have severe or persistent gastrointestinal symptoms [see *Warnings and Precautions* (5.6)].

Hypersensitivity Reactions

Inform patients that serious hypersensitivity reactions have been reported during postmarketing use of semaglutide, the active ingredient in WEGOVY. Advise patients on the symptoms of hypersensitivity reactions and instruct them to stop taking WEGOVY and seek medical advice promptly if such symptoms occur [see *Warnings and Precautions* (5.7)].

Diabetic Retinopathy Complications in Patients with Type 2 Diabetes

Inform patients with type 2 diabetes to contact their physician if changes in vision are experienced during treatment with WEGOVY [see *Warnings and Precautions* (5.8)].

Heart Rate Increase

Instruct patients to inform their healthcare providers of palpitations or feelings of a racing heartbeat while at rest during WEGOVY treatment [see *Warnings and Precautions* (5.9)].

Pulmonary Aspiration During General Anesthesia or Deep Sedation

Inform patients that WEGOVY may cause their stomach to empty more slowly which may lead to complications with anesthesia or deep sedation during planned surgeries or procedures. Instruct patients to inform healthcare providers prior to any planned surgeries or procedures if they are taking WEGOVY [see *Warnings and Precautions* (5.10)].

Pregnancy

WEGOVY may cause fetal harm. Advise patients to inform their healthcare provider of a known or suspected pregnancy. Advise patients who are exposed to WEGOVY during pregnancy to contact Novo Nordisk at 1-877-390-2760 or www.wegovypregnancyregistry.com [see *Use in Specific Populations* (8.1)].

Missed Doses

Inform patients if a dose of WEGOVY injection is missed and the next scheduled dose is more than 2 days away (48 hours), administer WEGOVY injection as soon as possible. If one dose is missed and the next scheduled dose is less than 2 days away (48 hours), do not administer the dose. Inform patients to resume their regular once-weekly dosing schedule [see *Dosage and Administration* (2.4)].

Inform patients if a dose of WEGOVY tablets is missed, skip the missed dose and take the next dose the following day [see *Dosage and Administration* (2.4)].

Lactation

Advise females not to breastfeed during treatment with WEGOVY tablets [*see Use in Specific Populations (8.2)*].

Marketed by:
Novo Nordisk Inc.
Plainsboro, NJ 08536

For additional information about WEGOVY contact:
Novo Nordisk Inc.
800 Scudders Mill Road
Plainsboro, NJ 08536
1-833-934-6891

WEGOVY® is a registered trademark of Novo Nordisk A/S.
Patent Information: <http://www.novonordisk-us.com/products/product-patents.html>
© 2026 Novo Nordisk

MEDICATION GUIDE	
WEGOVY® (wee-GOH-vee) (semaglutide) injection, for subcutaneous use	WEGOVY® (wee-GOH-vee) (semaglutide) tablets, for oral use
Read this Medication Guide and Instructions for Use before you start using WEGOVY and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.	
What is the most important information I should know about WEGOVY? WEGOVY may cause serious side effects, including: • Possible thyroid tumors, including cancer. Tell your healthcare provider if you get a lump or swelling in your neck, hoarseness, trouble swallowing, or shortness of breath. These may be symptoms of thyroid cancer. In studies with rodents, WEGOVY and other medicines that work like WEGOVY caused thyroid tumors, including thyroid cancer. It is not known if WEGOVY will cause thyroid tumors or a type of thyroid cancer called medullary thyroid carcinoma (MTC) in people. • Do not use WEGOVY if you or any of your family have ever had a type of thyroid cancer called medullary thyroid carcinoma (MTC), or if you have an endocrine system condition called Multiple Endocrine Neoplasia syndrome type 2 (MEN 2).	
What is WEGOVY? • WEGOVY injection is a prescription medicine used with a reduced-calorie diet and increased physical activity to: ○ reduce the risk of major cardiovascular events such as death, heart attack, or stroke in adults with known heart disease and with either obesity or overweight. ○ help adults and children aged 12 years and older with obesity, or some adults with excess weight (overweight) who also have weight-related medical problems to lose weight and keep the weight off. ○ treat adults with metabolic dysfunction-associated steatohepatitis (MASH) with moderate to advanced liver scarring (fibrosis), but not with cirrhosis of the liver. • WEGOVY tablets are a prescription medicine used with a reduced-calorie diet and increased physical activity to: ○ reduce the risk of major cardiovascular events such as death, heart attack, or stroke in adults with known heart disease and with either obesity or overweight. ○ help adults with obesity, or some adults with excess weight (overweight) who also have weight-related medical problems to lose weight and keep the weight off. • WEGOVY contains semaglutide and should not be used with other semaglutide-containing products or other GLP-1 receptor agonist medicines. • It is not known if WEGOVY injection is safe and effective: ○ to reduce the risk of major cardiovascular events (death, heart attack, or stroke) in people under 18 years. ○ to help children under 12 years of age lose weight and keep the weight off. ○ for the treatment of MASH in people under 18 years of age. • It is not known if WEGOVY tablets are safe and effective for use in people under 18 years of age.	
Do not use WEGOVY if: • you or any of your family have ever had a type of thyroid cancer called MTC or if you have an endocrine system condition called MEN 2. • you have had a serious allergic reaction to semaglutide or any of the ingredients in WEGOVY injection or WEGOVY tablets. See the end of this Medication Guide for a complete list of ingredients in WEGOVY injection and WEGOVY tablets. See “What are the possible side effects of WEGOVY?” for symptoms of a serious allergic reaction.	
Before using WEGOVY, tell your healthcare provider if you have any other medical conditions, including if you: • have or have had problems with your pancreas or kidneys. • have type 2 diabetes and a history of diabetic retinopathy. • are scheduled to have surgery or other procedures that use anesthesia or deep sleepiness (deep sedation).	

- are pregnant or plan to become pregnant. WEGOVY may harm your unborn baby. You should stop using WEGOVY 2 months before you plan to become pregnant.
 - **Pregnancy Exposure Registry:** There is a pregnancy exposure registry for women who use WEGOVY during pregnancy. The purpose of this registry is to collect information about the health of you and your baby. Talk to your healthcare provider about how you can take part in this registry or you may contact Novo Nordisk at 1-877-390-2760 or www.wegovypregnancyregistry.com.
- are breastfeeding or plan to breastfeed. Breastfeeding is not recommended during treatment with WEGOVY tablets. It is not known if WEGOVY when received through an injection passes into your breast milk. You should talk with your healthcare provider about the best way to feed your baby while using WEGOVY.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. WEGOVY may affect the way some medicines work and some medicines may affect the way WEGOVY works. Tell your healthcare provider if you are taking other medicines to treat diabetes, including sulfonylureas or insulin. WEGOVY slows stomach emptying and can affect medicines that need to pass through the stomach quickly.

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

How should I use WEGOVY?

- Use WEGOVY exactly as your healthcare provider tells you to.
- Use WEGOVY with a reduced-calorie diet and increased physical activity.
- If you take too much WEGOVY, you may have severe nausea, severe vomiting and severe low blood sugar. Call your healthcare provider or Poison Help line at 1-800-222-1222 or go to the nearest hospital emergency room right away. Advice is also available online at poisonhelp.org.

WEGOVY Injection

- Read the **Instructions for Use** that comes with WEGOVY.
- **Your healthcare provider should show you how to use WEGOVY before you use it for the first time.**
- WEGOVY is injected under the skin (subcutaneously) of your stomach (abdomen), thigh, or upper arm. **Do not** inject WEGOVY into a muscle (intramuscularly) or vein (intravenously).
- Change (rotate) your injection site with each injection. **Do not** use the same site for each injection.
- **Use WEGOVY 1 time each week, on the same day each week, at any time of the day.**
- If you need to change the day of the week, you may do so as long as your last dose of WEGOVY was given 2 or more days before.
- If you miss a dose of WEGOVY and the next scheduled dose is more than 2 days away (48 hours), take the missed dose as soon as possible. If you miss a dose of WEGOVY and the next schedule dose is less than 2 days away (48 hours), do not administer the dose. Take your next dose on the regularly scheduled day.
- If you miss doses of WEGOVY for 2 or more weeks, take your next dose on the regularly scheduled day or call your healthcare provider to talk about how to restart your treatment.
- You can take WEGOVY with or without food.

WEGOVY Tablets

- Take 1 WEGOVY tablet by mouth on an empty stomach in the morning with water (no more than 4 ounces). **Do not** take WEGOVY tablets with any other liquids besides water.
- **Do not** split, crush, chew or dissolve WEGOVY tablets. Swallow WEGOVY tablets whole.
- **Do not** take more than 1 WEGOVY tablet each day.
- After 30 minutes, you can eat, drink, or take other oral medicines.
- If you miss a dose of WEGOVY, skip the missed dose and go back to your regular schedule for the next dose.

What are the possible side effects of WEGOVY?

WEGOVY may cause serious side effects, including:

- See **“What is the most important information I should know about WEGOVY?”**

- **inflammation of your pancreas (pancreatitis).** Stop using WEGOVY and call your healthcare provider right away if you have severe pain in your stomach area (abdomen) that will not go away, with or without nausea or vomiting. Sometimes you may feel the pain from your abdomen to your back.
- **gallbladder problems.** WEGOVY may cause gallbladder problems including gallstones. Some gallbladder problems need surgery. Call your healthcare provider if you have any of the following symptoms:
 - pain in your upper stomach (abdomen)
 - fever
 - yellowing of skin or eyes (jaundice)
 - clay-colored stools
- **increased risk of low blood sugar (hypoglycemia) in patients with type 2 diabetes, especially those who also take medicines to treat type 2 diabetes mellitus such as an insulin or a sulfonylureas.** Low blood sugar in patients with type 2 diabetes who receive WEGOVY can be both a serious and common side effect. Talk to your healthcare provider about how to recognize and treat low blood sugar. You should check your blood sugar before you start taking WEGOVY and while you take WEGOVY. Signs and symptoms of low blood sugar may include:
 - dizziness or light-headedness
 - blurred vision
 - anxiety
 - irritability or mood changes
 - sweating
 - slurred speech
 - hunger
 - confusion or drowsiness
 - shakiness
 - weakness
 - headache
 - fast heartbeat
 - feeling jittery
- **dehydration leading to kidney problems.** Diarrhea, nausea, and vomiting may cause a loss of fluids (dehydration) which may cause kidney problems. It is important for you to drink fluids to help reduce your chance of dehydration. Tell your healthcare provider right away if you have nausea, vomiting, or diarrhea that does not go away.
- **severe stomach problems.** Stomach problems, sometimes severe, have been reported in people who use WEGOVY. Tell your healthcare provider if you have stomach problems that are severe or will not go away.
- **serious allergic reactions.** Stop using WEGOVY and get medical help right away, if you have any symptoms of a serious allergic reaction including:
 - swelling of your face, lips, tongue or throat
 - problems breathing or swallowing
 - severe rash or itching
 - fainting or feeling dizzy
 - very rapid heartbeat
- **change in vision in people with type 2 diabetes.** Tell your healthcare provider if you have changes in vision during treatment with WEGOVY.
- **increased heart rate.** WEGOVY can increase your heart rate while you are at rest. Your healthcare provider should check your heart rate while you take WEGOVY. Tell your healthcare provider if you feel your heart racing or pounding in your chest and it lasts for several minutes.
- **food or liquid getting into the lungs during surgery or other procedures that use anesthesia or deep sleepiness (deep sedation).** WEGOVY may increase the chance of food getting into your lungs during surgery or other procedures. Tell all your healthcare providers that you are taking WEGOVY before you are scheduled to have surgery or other procedures.

The most common side effects of WEGOVY in adults or children aged 12 years and older may include:

- | | | | |
|----------------|------------------------------|--|---------------|
| • nausea | • stomach (abdomen) pain | • dizziness | • gas |
| • diarrhea | • changes in skin sensations | • feeling bloated | • stomach flu |
| • vomiting | • headache | • belching | • heartburn |
| • constipation | • tiredness (fatigue) | • low blood sugar in people with type 2 diabetes | • hair loss |
| | • upset stomach | | |

Talk to your healthcare provider about any side effect that bothers you or does not go away. These are not all the possible side effects of WEGOVY.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store WEGOVY?

WEGOVY injection

- Store the WEGOVY pen in the refrigerator between 36°F to 46°F (2°C to 8°C).
- If needed, before removing the pen cap, WEGOVY can be stored from 46°F to 86°F (8°C to 30°C) in the original carton for up to 28 days.

- Do not store WEGOVY in the freezer or directly beside the refrigerator cooling element.
- **Do not freeze WEGOVY and do not use WEGOVY if it has been frozen.**
- Keep WEGOVY in the original carton to protect it from light.
- Throw away the pen if WEGOVY has been frozen, has been exposed to light or temperatures above 86°F (30°C), has been out of the refrigerator for 28 days or longer, or after use.

WEGOVY tablets

- Store WEGOVY tablets at room temperature between 68°F to 77°F (20°C to 25°C).
- Store tablets in the original closed WEGOVY bottle until you are ready to take one. Do not store in any other container.
- Store in a dry place away from moisture.

Keep WEGOVY and all medicines out of the reach of children.

General information about the safe and effective use of WEGOVY.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use WEGOVY for a condition for which it was not prescribed. Do not give WEGOVY to other people, even if they have the same condition that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about WEGOVY that is written for health professionals.

What are the ingredients in WEGOVY?

Active Ingredient: semaglutide

Inactive Ingredients in WEGOVY injection: disodium phosphate dihydrate, 1.42 mg; sodium chloride, 8.25 mg; water for injection; and hydrochloric acid or sodium hydroxide may be added to adjust pH.

Inactive Ingredients in WEGOVY tablets: salcaprozate sodium (SNAC) and magnesium stearate

Marketed by: Novo Nordisk Inc., Plainsboro, NJ 08536

WEGOVY® is a registered trademark of Novo Nordisk A/S.

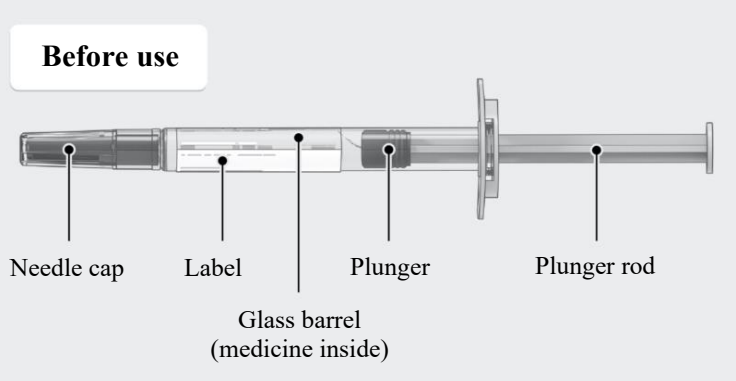
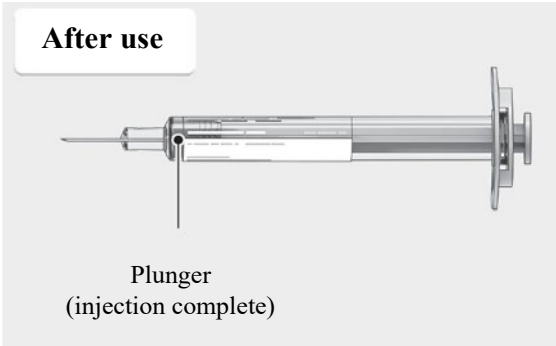
Patent Information: <http://novonordisk-us.com/products/product-patents.html>

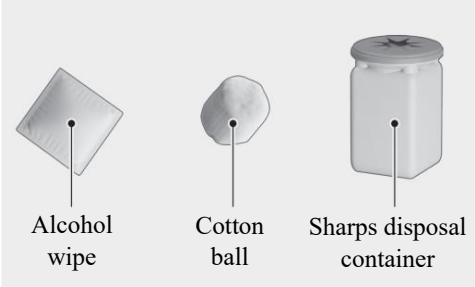
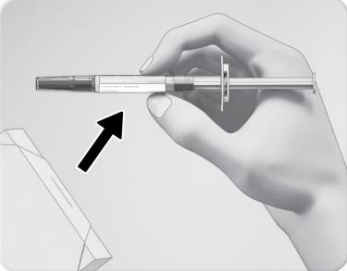
© 2026 Novo Nordisk

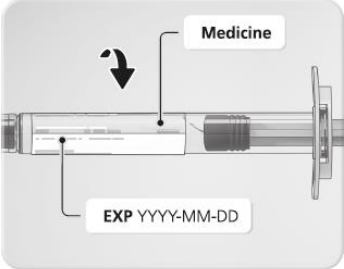
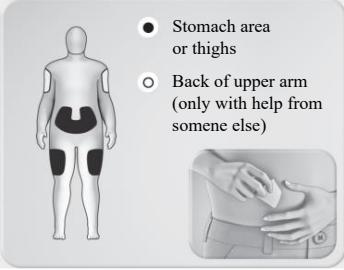
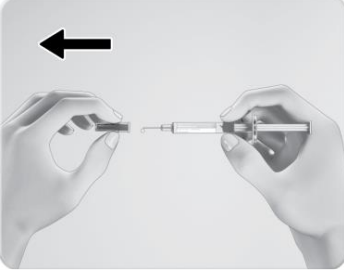
For more information, go to startWegovy.com or call 1-833-Wegovy-1.

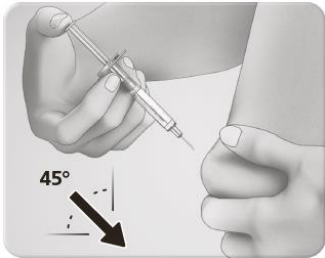
This Medication Guide has been approved by the U.S. Food and Drug Administration.

Revised: 03/2026

INSTRUCTIONS FOR USE WEGOVY® [wee-GOH-vee] (semaglutide) injection, subcutaneous only single-dose prefilled syringe	
Before using your prefilled syringe always read these instructions carefully. This leaflet instructs how to perform an injection under the skin (subcutaneous). The prefilled syringe might be different than any other device you have used previously. Before you use your prefilled syringe, talk to your healthcare provider about how to inject your prefilled syringe correctly.	
Get to Know Your Prefilled Syringe You should check the label on the carton and prefilled syringe to ensure it contains the correct medicine. Please make sure you have the correct dose prescribed by your healthcare provider.	Before use  Needle cap Label Plunger Plunger rod Glass barrel (medicine inside) After use  Plunger (injection complete)
Important Information You Need to Know Before Injecting with your Prefilled Syringe • Use the prefilled syringe exactly the way your healthcare provider tells you to. • The prefilled syringe contains 1 complete dose. It is for one-time use only. • Do not use the prefilled syringe if the carton is damaged or if the tamper-evident is broken.	

• Do not warm the prefilled syringe using any heat sources such as hot water or a microwave. • Do not use the prefilled syringes if the expiration date on the label or carton has expired. • Do not use the prefilled syringe if it has been frozen or thawed. People who are blind or have vision problems should not use the prefilled syringe without help from a person who knows how to use the prefilled syringe.	
Gather the Following Materials Before Your Injection • 1 WEGOVY prefilled syringe. • Alcohol wipe. • Cotton ball or gauze. • Sharps disposal container for used prefilled syringes.	Not Included in Your Carton  Alcohol wipe Cotton ball Sharps disposal container
Frequently Asked Questions Do I inject the full volume of the prefilled syringe? Yes, the prefilled syringe is for one-time (single) use and contains one complete dose. What if the prefilled syringe is damaged? Do not use a dropped, damaged or broken prefilled syringe. Take a new prefilled syringe for your injection. What if the needle is broken? Do not use a needle that appears to be bent, dropped, damaged or broken. Take a new prefilled syringe for your injection. If you have any questions about WEGOVY, go to startWEGOVY.com or call Novo Nordisk Inc. at 1-833-Wegovy-1.	
Prepare Your Prefilled Syringe 1. Take One Prefilled Syringe • Wash and dry your hands. • Open the carton. • Gently take out one prefilled syringe by holding the glass barrel. • Check the syringe label. Confirm you have the dose prescribed by your healthcare provider.	

Do not hold or touch the prefilled syringe by the plunger rod or needle cap. Keep the needle cap on, until you are ready to inject.	
2. Inspect your Prefilled Syringe • Check the expiration date (EXP) on the label has not passed. • Check that the medicine in the prefilled syringe is clear and colorless. If the medicine looks cloudy or contains particles, do not use the prefilled syringe. It is normal to see air bubbles, they do not affect your dose. Do not try to remove bubbles. Do not use the prefilled syringe if it appears to have been used, dropped, damaged or broken.	
3. Choose Your Injection Site • Inject into the skin of: • Stomach area (abdomen) at least 2 inches from the belly button. • Thighs. ○ Back of upper arm (only with help from someone else) Clean the injection site with an alcohol wipe and allow to dry. Your healthcare provider can help you choose the injection site that is best for you. Avoid using the exact same spot as the last time between injections.	
Inject Your Dose	
4. Pull Off the Needle Cap • Pull the needle cap straight off and throw it in a sharps disposal container. You might see drops of medicine from the needle tip. This is normal and does not affect your dose. Continue with your injection right away. Do not put the needle cap back on, to avoid needle stick injuries.	

5. Insert Your Prefilled Syringe - Pinch and hold a fold of skin at the injection site between your thumb and fingers. Hold the pinch throughout the injection. - Fully insert the needle into the pinched skin at a 45-degree angle. This is to inject under the skin (subcutaneous) and not the muscle.	
6. Inject Your Dose Keep a 45-degree angle. With a constant pressure, gently push the plunger rod all the way down, until the plunger stops. When the plunger is at the bottom and the prefilled syringe is empty, your dose is complete.	
7. Remove Your Syringe Pull out the empty syringe at a 45-degree angle. Your injection is complete. If blood appears at the injection site, lightly press with a cotton ball or gauze over it, without rubbing. Do not put the needle cap back on the syringe.	
After Injection	
8. Dispose of (Throw Away) Your Used Syringe - Put the used syringe in an FDA-cleared sharp disposal container right away after use. - If you do not have an FDA-cleared sharps disposal container, you may use a household container that is: - made of a heavy-duty plastic, - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,	

◦ upright and stable during use, ◦ leak-resistant, and, ◦ properly labeled to warn of hazardous waste inside the container. • When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: http://www.fda.gov/safesharpsdisposal • Do not dispose of your used sharps disposal container in your household trash unless your community guidelines permit this. Do not recycle your used sharps disposal container. Safely dispose of your syringe that is out of date or no longer needed Keep your syringe and all medicines out of the reach of children.	
How Should I Store My WEGOVY Prefilled Syringe? • Store the unused WEGOVY prefilled syringes in the refrigerator between 36°F to 46°F (2°C to 8°C). • If needed, the prefilled syringes can be stored out of the refrigerator between 46°F to 86°F (8°C to 30°C) for up to 28 days. Record the date your prefilled syringe was removed from the refrigerator and dispose of it, if not used within 28 days. • Do not freeze. • Always keep the prefilled syringes in the original carton to protect from light. Keep the prefilled syringe and all medicines out of the reach of children.	
Marketed by: Novo Nordisk Inc. Plainsboro, NJ 08536 For information about WEGOVY, contact: Novo Nordisk Inc. 800 Scudders Mill Road Plainsboro, NJ 08536 1-833-Wegovy-1 <i>Wegovy® is a registered trademark of Novo Nordisk A/S.</i> Patent Information: http://www.novonordisk-us.com/products/product-patents.html	

©2026 Novo Nordisk	
--------------------	--

The Instructions for Use has been approved by the U.S Food and Drug Administration.

Approved: 05/2026

Instructions for Use

WEGOVY®

(semaglutide) injection

WEGOVY comes in five strengths:

0.25 mg / 0.5 mL

0.5 mg / 0.5 mL

1 mg / 0.5 mL

1.7 mg / 0.75 mL

2.4 mg / 0.75 mL

Before you use your WEGOVY pen for the first time, talk to your healthcare provider or your caregiver about how to prepare and inject WEGOVY correctly.



Pull out to get started



Important information

Read this Instructions for Use before you start using WEGOVY. This information does not replace talking to your healthcare provider about your medical condition or treatment.

- Your WEGOVY pen is for 1 time use only. The WEGOVY pen is for subcutaneous (under the skin) use only.
- The dose of WEGOVY is already set on your pen.
- The needle is covered by the needle cover and the needle will not be seen.
- Do not remove the pen cap until you are ready to inject.
- Do not touch or push on the needle cover. You could get a needle stick injury.
- Your WEGOVY injection will start when the needle cover is pressed firmly against your skin.
- **Do not** remove the pen from your skin before the yellow bar in the pen window has stopped moving. The medicine may appear on the skin or squirt from the needle and you may not get your full dose of WEGOVY if:
 - the pen is removed too early or
 - you have not pressed the pen firmly against the skin for the entire injection.
- If the yellow bar does not start moving or stops during the injection, contact your healthcare provider or Novo Nordisk at startWegovy.com or call Novo Nordisk Inc. at 1-833-934-6891.
- The needle cover will lock when the pen is removed from your skin. **You cannot stop the injection and restart it later.**
- People who are blind or have vision problems should not use the WEGOVY pen without help from a person trained to use the WEGOVY pen.

How do I store WEGOVY?

- Store the WEGOVY pen in the refrigerator between 36°F to 46°F (2°C to 8°C).
- If needed, before removing the pen cap, WEGOVY can be stored from 46°F to 86°F (8°C to 30°C) in the original carton for up to 28 days.
- Keep WEGOVY in the original carton to protect it from light.
- **Do not freeze.**
- Throw away the pen if WEGOVY has been frozen, has been exposed to light or temperatures above 86°F(30°C), or has been out of the refrigerator for 28 days or longer.

Keep WEGOVY and all medicines out of the reach of children.

WEGOVY pen parts

Before use

Expiration date
(on the back)
Check that
WEGOVY has not
expired.

EXP:
LOT:

Always check you
have the medicine
and dose that your
healthcare provider
prescribed. Either:

0.25 mg / 0.5 mL

0.5 mg / 0.5 mL

1 mg / 0.5 mL

1.7 mg / 0.75 mL

2.4 mg / 0.75 mL

Pen window
Check that
WEGOVY is clear
and colorless. Air
bubbles are normal.
They do not affect
your dose.

Needle cover
Needle is hidden
inside.

Pen cap
Remove it just
before you are
ready to inject.

After use

Pen window
Check that
the yellow bar
has stopped
moving to
make sure you
received your
full dose.

Needle cover
locks after use.

How to use your WEGOVY pen

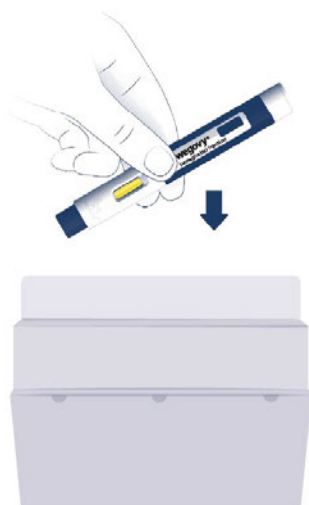
Do not use your WEGOVY pen without receiving training from your healthcare provider. Make sure that you or your caregiver know how to give an injection with the pen before you start your treatment.

Read and follow the instructions so that you use your WEGOVY pen correctly:

Preparation

Step 1. Prepare for your injection.

- **Supplies you will need to give your WEGOVY injection:**
 - WEGOVY pen
 - 1 alcohol swab or soap and water
 - 1 gauze pad or cotton ball
 - 1 sharps disposable container for used WEGOVY pens



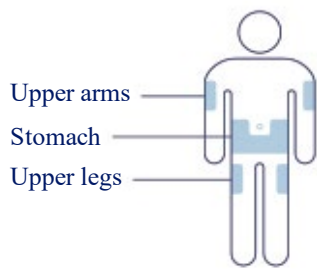
- **Wash your hands.**
- **Check your WEGOVY pen.**
Do not use your WEGOVY pen if:
 - The pen appears to have been used or any part of the pen appears broken, for example if it has been dropped.
 - The WEGOVY medicine is not clear and colorless through the pen window.
 - The expiration date (EXP) has passed.

Contact Novo Nordisk at 1-833-934-6891 if your WEGOVY pen fails any of these checks.

Step 2. Choose your injection site.

- Your healthcare provider can help you choose the injection site that is best for you
 - You may inject into your upper leg (front of the thighs), lower stomach (keep 2 inches away from your belly button) or upper arm.
- Do not inject into an area where the skin is tender, bruised, red, or hard. Avoid injecting into areas with scars or stretch marks.
- You may inject in the same body area each week, but make sure it is not in the same spot each time.

Clean the injection site with an alcohol swab or soap and water. Do not touch the injection site after cleaning. Allow the skin to dry before injecting.



Injection

Step 3. Remove pen cap.

- Pull the pen cap straight off your pen.

Step 4. Inject WEGOVY.

- **Push the pen firmly against your skin and keep applying pressure until the yellow bar has stopped moving.**
If the yellow bar does not start moving, press the pen more firmly against your skin.
- **You will hear 2 clicks during the injection.**
 - Click 1: the injection has started.
 - Click 2: the injection is ongoing.
- **If you have problems with the injection, refer to the “Troubleshooting” section.**



Throw away pen

Step 5. Throw away (dispose of) pen.

Safely dispose of the WEGOVY pen right away after each use. See “How do I throw away (dispose of) WEGOVY pens?”

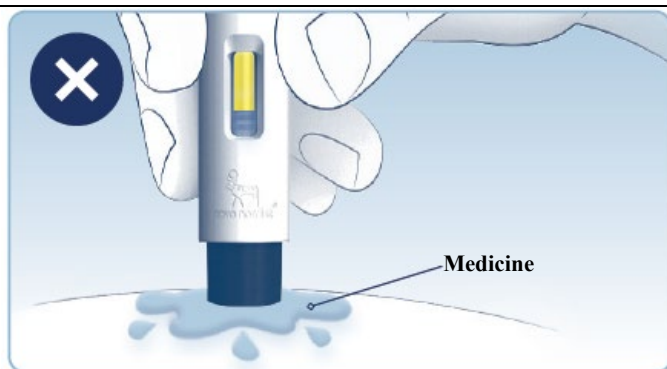
• What if blood appears after injection?

If blood appears at the injection site, press the site lightly with a gauze pad or cotton ball.



Troubleshooting

- If you have problems injecting, change to a more firm injection site, such as upper leg, or upper arm or consider standing up while injecting into the lower stomach.
- If medicine appears on the skin or squirts from the needle, make sure the next time you inject to keep applying pressure until the yellow bar has stopped moving. Then you can lift the pen slowly from your skin.



How do I throw away (dispose of) WEGOVY pens?

Put the used WEGOVY pen in an FDA-cleared sharps disposal container right away after use. **Do not throw away (dispose of)** the pen in your household trash.

If you do not have an FDA-cleared sharps disposal container, you may use a household container that is:

- made of a heavy-duty plastic,
- able to be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
- upright and stable during use,
- leak-resistant, and
- properly labeled to warn of hazardous waste inside the container.

When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. For more information about safe sharps disposal, and for specific sharps disposal in the state that you live in, go to the FDA's website at <http://www.fda.gov/safesharpsdisposal>.

- Do not reuse the pen.
- Do not recycle the pen or sharps disposal container, or throw them into household trash.

Important: Keep your WEGOVY pen, sharps disposal container and all medicines out of the reach of children.



How do I care for my pen?

Protect your pen

- Do not drop your pen or knock it against hard surfaces.
- Do not expose your pen to any liquids.
- If you think that your pen may be damaged, do not try to fix it. Use a new one.
- Keep the pen cap on until you are ready to inject. Your pen will no longer be sterile if you store an unused pen without the cap, if you pull the pen cap off and put it on again, or if the pen cap is missing. This could lead to an infection.



If you have any questions about WEGOVY, go to startWegovy.com or call Novo Nordisk Inc. at 1-833-Wegovy-1

Manufactured by:
Novo Nordisk A/S
Novo Allé
DK-2880 Bagsvaerd, Denmark

For information about WEGOVY, go to startWegovy.com or contact:
Novo Nordisk Inc.
800 Scudders Mill Road
Plainsboro, NJ 08536
1-833-Wegovy-1

Version: 2

WEGOVY® is a registered trademark of Novo Nordisk A/S.

PATENT Information: <http://novonordisk-us.com/products/product-patents.html>

© 2022 Novo Nordisk

This Instructions for Use has been approved by the U.S. Food and Drug Administration.

Revised: August 2022



Instructions for Use

WEGOVY® HD

(semaglutide) injection

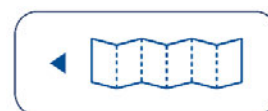
WEGOVY HD comes in the following strength:

7.2 mg/0.75 mL

Before you use your WEGOVY pen for the first time, talk to your healthcare provider or your caregiver about how to prepare and inject WEGOVY correctly.



Pull out to get started



Important information

Read this Instructions for Use before you start using WEGOVY. This information does not replace talking to your healthcare provider about your medical condition or treatment.

- **Your WEGOVY pen is for 1 time use only.** The WEGOVY pen is for subcutaneous (under the skin) use only.
- **The dose of WEGOVY is already set on your pen.**
- **The needle is covered by the needle cover and the needle will not be seen.**
- Do not remove the pen cap until you are ready to inject.
- Do not touch or push on the needle cover. You could get a needle stick injury.
- Your WEGOVY injection will start when the needle cover is pressed firmly against your skin.
- **Do not** remove the pen from your skin before the yellow bar in the pen window has stopped moving. The medicine may appear on the skin or squirt from the needle and you may not get your full dose of WEGOVY if:
 - the pen is removed too early **or**
 - you have not pressed the pen firmly against the skin for the entire injection.
- If the yellow bar does not start moving or stops during the injection, contact your healthcare provider or Novo Nordisk at startWegovy.com or call Novo Nordisk Inc. at 1-833-934-6891.
- The needle cover will lock when the pen is removed from your skin. **You cannot stop the injection and restart it later.**
- People who are blind or have vision problems should not use the WEGOVY pen without help from a person trained to use the WEGOVY pen.

How do I store WEGOVY?

- Store the WEGOVY pen in the refrigerator between 36°F to 46°F (2°C to 8°C).
- If needed, before removing the pen cap, WEGOVY can be stored from 46°F to 86°F (8°C to 30°C) in the original carton for up to 28 days.
- Do not store WEGOVY in the freezer or directly beside the refrigerator cooling element.
- **Do not freeze WEGOVY and do not use if it has been frozen.**
- Keep WEGOVY in the original carton to protect it from light.
- Throw away the pen if WEGOVY has been frozen, has been exposed to light or temperatures above 86°F (30°C), or has been out of the refrigerator for 28 days or longer or after use.

Keep WEGOVY and all medicines out of the reach of children.

WEGOVY pen parts

Before use

After use

Expiration date
(on the back)
Check that Wegovy has not expired

EXP:
LOT:

Always check you have the medicine and dose that your healthcare provider prescribed.

7.2 mg/0.75 mL

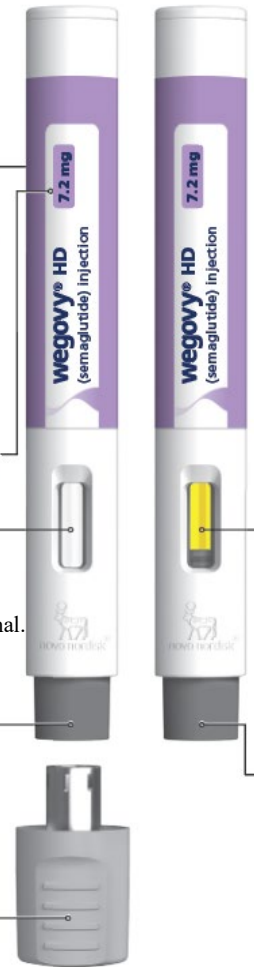
Pen window
Check that Wegovy is clear and colourless. Air bubbles are normal. They do not affect your dose.

Needle cover
Needle is hidden inside

Pen cap
Remove it just before you are ready to inject.

Pen window
Check that the yellow bar has stopped moving to make sure you received your full dose

Needle cover
Locks after use



How to use your WEGOVY pen

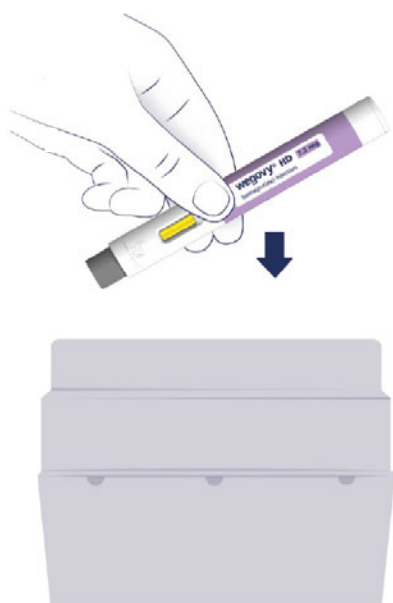
Do not use your WEGOVY pen without receiving training from your healthcare provider. Make sure that you or your caregiver know how to give an injection with the pen before you start your treatment.

Read and follow the instructions so that you use your WEGOVY pen correctly:

Preparation

Step 1. Prepare for your injection.

- **Supplies you will need to give your WEGOVY injection:**
 - WEGOVY pen
 - 1 alcohol swab or soap and water
 - 1 gauze pad or cotton ball
 - 1 sharps disposable container for used WEGOVY pens



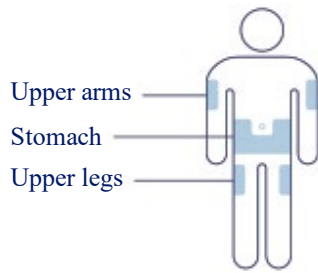
- **Wash your hands.**
- **Check your WEGOVY pen.**
Do not use your WEGOVY pen if:
 - The pen appears to have been used or any part of the pen appears broken, for example if it has been dropped.
 - The WEGOVY medicine is not clear and colorless through the pen window.
 - The expiration date (EXP) has passed.

Contact Novo Nordisk at 1-833-934-6891 if your WEGOVY pen fails any of these checks.

Step 2. Choose your injection site.

- Your healthcare provider can help you choose the injection site that is best for you.
 - You may inject into your upper leg (front of the thighs), lower stomach (keep 2 inches away from your belly button) or upper arm.
- Do not inject into an area where the skin is tender, bruised, red, or hard. Avoid injecting into areas with scars or stretch marks.
- You may inject in the same body area each week, but make sure it is not in the same spot each time.

Clean the injection site with an alcohol swab or soap and water. Do not touch the injection site after cleaning. Allow the skin to dry before injecting.



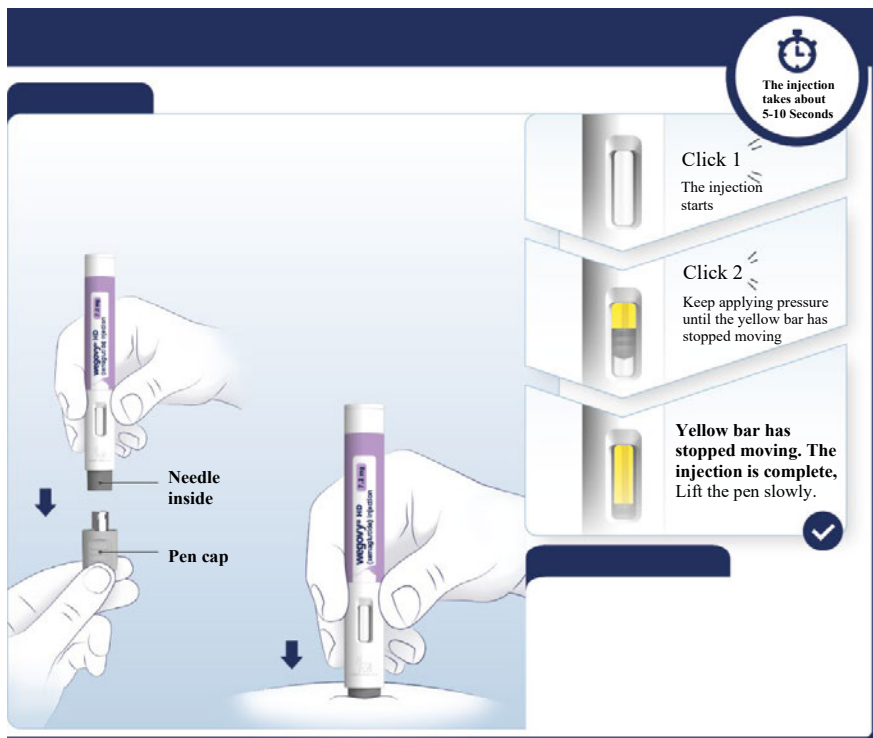
Injection

Step 3. Remove pen cap.

- Pull the pen cap straight off your pen.

Step 4. Inject WEGOVY.

- **Push the pen firmly against your skin and keep applying pressure until the yellow bar has stopped moving.**
If the yellow bar does not start moving, press the pen more firmly against your skin.
- **You will hear 2 clicks during the injection.**
 - Click 1: the injection has started.
 - Click 2: the injection is ongoing.
- **If you have problems with the injection, refer to the “Troubleshooting” section.**



Throw away pen

Step 5. Throw away (dispose of) pen.

Safely dispose of the WEGOVY pen right away after each use. See “How do I throw away (dispose of) WEGOVY pens?”

- **What if blood appears after injection?**

If blood appears at the injection site, press the site lightly with a gauze pad or cotton ball.

Troubleshooting

- If you have problems injecting, change to a more firm injection site, such as upper leg, or upper arm or consider standing up while injecting into the lower stomach.
- If medicine appears on the skin or squirts from the needle, make sure the next time you inject to keep applying pressure until the yellow bar has stopped moving. Then you can lift the pen slowly from your skin.



How do I throw away (dispose of) WEGOVY pens?

Put the used WEGOVY pen in an FDA-cleared sharps disposal container right away after use. **Do not throw away (dispose of)** the pen in your household trash.

If you do not have an FDA-cleared sharps disposal container, you may use a household container that is:

- made of a heavy-duty plastic,
- able to be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
- upright and stable during use,
- leak-resistant, and
- properly labeled to warn of hazardous waste inside the container.

When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. For more information about safe sharps disposal, and for specific sharps disposal in the state that you live in, go to the FDA's website at <http://www.fda.gov/safesharpsdisposal>.

- Do not reuse the pen.
- Do not recycle the pen or sharps disposal container, or throw them into household trash.

Important: Keep your WEGOVY pen, sharps disposal container and all medicines out of the reach of children.



How do I care for my pen?

Protect your pen

- Do not drop your pen or knock it against hard surfaces.
- Do not expose your pen to any liquids.
- If you think that your pen may be damaged, do not try to fix it. Use a new one.
- Keep the pen cap on until you are ready to inject. Your pen will no longer be sterile if you store an unused pen without the cap, if you pull the pen cap off and put it on again, or if the pen cap is missing. This could lead to an infection.



If you have any questions about WEGOVY, go to startWegovy.com or call Novo Nordisk Inc. at 1-833-Wegovy-1

Marketed by:
Novo Nordisk Inc.
Plainsboro, NJ 08536

For information about WEGOVY, go to startWegovy.com
or contact:

Novo Nordisk Inc.
800 Scudders Mill Road
Plainsboro, NJ 08536
1-833-Wegovy-1

Wegovy® is a registered trademark of Novo Nordisk A/S.

Patent Information: <http://novonordisk-us.com/products/product-patents.html>

© 2026 Novo Nordisk



This Instructions for Use has been approved by the U.S. Food and Drug Administration.

Revised: 03/2026

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

215256Orig1s031

CROSS DISCIPLINE TEAM LEADER REVIEW

Memorandum

Date: May 5, 2026

From: Justin Penzenstadler, PharmD
Cross Disciplinary Team Leader (Acting)
Division of Diabetes, Lipid Disorders, and Obesity (DDLO)

Through: Raymond E. Soccio, MD PhD
Supervisory Physician (Acting)
Division of Diabetes, Lipid Disorders, and Obesity (DDLO)

Subject: CDTL Summary Review
Introduction of a Manual Prefilled Syringe (mPFS)
Presentation

Drug Name: Semaglutide

Application Number(s): NDA 209637/S-039 (OZEMPIC), NDA 215256/S-031 (WEGOVY), NDA 218316/S-003 (WEGOVY)

Sponsor: Novo Nordisk, Inc

Recommended Regulatory Action

This review only summarizes the scientific content related to the introduction of the mPFS. I recommend approval of NDA 209637/S-039, NDA 215256/S-031, and NDA 218316/S-003.

Readers should refer to the combined regulatory project manager (RPM) and Associate Director of Labeling (ADL) review for a detailed discussion of labeling issues. I participated in multidisciplinary discussions involving labeling of these supplements, and I concur with the labeling changes proposed.

Executive Summary

These three supplements collectively introduce a single-dose manual prefilled syringe (mPFS) presentation for OZEMPIC (semaglutide) injection and WEGOVY (semaglutide) injection. NDA 218316/S-003 is a labeling-only supplement for the WEGOVY oral tablet NDA, updated to reflect the new mPFS presentation approved under NDA 215256/S-031.

The mPFS is assembled by adding a (b) (4) plunger rod and finger grip to the prefilled syringe already used in the currently marketed WEGOVY single-dose

autoinjector. (b) (4)

(b) (4)

The formulation change for OZEMPIC is minor: the mPFS will use the preservative-free WEGOVY formulation (substituting sodium chloride for propylene glycol as (b) (4) and removing phenol), as the device is intended for single-dose use. This formulation is already approved and marketed under WEGOVY. There are no formulation changes for WEGOVY.

CMC and Clinical Pharmacology reviews both recommend approval. I concur.

CMC Review

The proposed mPFS utilizes the identical prefilled syringe component currently used in the WEGOVY single-dose autoinjector. The mPFS is assembled by adding a (b) (4) plunger rod and finger grip to the prefilled syringe already used in the currently marketed WEGOVY single-dose autoinjector. It is notable that the proposed mPFS presentation does not alter the container closure system or drug product formulation. Manufacturing will be performed at a (b) (4) (b) (4). OPMA-Facility recommended approval of this site.

The CMC reviewers noted that critical quality attributes for the new presentation (for example, dose accuracy, break-loose and glide forces) all met acceptance criteria at release, under accelerated and long-term storage conditions. There are no outstanding CMC deficiencies. Drs Sarah Zimmerman and Rohit Kolhatkar recommend approval. I concur.

Clinical Pharmacology Review

The Clinical Pharmacology review was conducted by Drs. Chongwoo Yu and Li Wang.

A key question is whether the proposed mPFS delivers semaglutide with PK comparable to the currently approved pen-injectors, given differences in injection parameters between the approved presentations and the proposed mPFS. In particular, the needle length differs (12.7 mm nominal for the mPFS vs. 6 mm for the WEGOVY autoinjector and 4–8 mm for the OZEMPIC pen) which is a surrogate for injection depth, the needle bore differs (a 29G needle in the WEGOVY autoinjector and mPFS, versus various gauges of pen needles compatible with OZEMPIC), the injection angle may differ (45 degrees for mPFS vs. perpendicular for autoinjectors), and the injection rate and pressure will differ, because the manual prefilled syringe is user-dependent and the currently approved WEGOVY and OZEMPIC presentations have injection pressures that are device-controlled.

The Applicant did not conduct a prospective crossover bioequivalence (BE) study comparing the mPFS directly to the approved pen-injectors. Instead, the Applicant submitted a justification based on cross-study PK comparisons across three separate studies (Studies 4010, 7560, and 4590) conducted in different cohorts using various devices. For OZEMPIC, an additional formulation bridging study (Study 4588) was referenced to bridge the preserved OZEMPIC formulation to the preservative-free mPFS formulation. The cross-study PK comparison suggests that AUC is comparable across devices and needle lengths, while Cmax appears modestly higher with the mPFS-like administration.

OCP recommends approval of all three supplements from a clinical pharmacology perspective. I concur.

OCP proposed adding language to the Instructions for Use (IFU) instructing patients to inject over a 6-second duration. I am overruling this recommendation for the following reasons. First, through email discussions, the Human Factors reviewer noted that patients are unlikely to follow a timed injection instruction in practice; I agree with this assessment and do not favor labeling solutions that are unlikely to be implemented. Second, the currently marketed WEGOVY and OZEMPIC autoinjectors do not actually deliver the injection over a fixed 6-second duration — injection time varies depending on tissue resistance, injection volume, and needle bore, and the 6-second instruction on existing labeling is designed to ensure complete dose delivery across a range of conditions, not to prescribe a precise injection rate. Third, I am not aware of other approved labeling or scientific precedent recommending a specific injection duration for a manual prefilled syringe, which I interpret as an absence of positive evidence that injection duration meaningfully affects bioavailability, and therefore safety or efficacy, for this type of product.

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

JUSTIN A PENZENSTADLER
05/05/2026 05:00:01 PM

RAYMOND E SOCCIO
05/05/2026 05:07:48 PM

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

215256Orig1s031

PRODUCT QUALITY REVIEW(S)

Offices of Pharmaceutical Quality
Quality Assessment
Supplemental New Drug Application (sNDA) / Abbreviated New Drug Application (sANDA)

1. Application Type: NDA

Application/Supplement Number: 215256/S-031

Filing Category: PA based on *CANA IX.B.4*.

Supplement Managed By: OND

Review Cycle # 1

Drug Product Name and Strength: Wegovy (semaglutide) injection, 0.25 mg, 0.5 mg, 1 mg, 1.7 mg, 2.4 mg, 7.2 mg

Pharmacological Category/Indication(s): to reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with established cardiovascular disease and either obesity or overweight; to reduce excess body weight and maintain weight reduction; for the treatment of noncirrhotic metabolic dysfunction-associated steatohepatitis (MASH), formerly known as nonalcoholic steatohepatitis (NASH).

Applicant Name (and US Agent if Applicable): Novo Nordisk Inc.

Recommendation: Approval

2. Submission(s) Being Reviewed:

Submission	eCTD Sequence #	Received Date
Original Supplement	1202	01/05/2026
Amendment	1310	02/11/2026
Amendment	1311	02/12/2026
Amendment	1312	02/12/2026
Amendment	1318	03/05/2026
Amendment	1322	03/10/2026
Amendment	1333	03/19/2026
Amendment	1338	03/27/2026

3. Supplement Provides For: an additional presentation of WEGOVY (semaglutide) injection in a single dose manual prefilled syringe (mPFS).

4. Disciplines Involved/Consults Needed:

Disciplines/Consults	Recommendation	Date	Reviewer
OPMA-Microbiology	Adequate	02/22/2026	David Quan
OPMA-Facility	Adequate	03/31/2026	Ruth Moore

5. Executive Summary:

20 Page(s) have been Withheld in Full as b4 (CCI/TS) immediately following this page

Offices of Pharmaceutical Quality
Quality Assessment
Supplemental New Drug Application (sNDA) / Abbreviated New Drug Application (sANDA)

The firm is using the same analytical methods for the proposed mPFS configuration with the exception of (b) (4). The current methods were transferred to the proposed (b) (4) site. Comparative testing between the proposed (b) (4) site with the Novo Nordisk Denmark site suggests that the proposed (b) (4) site is capable of performing the required testing. The methods remain suitable for their intended use.

Labeling

USPI labeling was revised for the single-dose prefilled syringe configuration. Recommendations were provided to revise Section 3 to add clarity and align with the formatting of the OZEMPIC labeling. Section 11 has been revised to provide the formulation for the mPFS configuration. Section 16 has been revised to provide the NDC for the proposed mPFS as well as to revise the storage conditions to list C prior to F (e.g. 2°C to 8°C (36°F to 46°F)).

3 DOSAGE FORMS AND STRENGTHS

[Injection]: clear, colorless solution available as follows:

Single-Dose Prefilled Pens

Dose per Injection	Total Strength per Total Volume
0.25 mg	0.25 mg / 0.5 mL
0.5 mg	0.5 mg / 0.5 mL
1 mg	1 mg / 0.5 mL
1.7 mg	1.7 mg/0.75 mL
2.4 mg	2.4 mg/0.75 mL
7.2 mg (WEGOVY HD)	7.2 mg/0.75 mL

Single-Dose Prefilled Syringes

Dose per Injection	Total Strength per Total Volume
0.25 mg	0.25 mg / 0.5 mL
0.5 mg	0.5 mg / 0.5 mL
1 mg	1 mg / 0.5 mL
1.7 mg	1.7 mg/0.75 mL
2.4 mg	2.4 mg/0.75 mL

Tablets: available as:

Tablet strength	Description
1.5 mg	White to light yellow, round shaped debossed with "1.5" on one side and "novo" on the other side
4 mg	White to light yellow, round shaped debossed with "4" on one side and "novo" on the other side
9 mg	White to light yellow, round shaped debossed with "9" on one side and "novo" on the other side
25 mg	White to light yellow, oval shaped debossed with "25" on one side and "novo" on the other side

11 DESCRIPTION

WEGOVY contains semaglutide, a human GLP-1 receptor agonist (or GLP-1 analog). The peptide backbone is produced by yeast fermentation. The main protraction mechanism of semaglutide is albumin binding, facilitated by modification of position 26 lysine with a hydrophilic spacer and a C18 fatty di-acid. Furthermore, semaglutide is modified in position 8 to provide stabilization against degradation by the enzyme dipeptidyl-peptidase 4 (DPP-4). A minor modification was made in position 34 to ensure the attachment of only one fatty di-acid. The molecular formula is $C_{187}H_{291}N_{45}O_{59}$ and the molecular weight is 4113.58 g/mol.



A Author

FDA to Applicant: Revisions to improve clarity and for consistency with the presentation in the Ozempic PI (Section 3) and, as applicable, Section

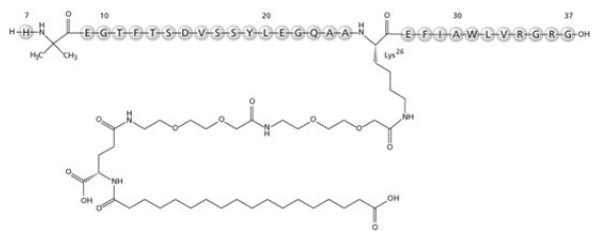
[See more](#)

C CIVT (Christina Talley)

Applicant to FDA: We accept this change.

Offices of Pharmaceutical Quality
Quality Assessment
Supplemental New Drug Application (sNDA) / Abbreviated New Drug Application (sANDA)

Figure 1. Structural Formula of Semaglutide



WEGOVY injection is a sterile, aqueous, clear, colorless solution. Each 0.5 mL single-dose pen contains a solution of WEGOVY containing 0.25 mg, 0.5 mg or 1 mg of semaglutide; and each 0.75 mL single-dose pen contains a solution of WEGOVY containing 1.7, 2.4 mg or 7.2 mg of semaglutide. Each 0.5 mL single-dose prefilled syringe contains a solution of WEGOVY containing 0.25 mg, 0.5 mg or 1 mg of semaglutide; and each 0.75 mL single-dose prefilled syringe contains a solution of WEGOVY containing 1.7, 2.4 mg of semaglutide. Each 1 mL of WEGOVY contains the following inactive ingredients: disodium phosphate dihydrate, 1.42 mg; sodium chloride, 8.25 mg; and water for injection. WEGOVY has a pH of approximately 7.4. Hydrochloric acid or sodium hydroxide may be added to adjust pH.

WEGOVY tablets include semaglutide as a white to almost white hygroscopic powder. Each tablet of WEGOVY contains 1.5 mg, 4 mg, 9 mg or 25 mg of semaglutide and the following inactive ingredients: magnesium stearate and salcaprozate sodium (SNAC).

16 HOW SUPPLIED/STORAGE AND HANDLING

WEGOVY Injection

How Supplied

WEGOVY injection is a clear, colorless solution in a prefilled, disposable, single-dose pen or single dose syringe with an integrated needle. It is supplied in cartons containing 4 pen or 4 syringes in the following packaging configurations:

Device Type	Name	Total Strength per Total Volume	NDC
Pen	WEGOVY	0.25 mg/0.5 mL	0169-4525-14
Pen		0.5 mg/0.5 mL	0169-4505-14
Pen		1 mg/0.5 mL	0169-4501-14
Pen		1.7 mg/0.75 mL	0169-4517-14
Pen		2.4 mg/0.75 mL	0169-4524-14
Pen	WEGOVY HD	7.2 mg/0.75 mL	0169-4572-14
Syringe	WEGOVY	0.25 mg/0.5 mL	XXXX-XXXX-XX
Syringe		0.5 mg/0.5 mL	XXXX-XXXX-XX
Syringe		1 mg/0.5 mL	XXXX-XXXX-XX
Syringe		1.7 mg/0.75 mL	XXXX-XXXX-XX
Syringe		2.4 mg/0.75 mL	XXXX-XXXX-XX

Recommended Storage

Store the WEGOVY prefilled single-dose pen or single-dose syringe in the refrigerator from 2°C to 8°C (36°F to 46°F). If needed, prior to the pen or syringe cap removal, the pen can be kept from 8°C to 30°C (46°F to 86°F) up to 28 days. Do not store WEGOVY injection in the freezer or directly adjacent to the refrigerator

cooling element. Do not freeze WEGOVY injection and do not use if it has been frozen. Protect WEGOVY injection from light. WEGOVY injection must be kept in the original carton until time of administration. Discard the WEGOVY pen or syringe after use.

WEGOVY Tablets

How Supplied

WEGOVY tablets are available as:

53

Author

FDA to Applicant: For scientific communications directed to prescribers, we use C and then F. For the MG, this is acceptable to include F and then C. This See more

CIVT (Christina Talley)

Applicant to FDA: We accept this change.

Offices of Pharmaceutical Quality
Quality Assessment
Supplemental New Drug Application (sNDA) / Abbreviated New Drug Application (sANDA)

Tablet strength	Description	Package Configuration	NDC Number
1.5 mg	White to light yellow, round shaped debossed with "1.5" on one side and "novo" on the other side	Bottle of 30 tablets	0169-4415-31
4 mg	White to light yellow, round shaped debossed with "4" on one side and "novo" on the other side	Bottle of 30 tablets	0169-4404-31
9 mg	White to light yellow, round shaped debossed with "9" on one side and "novo" on the other side	Bottle of 30 tablets	0169-4409-31
25 mg	White to light yellow, oval shaped debossed with "25" on one side and "novo" on the other side	Bottle of 30 tablets	0169-4425-31

Recommended Storage

Store at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature]. Store and dispense WEGOVY tablets in the original bottle. Store WEGOVY tablet in the original bottle until use to protect tablets from moisture. Store WEGOVY tablets in a dry place away from moisture.

An example of the carton labeling for the proposed mPFS presentation was provided:



Assessment: Adequate

Offices of Pharmaceutical Quality
Quality Assessment
Supplemental New Drug Application (sNDA) / Abbreviated New Drug Application (sANDA)

The 7.2 mg WEGOVY single-dose auto-injector Pen was approved in NDA 215256 S-029 on 3/19/2026. The 7.2 mg strength was not included in this proposed mPFS presentation. Of note, due to the tablet formulation approved under NDA 218316, and the drug product labels being combined, concurrent review of NDA 218316 S-003 for these same labeling changes is being performed. There are no quality changes to NDA 218316 S-003 as a result of the subject supplement NDA 215256 S-031.

The firm has implemented the recommended edits for CMC USPI Sections 3, 11, and 16. The carton container has been provided for the 0.25 mg strength as an example. The firm has not revised the temperature format for the carton label to match the 2°C to 8°C (36°F to 46°F) format, however the firm provided justification in sister supplement NDA 209637 S-039 labeling response to maintain the 36°F to 46°F (2°C to 8°C) due to the carton labeling being patient facing materials. This formatting would be in alignment with the IFU. Consult with DMEPA does not have any concerns about potential medication errors due to the formatting, and the firm's justification is acceptable.

Final Labeling is deferred to OND.

7. Recommendations:

☒ Supplement is CMC Approvable

☐ Supplement is NOT CMC Approvable (Provide ANDA CR Major Justification statement):

(Choose ☐ IR, ☐ NDA CR ☐ ANDA CR-Minor, ☐ ANDA CR-Major)

<u>Comments / Deficiencies to be communicated:</u> None

--END--



Sarah
Zimmermann

Digitally signed by Sarah Zimmermann

Date: 4/30/2026 11:11:19AM

GUID: 59aeccce003cb2b7276f6582f89c37ee



Rohit
Kolhatkar

Digitally signed by Rohit Kolhatkar

Date: 4/30/2026 12:58:18PM

GUID: 57bf531500b52a2eccd5395bec77ebc2

Comments: concur with approval recommendation from CMC perspective

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

215256Orig1s031

CLINICAL PHARMACOLOGY
REVIEW(S)

Office of Clinical Pharmacology Review Addendum

NDA Numbers	215256 / S-031 and 209637 / S-039																	
Link to EDR	\\CDSESUB1\evsprod\NDA215256\1202 [WEGOVY: NDA 215256 / SDN 1235] \\CDSESUB1\evsprod\NDA209637\1476 [OZEMPIC: NDA 209637 / SDN 1791]																	
Submission Date	1/5/2026																	
Submission Type	CMC Prior Approval Supplement (PAS)																	
Brand Name	WEGOVY and OZEMPIC																	
Generic Name	Semaglutide																	
Dosage Form and Strength	[WEGOVY] Pre-filled syringe for single dose manual injection (mPFS): • 0.25 mg (0.5 mg/mL) • 0.5 mg (1.0 mg/mL) • 1.0 mg (2.0 mg/mL) • 1.7 mg (2.27 mg/mL) • 2.4 mg (3.2 mg/mL) [OZEMPIC] Single-patient-use pen: • 0.25 mg (0.68 mg/mL) • 0.5 mg (0.68 mg/mL) • 1 mg (1.34 mg/mL) • 2 mg (2.68 mg/mL)																	
Route of Administration	Subcutaneous (SC)																	
Dosage and Administration	[WEGOVY] • Administer WEGOVY injection once weekly (QW) as an adjunct to diet and increased physical activity, on the same day each week, at any time of day, with or without meals. • SC Injection in the abdomen, thigh, or upper arm. • Initiate at 0.25 mg QW for 4 weeks. Then follow the dosage escalation schedule below, titrating every 4 weeks to achieve the maintenance dosage. <table border="1"> <thead> <tr> <th></th><th>Weeks</th><th>Once-weekly Subcutaneous Injection Dosage</th></tr> </thead> <tbody> <tr> <td>Starting Dosage</td><td>1 through 4</td><td>0.25 mg</td></tr> <tr> <td rowspan="3">Dosage Escalation</td><td>5 through 8</td><td>0.5 mg</td></tr> <tr> <td>9 through 12</td><td>1 mg</td></tr> <tr> <td>13 through 16</td><td>1.7 mg</td></tr> <tr> <td>Maintenance Dosage</td><td>17 and onward</td><td>(b) (4)</td></tr> </tbody> </table>			Weeks	Once-weekly Subcutaneous Injection Dosage	Starting Dosage	1 through 4	0.25 mg	Dosage Escalation	5 through 8	0.5 mg	9 through 12	1 mg	13 through 16	1.7 mg	Maintenance Dosage	17 and onward	(b) (4)
	Weeks	Once-weekly Subcutaneous Injection Dosage																
Starting Dosage	1 through 4	0.25 mg																
Dosage Escalation	5 through 8	0.5 mg																
	9 through 12	1 mg																
	13 through 16	1.7 mg																
Maintenance Dosage	17 and onward	(b) (4)																

</

	To reduce the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction or non-fatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease.
Applicant	Novo Nordisk, Inc.
Associated IND	IND 151138 (WEGOVY) and IND 079754 (OZEMPIC)
OCP Review Team	Chongwoo Yu, PhD Li Wang, PhD
OCP Final Signatory	Li Wang, PhD Team Leader, Division of Cardiometabolic and Endocrine Pharmacology (DCEP)
OND Division	Division of Diabetes, Lipid Disorders, and Obesity (DDLO)

Table of Contents

1. EXECUTIVE SUMMARY	5
1.1 Recommendations.....	5
1.2 Post-Marketing Requirements and Commitments.....	5
2. SUMMARY OF CLINICAL PHARMACOLOGY ASSESSMENT.....	5
2.1 Comparison of Delivery Devices.....	5
2.2 Cross-study Pharmacokinetic (PK) Comparison.....	6
2.3 Drug Delivery.....	8
2.3.1 Extractable Volume.....	8
2.3.2 Injection Force	8
2.3.3 Injection Rate: Duration of Injection Time	8
2.3.4 Literature Reports: Needle Lengths	8
2.3.5 Physicochemical Property: Viscosity.....	9
2.4 Conclusion.....	9

1. EXECUTIVE SUMMARY

Reference is made to Dr. Chongwoo Yu's Clinical Pharmacology reviews for NDA 215256 / S-031 (WEGOVY; dated February 20, 2026) and NDA 209637 / S-039 (OZEMPIC; dated March 2, 2026) in DARRTS. The purpose of this review addendum is to summarize additional supporting information and the Clinical Pharmacology review team's rationale for recommending approval of the supplemental new drug applications (sNDAs) for both WEGOVY and OZEMPIC. The purpose of these sNDAs is to propose an additional presentation of WEGOVY and OZEMPIC in a single dose manual injection prefilled syringe (mPFS) in addition to the currently marketed pen-injectors. For the background of these submissions, refer to the aforementioned reviews.

1.1 Recommendations

The Office of Clinical Pharmacology (OCP), Division of Cardiomatabolic and Endocrine Pharmacology (DCEP) has reviewed the information contained in NDA 215256/S-031 and NDA 209637/S-039 and recommends approval of this NDA.

1.2 Post-Marketing Requirements and Commitments

None.

2. SUMMARY OF CLINICAL PHARMACOLOGY ASSESSMENT

2.1 Comparison of Delivery Devices

The proposed semaglutide manual prefilled syringe (mPFS) uses the prefilled syringe component of the single dose device (SDD) pen-injector (approved under WEGOVY). Table 1 compares the technical features related to delivery with the PDS290 pen-injector (approved under OZEMPIC), the SDD pen-injector, and the proposed semaglutide mPFS.

Table 1: Comparison of Semaglutide Delivery Devices

Characteristic	PDS290 pen-injector 	Single dose pen-injector for semaglutide 	Semaglutide mPFS 
Approved products	Ozempic®	Wegovy®	Proposed new delivery system for Ozempic® and Wegovy®
Intended use	Intended for once-weekly subcutaneous injection of semaglutide		
Type of delivery system	• Prefilled, multiple-dose, disposable, manually-activated pen-injector • Separate, compatible pen-needle	Prefilled, single-dose, disposable, auto-injector (Staked-in needle)	Prefilled, single-dose, disposable syringe (Staked-in needle)
Dose sizes	0.25 mg, 0.5 mg or 1 mg (selectable dose)	0.25 mg, 0.5 mg, 1 mg, 1.7 mg and 2.4 mg (dose-specific pen-injectors)	• 0.25 mg, 0.5 mg, 1 mg (Ozempic® and Wegovy®) • 1.7 mg and 2.4 mg (Wegovy®) (dose-specific prefilled syringes)
Dose volumes	(b) (4)		
Rate of injection	Dependent on the (b) (4) mechanism in the device	Dependent on the (b) (4) mechanism in the device	Controlled by the user

Primary packaging	Cartridge system (see 3.2.P.7 Cartridge 3.0 ml, System Report for EMK0502)	Syringe system (see 3.2.P.7 Prefilled syringe 1 ml System Report for EMK0595).	
Needle information	Nominal needle length of separate, compatible needles: 4 mm to 8 mm	Nominal needle extension: 6 mm	Nominal needle length: 12.7 mm
	Needle bore: 30-32 G	Needle bore: 29 G	Needle bore: 29 G
Injection site	Upper arm, abdomen, thigh		
Injection process	- The user attaches a compatible needle before injection. - The user inserts the needle perpendicularly into the skin. - The user injects by activating the device by pressing on the dose button.	- An integrated staked needle is present within the device. - The user activates the device by pressing its shield down on the skin perpendicularly. - The activated device drives the needle into the skin and injects the dose.	- An integrated staked needle is present on the prefilled syringe. - The user pinches the skin and manually inserts the needle at a 45° angle - User injects by manually pressing down on the plunger

Source: Table 2, Module 3.2.P.2.2, NDA 209637 / S-039 (submitted on January 5, 2026)

2.2 Cross-study Pharmacokinetic (PK) Comparison

As mentioned in the aforementioned Dr. Chongwoo Yu's Clinical Pharmacology reviews, the Applicant proposed to use results from available PK studies to bridge the different formulations (for OZEMPIC) and different injection parameters between the proposed mPFS and currently marketed pen-injectors for WEGOVY and OZEMPIC, respectively. In particular, the Applicant is using a cross-study PK comparison between Studies 4010 and 7560 to support that the PK parameters (i.e., AUC and C_{max}) are comparable despite the different needle lengths and injection rates.

In general, a cross-study PK comparison is discouraged due to several factors including the difference of study design, device and formulation, study population heterogeneity (e.g., varying demographics [age, sex, race, weight], disease states, etc.), and factors that can affect the bioanalytical method performance (e.g., different laboratories, bioanalytical methods with different dynamic range, and sample preparation, etc.) that may introduce bias and lead to unreliable conclusions. In order to determine the adequacy of the Applicant's approach, the Clinical Pharmacology review team looked further into these aspects of each study.

Study 4010

Study design: This was a randomized, double-blind, single dose, two-period, cross-over, PK study conducted in 28 healthy White subjects (hemoglobin A1C [HbA_{1c}] <6.5%; 16 females and 12 males; mean age of 48 years [range: 29-53 years]; mean body weight of 75.0 kg [range: 54.5-101.0 kg]; mean body mass index [BMI] of 25.7 kg/m² [range: 21.1-29.8 kg/m²]; 27 completed) comparing two different SC single dose treatments.

Treatments:

- Semaglutide A (synthetic, preserved formulation): 0.5 mg (1.34 mg/mL); Needle (b) (4), 12 mm × needle bore 30 G) and manual syringe (b) (4)
- Semaglutide B (recombinant, preserved formulation): 0.5 mg (1.34 mg/mL); Needle (b) (4), 12 mm × needle bore 30 G) and manual syringe (b) (4)

Study site and year: (b) (4) study completed in May 2013

Bioanalytical method:

- Platform: liquid chromatography – tandem mass spectrometry (LC-MS/MS)
- Dynamic range: 0.729-60.8 nmol/L
- Bioanalytical study site: (b) (4)

Study 7560

Study design: This was a randomized, open-label, cross-over, PK study conducted in 20 healthy subjects (HbA_{1c} <6.5%; 6 females and 14 males; 10 White, 7 Black, 3 Asian; mean age of 40.5 years [range: 25-54 years]; mean body weight of 80.8 kg [range: 66.0-97.8 kg]; mean BMI of 27.0 kg/m² [range: 22.7-29.8 kg/m²]; 18 completed) comparing two different SC single dose treatments.

Treatments:

- Semaglutide B (recombinant, preserved formulation); 0.5 mg (0.68 mg/mL); PDS290 pen-injector (needle length: 6 mm x needle bore: 32 G)
- Semaglutide B (recombinant, preserved formulation); 0.5 mg (1.34 mg/mL); PDS290 pen-injector (needle length: 6 mm x needle bore: 32 G)

Study site and year: Altasciences Clinical/Professional (Los Angeles, CA); study completed in May 2023

Bioanalytical method:

- Platform: LC-MS/MS
- Dynamic range: 0.729-60.8 nmol/L
- Bioanalytical study site: (b) (4)

The dose (i.e., single dose of 0.5 mg at 1.34 mg/mL) and formulation (i.e., recombinant, preserved formulation) were identical and the PK sampling/washout periods were similar. Study 4010 was conducted in Germany while Study 7560 was conducted in the US. Though Study 7560 had more diverse races enrolled, majority in both studies were White. The demographics and baseline characteristics of the participants from both studies were comparable. It should be noted that no clinically significant differences in semaglutide PK were observed based on age (<65 years, 65 to 74, ≥75 years old), sex, race (White, Asian, or Black or African American), ethnicity, body weight, upper GI disease (i.e. chronic gastritis and/or gastroesophageal reflux disease), renal impairment [estimated glomerular filtration rate (eGFR) ≥30 to <90 mL/minute], or mild, moderate, and severe hepatic impairment (Child-Pugh Class A-C) or fibrosis stage (F2 or F3 in patients with MASH) according to the WEGOVY product label. The same LC-MS/MS bioanalytical method was used, and study sample analysis were conducted at the same bioanalytical laboratory (b) (4). It should also be noted that the proposed mPFS does not involve complex engineering features of the pen-injector. Considering this information, while not ideal, the Clinical Pharmacology review team concludes that the Applicant's cross-study PK comparison approach is reasonable in this case to support that PK parameters between the proposed mPFS (i.e., 12 mm needle length and user dependent injection rate) and the approved pen-

injectors (i.e., 6 mm needle length and user independent injection rate) are comparable, together with other supporting information and data described below in this review.

2.3 Drug Delivery

2.3.1 Extractable Volume

The Applicant assessed the extractable volume using the proposed mPFS. In the extraction volume assessment involved a sample size of (b) (4) for each respective semaglutide drug product (i.e., 0.5 mg/mL, 2.0 mg/mL, and 3.2 mg/mL) and the acceptance criteria was a minimum single dose injection volume of (b) (4) for semaglutide 0.5 mg/mL or (b) (4); and (b) (4) mL for semaglutide 3.2 mg/mL, respectively. The Applicant's human factors validation study (i.e., Human Factors Engineering Report [UT342]) documents that users can deliver the intended volume (i.e., 0.5 or 0.75 mL) to the intended administration site with reference to the available instructions with the proposed semaglutide mPFS. The Office of Product Quality (OPQ) review team (primary reviewer: Dr. Sarah Zimmermann) concurs with the Applicant's conclusion from a product quality standpoint.

2.3.2 Injection Force

The Applicant conducted a foundational data study (FE265) to determine: (1) maximum injection force (young and elderly females); and (2) how injection forces differ depending on grip. The Applicant concluded that the Chuck Pinch grip provided a greater average maximum force compared to the precision grip in females of 10-12 years old (N=44) and 65+ years old (N=42). Based on this study outcome, the Applicant concluded that there were no difficulties regarding the injection force needed to deliver the desired dose using the proposed mPFS and the grip represented in the Information for Use (IFU) illustration was updated to the "chuck pinch" grip.

2.3.3 Injection Rate: Duration of Injection Time

The injection duration time of both the currently marketed WEGOVY and OZEMPIC pen-injectors are 6 seconds. The IFU of OZEMPIC instructs users to "count 6 seconds while keeping the dose button pressed." The injection rate of the proposed mPFS is user dependent. One way to ensure semaglutide is dosed with a comparable injection rate between the currently approved pen-injectors and the proposed mPFS is to specify the injection duration time (i.e., 6 sec.) on the IFU of the proposed mPFS. The Clinical Pharmacology review team has proposed to add "Keep a 45-degree angle. With a slow and constant pressure, slowly count to 6 while pushing the plunger rod all the way down, until the plunger stops" to the IFU of the proposed mPFS for both WEGOVY and OZEMPIC.

2.3.4 Literature Reports: Needle Lengths

As mentioned in Section 2.2.4 of Dr. Chongwoo Yu's Clinical Pharmacology review on NDA 215256 / S-032 dated February 20, 2026, the Applicant submitted literature reports including the following as supporting evidence of comparable PK or pharmacodynamics (PD) despite the difference of needle lengths:

- Hirose *et al.*, 2013 (Comparison of insulin PK injected with a new 4-mm needle vs 6- and 8-mm needles accounting for endogenous insulin and C-peptide secretion kinetics in non-diabetic adult males): Shorter needles of 4 mm reliably achieved similar PK profiles when compared to injections with longer needles of 8 mm
- Schwartz *et al.*, 2004 (Comparing glycemic control achieved with a 6 mm needle vs. a 12.7 mm needle in obese patients with diabetes mellitus): Insulin administered SC with 6 mm or 12.7 mm needles result in equivalent glycemic outcomes and no clinically relevant differences in PD of insulins.

The applicability of these literature reports to semaglutide is discussed in Section 2.3.5 below.

2.3.5 Physicochemical Property: Viscosity

Viscosity is a fundamental physicochemical property measuring a fluid's internal resistance to flow, shear stress, or deformation. It represents a fluid's "thickness" or internal friction, where higher viscosity requires greater force to expel from syringes or auto-injectors (i.e., injection force). Semaglutide injections have a comparable viscosity to insulin injections while monoclonal antibodies (mAbs) have a much higher and variable viscosity (per Elsa, FDA's generative Artificial Intelligence tool):

- Water: 1.002 cP (centipoise)
- Insulin injections: (b) (4) cP
- WEGOVY and OZEMPIC: (b) (4) cP
- mAb injections: (b) (4) cP

The following factors are known to affect viscosity:

- **Protein concentration:** mAbs are often formulated at 100-150 mg/mL or higher for SC delivery, while semaglutide and insulin injections are at much lower concentrations (0.68-2.68 mg/mL for OZEMPIC; 0.5-3.2 mg/mL for WEGOVY; and (b) (4) mg/mL for insulin)
- **Molecular size:** mAbs (~150 kDa) are significantly larger than insulin (~6 kDa) or semaglutide (~4 kDa)
- **Protein-protein interactions:** High-concentration mAb formulations experience increased intermolecular interactions

Given the comparable viscosity, lower protein concentration, and smaller molecular size of semaglutide compared to insulin, the Clinical Pharmacology review team finds the Applicant's extrapolation of insulin PK and PD studies (mentioned in Section 2.3.4) between PFS and auto-injector in literature to semaglutide to be reasonable.

2.4 Conclusion

In totality, the Clinical Pharmacology review team finds the Applicant's overall justifications addressing the impact of injection parameters on semaglutide PK to be reasonable. The sNDA is acceptable from the Clinical Pharmacology perspective and the Clinical Pharmacology review team recommends **approval** for these sNDAs.

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

CHONGWOO YU
04/23/2026 04:19:42 PM

LI WANG
04/23/2026 08:55:31 PM

Office of Clinical Pharmacology Review

NDA Number	215256 / S-031		
Link to EDR	\\CDSESUB1\evsprod\NDA215256\1202 [SDN 1235]		
Submission Date	1/5/2026		
Submission Type	CMC Prior Approval Supplement (PAS)		
Brand Name	WEGOVY		
Generic Name	Semaglutide		
Dosage Form and Strength	Pre-filled syringe for single dose manual injection (mPFS): • 0.25 mg (0.5 mg/mL) • 0.5 mg (1.0 mg/mL) • 1.0 mg (2.0 mg/mL) • 1.7 mg (2.27 mg/mL) • 2.4 mg (3.2 mg/mL)		
Route of Administration	Subcutaneous (SC)		
Dosage and Administration	• Administer WEGOVY injection once weekly (QW) as an adjunct to diet and increased physical activity, on the same day each week, at any time of day, with or without meals. • SC Injection in the abdomen, thigh, or upper arm. • Initiate at 0.25 mg QW for 4 weeks. Then follow the dosage escalation schedule below, titrating every 4 weeks to achieve the maintenance dosage.		
		Weeks	Once-weekly Subcutaneous Injection Dosage
	Starting Dosage	1 through 4	0.25 mg
	Dosage Escalation	5 through 8	0.5 mg
		9 through 12	1 mg
		13 through 16	1.7 mg
	Maintenance Dosage	17 and onward	(b) (4)
	(b) (4)		
Approved Indications	WEGOVY injection is indicated in combination with a reduced calorie diet and increased physical activity: • To reduce the risk of major adverse cardiovascular (CV) events (CV death, non-fatal myocardial infarction, or non-fatal stroke) in adults with established CV disease and either obesity or overweight. • To reduce excess body weight and maintain weight reduction long term in:		

	- Adults and pediatric patients aged 12 years and older with obesity. - Adults with overweight in the presence of at least one weight-related comorbid condition. • For the treatment of noncirrhotic metabolic dysfunction-associated steatohepatitis (MASH), formerly known as nonalcoholic steatohepatitis (NASH), with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis) in adults.
Applicant	Novo Nordisk, Inc.
Associated IND	IND 151138
OCP Review Team	Chongwoo Yu, PhD Li Wang, PhD
OCP Final Signatory	Li Wang, PhD Team Leader, Division of Cardiometabolic and Endocrine Pharmacology (DCEP)
OND Division	Division of Diabetes, Lipid Disorders, and Obesity (DDLO)

Table of Contents

1. EXECUTIVE SUMMARY	4
1.1 Recommendations.....	4
1.2 Post-Marketing Requirements and Commitments.....	5
2. SUMMARY OF CLINICAL PHARMACOLOGY ASSESSMENT.....	5
2.1 Regulatory History	5
2.2 Applicant's Justification and Supporting Data/Information	6
2.2.1 Formulation	6
2.2.2 Impact of Differences in Device-related Injection Parameters on Semaglutide PK.....	6
2.2.3 PK Data	8
2.2.4 Literature Reports.....	9
2.3 Clinical Pharmacology Review Team's Assessment	9
2.3.1 Assessment of PK Data	9
2.3.2 Assessment of the Effect of Injection Parameters on Semaglutide PK.....	11
2.3.3 Assessment of Literature Reports.....	13
2.4 Conclusion	13

1. EXECUTIVE SUMMARY

The Applicant submitted a Chemistry, Manufacturing, and Controls (CMC) Prior Approval Supplement (PAS) to propose an additional presentation of WEGOVY in a single dose manual injection prefilled syringe (mPFS) (b) (4)

WEGOVY is currently marketed in a single dose device (SDD) pen-injector.

The proposed WEGOVY mPFS is intended for once-weekly (QW) subcutaneous (SC) injection of semaglutide 0.25 mg, 0.5 mg, 1.0 mg, 1.7 mg, and 2.4 mg solution. The WEGOVY mPFS is a drug-device combination product consisting of the semaglutide solution for injection in a single dose PFS assembled with a plunger rod and a finger grip for manual injection. The container closure system for the mPFS is the same prefillable syringe component as is contained in the current WEGOVY SDD pen-injector for semaglutide. The semaglutide formulation in the mPFS is the same as the current WEGOVY semaglutide formulation in the SDD pen-injector.

In this submission, the Applicant adopted an approach of justifying that the pharmacokinetics (PK) of semaglutide remains unchanged when administered using the proposed mPFS, compared to the SDD pen-injector, irrespective of the difference in injection parameters. The Sponsor is referring to three relative bioavailability (BA) studies: Study 4590 (NDA 215256; SDN 001; submitted on December 4, 2020), Study 4010 (NDA 209637; SDN 001; submitted on December 5, 2016), and Study 7560 (NDA 209637/S-039; SDN 1791; submitted on January 5, 2026) for their justification. Studies 4590 and 4010 have been reviewed as part of previous NDA evaluations and Study 7560 was not fully reviewed for bioequivalence (BE) assessment but data was used for cross-study comparison to support the approval of this supplemental new drug application (sNDA).

1.1 Recommendations

The Office of Clinical Pharmacology (OCP), Division of Cardiomatabolic and Endocrine Pharmacology (DCEP) has reviewed the information contained in NDA 215256/S-031 and recommends **approval** of this NDA. The key review issues with specific recommendations and/or comments are summarized below:

Table 1: Summary of Review Issues and Recommendations

Review Issue	Recommendations and Comments
Unchanged PK	Applicant's justification demonstrating unchanged PK between the newly proposed mPFS and the currently marketed SDD pen-injector is acceptable.
Bridge between the proposed mPFS and the currently marketed SDD pen-injector formulations	There is no change in formulations.
Labeling	The only change proposed is adding the new presentation (mPFS) which is acceptable.

1.2 Post-Marketing Requirements and Commitments

None.

2. SUMMARY OF CLINICAL PHARMACOLOGY ASSESSMENT

2.1 Regulatory History

Reference is made to the Type C, Guidance meeting Written Responses letter issued on August 29, 2024, and the Information Request letter issued on November 15, 2024, that address the Applicant's questions regarding their proposal of introducing the additional WEGOVY mPFS presentation.

In summary, the Applicant proposed to use available relative BA study results to bridge the preservative-free formulation of WEGOVY in SDD pen-injector and the preserved formulation of OZEMPIC in PDS290 pen-injector to the preservative-free formulation in the proposed mPFS. The Applicant also proposed a device bridging strategy between the SDD pen-injector or PDS290 pen-injector and the proposed mPFS for both WEGOVY and OZEMPIC. The Applicant acknowledged that a difference in the needle length and injection angle may have an impact on the PK profile of the drug. To mitigate uncertainty surrounding the precision of injection to target site, the Applicant proposed specific injection instructions to ensure the drug is delivered to the intended tissue and conducting a full human factors program. In addition, the Applicant stated that they have some interim data to suggest no case related to adverse/serious adverse events have been observed with these delivery systems.

In response to the Applicant's question, the Agency recommended the Applicant to conduct a PK comparability study of the proposed mPFS and auto-injector to establish a scientific bridge. Alternatively, the Applicant may submit additional data (e.g., literature or in house) that characterizes how changes in presentation (e.g., auto-injector and mPFS) and associated changes in injection parameters (e.g., depth, needle bore, injection angle, injection pressure, etc.) affect the PK of semaglutide, or other related molecules. If there are PK differences observed, or some degree of uncertainty in the data itself or applicability of the data to semaglutide, the Applicant should justify how such potential PK change is not clinically meaningful. The Agency also noted that, if the Applicant does use examples of other peptide products, they will need to provide justification on why the PK differences would be expected to be similar between semaglutide and the other peptide products.

Subsequently, on September 18, 2024 (NDA 215256, SDN: 711), the Applicant submitted a Request for Clarification on the Agency's comments included in the August 29, 2024, Type C meeting Written Responses, in which the Applicant presented additional data to support the device bridging strategy for both WEGOVY and OZEMPIC in lieu of a new PK comparability study. Reference is made to the Information Request letter dated November 15, 2024. In response, the Agency clarified that based on the information provided in the June 14, 2024, meeting package, and additional information submitted in the Applicant's September 18, 2024, submission, the Agency found the Applicant's proposal acceptable for submission of their sNDAs. The Agency stated that the final determination on the acceptability of the device bridging strategy will be made at the time of the sNDA review.

2.2 Applicant's Justification and Supporting Data/Information

2.2.1 Formulation

Semaglutide solution for injection is a colorless or almost colorless liquid, free from turbidity and essentially free from particulate matter, intended for SC injection. The drug product solution is provided as isotonic solution with a pH of 7.4 ready for injection. The proposed mPFS variants contain the preservative-free semaglutide drug product formulation and concentrations, which are identical to those of the approved SDD pen-injector variants. Details on the composition of semaglutide drug products in the approved SDD pen-injector (i.e., WEGOVY injection), the PDS290 pen-injector (i.e., OZEMPIC injection), and the proposed mPFS are presented below (Table 2).

Table 2: Semaglutide Formulations and Devices

Device	Preservative-free formulation		Preserved formulation
	Single-dose pen-injector	Proposed mPFS	PDS290 pen-injector ^a
Active substance (concentration)			
Semaglutide dose			
0.25 mg	0.5 mg/mL		0.68 mg/mL, 1.34 mg/mL
0.5 mg	1.0 mg/mL		0.68 mg/mL, 1.34 mg/mL, 1.34 mg/mL
1.0 mg	2.0 mg/mL		-
1.7 mg	2.27 mg/mL		-
2.4 mg	3.2 mg/mL		-
Excipients (quantity per mL)			
Disodium phosphate dihydrate	1.42 mg		1.42 mg
Propylene glycol	-		14.0 mg
Sodium chloride	8.25 mg		-
Phenol	-		5.50 mg ^b
Hydrochloric acid	(b) (4)		
Sodium hydroxide			
Water for injections			

^aThe PDS290 pen-injector containing the preserved semaglutide formulation is approved for Ozempic® in the US. This is also approved for Wegovy® in markets outside the US, in the following concentrations: 0.25 mg (0.68 mg/mL), 0.5 mg (1.34 mg/mL), 1.0 mg (1.34 mg/mL), 1.7 mg (2.27 mg/mL) and 2.4 mg (3.2 mg/mL)

(b) (4)

^bTo reach pH 7.4.

Abbreviations: mPFS = pre-filled syringe for manual injection;

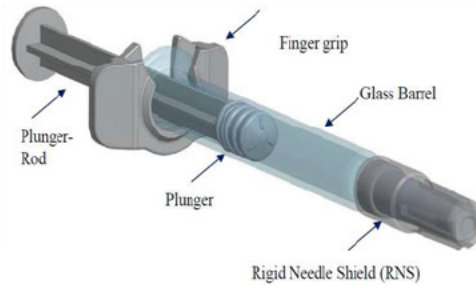
(b) (4)

Source: Table 1-2, Module 2.7.1, NDA 215256 / S-031 (SDN: 1235), Submitted on January 5, 2026

2.2.2 Impact of Differences in Device-related Injection Parameters on Semaglutide PK

The 1 mL PFS is assembled in a mPFS with a (b) (4) plunger rod and (b) (4) finger grip extension (Figure 1).

Figure 1: PFS for manual injection (not shown in true colors)



Source: Figure 1, Module 3.2.P.7, NDA 215256 / S-031 (SDN: 1235), Submitted on January 5, 2026

The PFS part of the SDD pen-injector is identical to the proposed mPFS, except that the mPFS includes a plunger rod and a finger grip to enable manual administration, whereas the SDD pen-injector is an automated device in which only part of the needle is exposed during administration. Manual administration compared to automated injection may lead to differences in the following injection parameters: needle length, angle of injection, rate of injection, and injection pressure.

Summary of Injection Parameters

Table 3 provides the overview of the injection parameters in the approved and proposed presentations.

Table 3: Summary of Injection Parameters for the Approved and Proposed Presentations

Parameter	PDS290 pen-injector (Ozempic®)	Single dose auto-injector (Wegovy®)	Proposed mPFS	Difference in the proposed mPFS
Effective injection depth	4 mm	6 mm	8.9 mm ^a	Additional length compared to Ozempic® and Wegovy®.
Needle bore	32G	29G	29G	No change compared to Wegovy®
Injection pressure	(b) (4)			

^aAs angle injections reduce the effective needle length, the needle length of 12 mm is presented as 8.9 mm due to a recommended needle insertion at 45° (see Figure 1). The effect of a skin fold on subcutaneous adipose layer depth in understanding the achieved injection depth is not included in the evaluation.

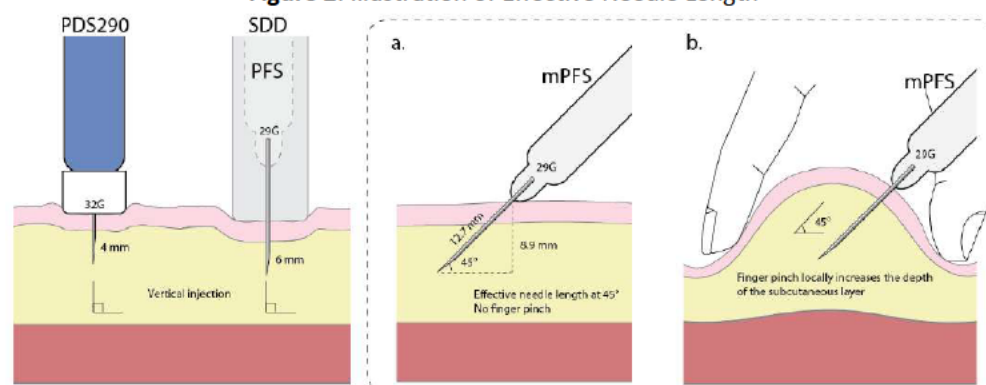
^b The user is not required to exert additional force with the delivery device onto the skin beyond what is needed for the needle to penetrate the skin.

Source: Table 1, Page 6, NDA 215256 (SDN: 711), Submitted on September 18, 2024

Effect of Needle Length and Injection Angle

Angle injections reduce the effective needle length, and skinfold increases the depth of the SC adipose layer, as discussed in de Lucio *et al.* (2023) in their study modelling the effect of the skinfold (pinch) (Figure 2).

Figure 2: Illustration of Effective Needle Length



Injection with the PDS290 pen-injector (Ozempic®) and single dose auto-injector (Wegovy®) will be perpendicular to the skin layer. The effective needle penetration at this angle will be equivalent to the needle length of the pen-needle (4 mm), or the needle extension of the single-dose device (6 mm). Angle injections reduce the effective needle length (see inset a). The ability to deliver the injection in the subcutaneous adipose layer is further enhanced by pinching of the skin (see inset b). Calculation of effective needle length, according to Hirsch et al., 2014 [1]. Illustration of effect of finger pinching on subcutaneous adipose layer, according to de Lucio et al., 2023 [2]

Source: Figure 1, Page 5, NDA 215256 (SDN: 711), Submitted on September 18, 2024

2.2.3 PK Data

A summary of individual PK studies that the Applicant is primarily relying on in support of their proposed introduction of mPFS is provided in Table 4.

Table 4: Summary of Clinical PK Studies Providing Data for the Current Summary

Study ID, Region, Analysis method	Study design and objectives	Participants exposed (M/F)	Treatment; Dose; Device	Results
Study 4010 DE LC-MG	A randomised, double-blind, two-period, cross-over design study investigating the semaglutide concentration profiles after single-dose s.c. injections of 0.5 mg synthetic semaglutide (semaglutide A) and 0.5 mg recombinant semaglutide (semaglutide B) administered using syringe and needle, in healthy participants.	28 participants (12/16)	1. Semaglutide A (synthetic, preserved formulation); 0.5 mg (1.34 mg/mL); Needle (b) (4) 12 mm x 30 G) and manual syringe (b) (4) 2. Semaglutide B (recombinant, preserved formulation); 0.5 mg (1.34 mg/mL); Needle (b) (4) 12 mm x 30 G) and manual syringe (b) (4)	- Bioequivalence was demonstrated between synthetic semaglutide and recombinant semaglutide. - No apparent or unexpected safety or tolerability issues were observed for either synthetic semaglutide or recombinant semaglutide.
Study 4590 DE LC-MS/MS	A randomised, open-label, parallel group study comparing the PK profile of semaglutide s.c. dosed with the single-dose pen-injector to PK profile obtained after dosing with the PDS290 pen-injector with their respective drug products, in participants with overweight or obesity.	68 participants (48/16)	1. Semaglutide D (preservative-free formulation); 0.25 mg (0.5 mg/mL), 0.5 mg (1.0 mg/mL), 1 mg (2.0 mg/mL), 1.7 mg (2.27 mg/mL), 2.4 mg (3.2 mg/mL); Single-dose pen-injector (needle: 6 mm x 29G). 2. Semaglutide B (preserved formulation); 0.25 mg, 0.5 mg (1.0 mg/mL), 1 mg, 1.7 mg, 2.4 mg (3.0 mg/mL); PDS290 pen-injector (needle: 6 mm x 32G).	- Bioequivalence was demonstrated between the semaglutide drug product used with the single-dose pen-injector and the semaglutide drug product used with the PDS290 pen-injector for the semaglutide 2.4 mg dose and for the semaglutide 1.0 mg dose. - The treatments had similar effect on body weight. - No unexpected safety or tolerability issues were identified.
Study 7560 US LC-MS/MS	A randomised, open-label, cross-over design study investigated the PK profile of semaglutide after two single administrations of 0.5 mg semaglutide (PDS290 pen-injector) given by s.c. injection with different semaglutide concentrations and separated by 7 to 11 weeks, in healthy participants.	20 participants (14/6)	1. Semaglutide B (recombinant, preserved formulation); 0.5 mg (0.68 mg/mL); PDS290 pen-injector (needle: 6 mm x 32G). 2. Semaglutide B (recombinant, preserved formulation); 0.5 mg (1.34 mg/mL); PDS290 pen-injector (needle: 6 mm x 32G).	- Bioequivalence between 0.5 mg of semaglutide B with drug product concentrations of 0.68 mg/mL and 1.34 mg/mL was confirmed. The estimated treatment ratio and 90% CI for AUC and C_{max} were within the acceptance interval of [0.80; 1.25]. - No unexpected safety or tolerability issues were identified.

Source: Table 2-1, Module 2.7.1, NDA 215256 / S-031 (SDN: 1235), Submitted on January 5, 2026

2.2.4 Literature Reports

The Applicant states that numerous investigations have evaluated the impact of the nominal needle length for SC delivery of other peptide-based therapeutics, such as insulins. Insulin and semaglutide are both peptide-based therapeutics administered via the SC route, and their absorption from the injection site relies on similar physiological processes within the SC tissue. The Applicant believes that this similarity supports that studies conducted with insulin can be leveraged to predict how factors like needle length may affect the PK of semaglutide.

The Applicant reports literature data supporting that when insulin is deposited into the SC layer, the precise depth of the injection within this tissue does not significantly alter the PK profile of the drug product. The absorption of insulin is comparable whether the injection is relatively superficial (e.g., a few millimeters beneath the skin) or deep (e.g., just above the fascia) (Frid and Linde, 1992). Consistent with these findings, the Applicant reports that shorter needles of 4 mm reliably achieve similar PK profiles when compared to injections with longer needles of 8 mm (Hirose *et al.*, 2013). Additional studies have demonstrated that insulin administered SC with 6 mm, 8 mm, or 12.7 mm needles result in equivalent glycemic outcomes and no clinically relevant differences in PK or PD of insulins (Schwartz *et al.*, 2004; Ross *et al.*, 1999). In these studies, insulin was injected using needles ranging 6 mm to 12.7 mm, with injection techniques for longer needles adjusted in accordance with clinical practice. The Applicant believes that these findings further suggest that the same absorption of insulin can be achieved with different nominal needle lengths. In conclusion, the Applicant believes that literature reports support that semaglutide administered SC with a 12.7 mm needle would result in PK comparable to administrations with shorter nominal needle lengths.

2.3 Clinical Pharmacology Review Team's Assessment

2.3.1 Assessment of PK Data

The Applicant is referring to three PK studies to support the approval of the proposed mPFS presentation (Table 5). Outcome of each study and its relevance to the mPFS is summarized below.

Table 5: PK Studies Supporting Evaluation of Differences in Injection Parameters Between Devices for SC Delivery of Semaglutide

Clinical study	Study 4010	Study 7560	Study 4590		
Device	Manual syringe (b) (4)	PDS290 pen-injector	Single-dose pen-injector	PDS290 pen-injector	Proposed mPFS
Needle type	Single-use hypodermic needle (b) (4)	Pen-needle (Novofine®)	Staked-in needle	Pen-needle (Novofine®)	Staked-in needle
Needle length	12 mm ^a	6 mm	6 mm	6 mm	12.7 mm ^a
Needle bore	30 G	32 G	29 G	32 G	29 G
Injection pressure ^b	(b) (4)				
Rate of injection	User-dependent	User independent	User independent	User independent	User-dependent

^aAngled injections during administration with manual syringes reduce the depth of injection, resulting in shorter effective needle length compared to nominal needle length.

^bInjection pressure is the force applied to the skin during administration. This is only applicable for shield-activated devices such as the single-dose pen-injector.

Abbreviation: mPFS = pre-filled syringe for manual injection.

Source: Table 1-1, Module 2.7.1, NDA 215256 / S-031 (SDN: 1235), Submitted on January 5, 2026

Study 4010

This was a randomized, double-blind, single dose, two-period, cross-over, PK study conducted in 28 healthy subjects comparing the following two treatments:

- Semaglutide A (synthetic, preserved formulation); 0.5 mg (1.34 mg/mL); Needle (b) (4), 12 mm × needle bore 30 G) and manual syringe (b) (4)
- Semaglutide B (recombinant, preserved formulation); 0.5 mg (1.34 mg/mL); Needle (b) (4), 12 mm × needle bore 30 G) and manual syringe (b) (4)

A single dose of 0.5 mg synthetic semaglutide and 0.5 mg of recombinant semaglutide was administered SC in this study. Reference is made to Dr. Shalini Wickramaratne Senarath Yapa's Clinical Pharmacology review of original NDA 209637 dated August 22, 2017, for the detailed study design and outcome. In summary, BE was demonstrated between synthetic semaglutide and recombinant semaglutide.

Study 4590

This was a randomized, single-center, parallel-group, open label, PK study conducted in 68 subjects with overweight or obesity comparing the following two treatments:

- Semaglutide D (preservative-free formulation) using a SDD pen-injector (needle length: 6 mm x needle bore: 29 G)
- Semaglutide B (preserved formulation) using a PDS290 pen-injector (needle length: 6 mm x needle bore: 32 G)

Dose was titrated up 0.25 mg → 0.5 mg → 1 mg → 1.7 mg → 2.4 mg QW during the 20-week treatment period of the study. Reference is made to Dr. Sang Chung's Clinical Pharmacology review of original NDA 215256 dated May 21, 2021, for the detailed study design and outcome. In summary, BE was demonstrated between the aforementioned semaglutide drug products used for semaglutide 2.4 mg QW (at 3.2 mg/mL for SDD pen-injector and at 3.0 mg/mL for PDS290 pen-injector) and 1.0 mg QW (at 2.0 mg/mL for SDD pen-injector and at 3.0 mg/mL for PDS290 pen-injector), respectively.

Study 7560

This was a randomized, open-label, cross-over, PK study conducted in 20 healthy subjects comparing the following two treatments:

- Semaglutide B (recombinant, preserved formulation); 0.5 mg (0.68 mg/mL); PDS290 pen-injector (needle length: 6 mm x needle bore: 32 G)
- Semaglutide B (recombinant, preserved formulation); 0.5 mg (1.34 mg/mL); PDS290 pen-injector (needle length: 6 mm x needle bore: 32 G)

Two single administrations of 0.5 mg semaglutide SC with different semaglutide concentrations were given using PDS290 pen-injector separated by 7 to 11 weeks. In summary, the Applicant concludes that BE between 0.5 mg of semaglutide B with drug product concentrations of 0.68 mg/mL and 1.34 mg/mL

was confirmed. It should be noted that this study was submitted to NDA 209637/S-039 (SDN: 1791) on January 5, 2026, and has not been reviewed in detail for BE assessment. The Applicant is referring to this study for a cross-study comparison of PK parameters between the single dose of 0.5 mg semaglutide B (1.34 mg/mL) in two different presentations that involves different needle strengths (i.e., 12 mm vs. 6 mm) as shown in Table 6.

Table 6: Key Results from PK Studies 4010 and 7560

Parameter	Study 4010	Study 7560
Formulation	Semaglutide B, 1.34 mg/mL	
Dose	0.5 mg	
Needle length	12 mm	6 mm
Device	Syringe (b) (4) and needle (b) (4)	PDS290 pen-injector and pen-needle (Novofine®)
AUC _{0-last} (nmol*h/L) (geometric mean, CV)	3424 (24)	3246 (29.5)
C _{max} (nmol/L) (geometric mean, CV)	11.5 (18.9)	11.4 (40.9)
T _{max} (median, range)	95.6 (24.0-121.8)	78.0 (30.0-838.4)

Abbreviations: AUC_{last}: area under the semaglutide concentration time curve from time 0 until last quantifiable measurement after single dosing; C_{max}: maximum concentration, T_{max}: Time to maximum concentration CV: Coefficient of variation in %.

Source: Table 3-1, Module 2.7.1, NDA 215256 / S-031 (SDN: 1235), Submitted on January 5, 2026

2.3.2 Assessment of the Effect of Injection Parameters on Semaglutide PK

Needle Length

The proposed mPFS has a nominal needle length of 12.7 mm, which is longer than the 6 mm needles used in the SDD pen-injector and the PDS290 pen-injector. When injections are administered at a 45° angle, the effective needle length of the proposed mPFS is approximately 8.9 mm (Hirsch *et al.*, 2014) as illustrated in Figure 2.

The Applicant is comparing PK parameters from Studies 4010 and 7560 to evaluate the effect of needle length on semaglutide PK. A single dose of 0.5 mg semaglutide was characterized in both studies using the same drug product formulation of semaglutide (Formulation B [recombinant preserved semaglutide formulation], 1.34 mg/mL). The SC administration was done using a syringe with a 12 mm needle in Study 4010 and with the PDS290 pen-injector with a 6 mm needle in Study 7560. The study populations consisted of healthy adults aged 18-55 years with comparable mean body weight (75.0 kg and 80.8 kg) and mean body mass index (BMI) (25.7 kg/m² and 27.0 kg/m²) in Studies 4010 and 7560, respectively. Semaglutide exposure following SC injection with two different needle lengths was comparable with similar values of C_{max} and AUC_{0-last}. Study 4010 showed a delayed T_{max} compared to Study 7560 (Table 6). The PK sampling around T_{max} was the same in the two studies (i.e., 60, 72, 96, and 120 hours post-dose); however, an additional sample at 84 hours post-dose was also included in Study 7560. The Applicant believes that this additional sample, together with between-study variability, may explain why the observed median T_{max} occurred slightly later in Study 4010 (95.6 hours) than in Study 7560 (78.0 hours). Overall, the exposure is similar between the two studies and the slightly delayed T_{max} for semaglutide

administered with the manual syringe is not considered clinically meaningful by the Applicant. The Clinical Pharmacology review team finds the Applicant's justification to be reasonable.

Needle Bore

As summarized above, BE was established between the SDD pen-injector (i.e., needle bore: 29G) and PDS290 pen-injector (i.e., needle bore: 32G). The Applicant does not expect any impact on semaglutide PK due to the different needle bore as it is same in both the SDD pen injector and the proposed mPFS. The Clinical Pharmacology review team finds the Applicant's justification to be reasonable.

Injection Angle

Per Applicant, patients using the proposed mPFS will be instructed to inject at a 45-degree angle and into a lifted skinfold, a technique that is standard practice for manual SC injections. The angled injection reduces the depth of the injection to approximately 8.9 mm (Figure 2) compared to the nominal needle length while the formation of a skinfold increases the thickness of the SC. adipose layer. Thus, the Applicant believes that injections with the proposed mPFS will result in SC delivery of semaglutide similar to the approved SDD pen-injector. The Clinical Pharmacology review team finds the Applicant's justification to be reasonable.

Injection Rate

In Study 4010, semaglutide was administered manually with syringe and needle, allowing variability in the rate of injection. As comparable PK profiles of semaglutide were observed between the two devices, syringe and PDS290 pen-injector, based on cross-study comparison (Table 6), the Applicant believes that difference in rate of injection between the two devices do not alter the PK of semaglutide. In addition, the Applicant believes that PK of semaglutide is not affected by the rate of injection for the SDD pen-injector, supported by data from Study 4590, wherein BE has been established between the SDD pen-injector and the PDS290 pen-injector. Accordingly, the Applicant believes these results support their conclusion that the PK of semaglutide will remain unchanged despite the variability in the rate of injections with the proposed mPFS. The Clinical Pharmacology review team finds the Applicant's justification to be reasonable.

Injection Pressure

Injection pressure, defined as the applied pressure to the skin during administration, is another parameter that can potentially affect PK. The proposed mPFS varies from the SDD pen-injector with respect to injection pressure applied during administration of semaglutide. While the single dose pen-injector is shield-activated and exerts an injection pressure of approximately (b) (4) on the skin during administration, the proposed mPFS and the PDS290 pen-injector do not exert pressure in this manner, as administration is manually performed in the proposed mPFS and button-activated in the PDS290 pen-injector.

Results from Study 4590 confirmed BE between the SDD pen-injector and PDS290 pen-injector, which supports that injection pressure does not influence the PK of semaglutide; therefore, the Applicant concludes that no differences in PK related to variations in injection pressure is expected with the

proposed mPFS. The Clinical Pharmacology review team finds the Applicant's justification to be reasonable.

2.3.3 Assessment of Literature Reports

The Applicant reports that numerous investigations have evaluated the impact of the nominal needle length on SC delivery of peptide-based therapeutics, such as insulins. Insulin and semaglutide are both peptide-based therapeutics administered via the SC route, and their absorption from the injection site relies on similar physiological processes within the SC tissue. The Applicant believes that this similarity supports that studies conducted with insulin can be leveraged to predict how factors like needle length may affect the PK of semaglutide. See Section 2.2.4 above for the Applicant's justification.

Semaglutide is a synthetic peptide based on human glucagon-like peptide-1 (GLP-1) with 94% homology. It consists of 31 amino acids and is a smaller (i.e., 4,113 Da), simpler peptide compared to full-sized proteins, while insulin is a protein hormone that has a much larger (i.e., 5,808 Da) and complex molecular structure (i.e., 51 amino acids) compared to GLP-1 analogs, consisting of two peptide chains (A and B chains) linked by disulfide bonds. Both semaglutide and insulin are typically administered via SC injection. Since semaglutide and insulin are different types of molecules, the applicability of insulin data to semaglutide is questionable. Therefore, insulin data from literature reports should not be used as primary evidence supporting that there is no impact of injection parameters on semaglutide PK. However, considering that insulin is structurally larger and more complex than semaglutide, the Clinical Pharmacology review team finds the Applicant's justification as supporting evidence to be reasonable.

2.4 Conclusion

In totality, the Clinical Pharmacology review team finds the Applicant's overall justifications addressing the impact of injection parameters on semaglutide PK to be reasonable. The sNDA is acceptable from the Clinical Pharmacology perspective and the Clinical Pharmacology review team recommends **approval** for this sNDA.

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

CHONGWOO YU
02/20/2026 09:35:22 AM

LI WANG
02/20/2026 09:54:24 AM

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

215256Orig1s031

OTHER REVIEW(S)

**MEMORANDUM
REVIEW OF REVISED LABEL AND LABELING**

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

***** This document contains proprietary information that cannot be released to the public*****

Date of This Review:	May 6, 2026
Requesting Office or Division:	Division of Diabetes, Lipid Disorders, and Obesity (DDLO)
Application Type and Number:	NDA 209637/S-39 and NDA 215256/S-31
Product Name, Dosage Form, and Strength:	Ozempic (semaglutide) injection, 0.25 mg/0.5 mL, 0.5 mg/0.5 mL, 1 mg/0.5 mL Wegovy (semaglutide) injection, 0.25 mg/0.5 mL, 0.5 mg/0.5 mL, 1 mg/0.5 mL, 1.7 mg/0.75 mL, 2.4 mg/0.75 mL
Applicant Name:	Novo Nordisk Inc (Novo Nordisk)
FDA Received Date:	May 5, 2026
TTT ID #:	2026-18700-1; 2026-18467-1
DMEPA 1 Safety Evaluator:	Avinash Konkani, PhD, MS, BE
DMEPA 1 Team Leader:	Matthew Barlow, RN, BSN

1 PURPOSE OF MEMORANDUM

Novo Nordisk Inc submitted revised Instructions for Use (IFU) received on May 5, 2026 for Ozempic and Wegovy. The Division of Diabetes, Lipid Disorders, and Obesity (DDLO) requested that we review the revised IFUs for Ozempic and Wegovy (Appendix A) to determine if they are acceptable from a medication error perspective. The revisions are in response to recommendations that we made during a previous human factors study results review.^a

2 DISCUSSION

We have reviewed Novo Nordisk's revised IFU along with their responses to our recommendations. Our assessment of the revisions is noted below.

- **Recommendation #1:** Based on our overall assessment of the root cause analysis and subjective feedback for the task of "Pinch the skin", we note some participants misunderstood the illustrations under Steps 5-7 in the Instructions for Use (IFU). Therefore, to improve clarity and user comprehension of the task of "Pinch the skin", we recommend revising the current figure to clearly and prominently depict the skin pinching technique. For example, you could consider revising the figure to zoom in on the pinched skin and syringe, rather than displaying the anatomical (i.e., abdomen) location because some study participants interpreted these images to only apply to injections to the abdomen.
 - **Response from Novo Nordisk (see Appendix A):** *"Accepted. All illustrations in steps 5,6 and 7 are updated with more zoomed in view"*.
 - **Review of response:** We determined that Novo Nordisk's revised illustrations under steps 5, 6 and 7 in the IFU are acceptable. Therefore, we have no additional recommendations for the illustrations under steps 5, 6 and 7 in the IFU at this time.
- **Recommendation #2:** We note some participants overlooked the instructions to pinch the skin in the IFU. Therefore, we recommend revising the current instructional text "Pinch the skin and fully insert the prefilled syringe in a 45-degree angle" by separating the current statement into two distinct, sequential steps with enhanced formatting for emphasis. For example:
 - 5 a: Gently pinch and hold** a fold of skin at the injection site between your thumb and fingers. Hold the pinch throughout the injection.
 - 5 b: Fully Insert the needle** into the pinched skin at a **45-degree angle** until it stops.

Response from Novo Nordisk (See Appendix A): *"Novo Nordisk acknowledges FDA's comment and recommendation. The instructional text has been revised by separating the pinch instruction and the needle insertion instruction into two*

^a Konkani, A. Human Factors Study Results Review for Ozempic and Wegovy (NDA 209637/S-39 and NDA 215256/S-31). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2026 APR 3. TTT ID: 2026-18700; 2026-18467.

distinct, sequential bullets, consistent with the bullet formatting used throughout the IFU. The updated text is provided in track changes in section 5."

- **Review of response:** We determined that Novo Nordisk's revised instructional text to pinch the skin in the IFU is acceptable. Therefore, we have no additional recommendations for instructional text to pinch the skin at this time.
- **Recommendation #3:** We note that the figures in your proposed IFU lack numbering and are not specifically referenced within the corresponding task instructions. This omission may create confusion for users attempting to correlate visual images with the written steps. To improve clarity and readability, we recommend assigning sequential lettering (e.g., Figure A, Figure B, Figure C) to all illustrations throughout the IFU. Additionally, incorporate references to these figures within the instructions, such as "See Figure X" or "(refer to Figure X)" at the appropriate point in each step to establish clear linkages between the written instructions and visual images.
 - **Response from Novo Nordisk:** *"We acknowledge the need for correct usability and linking the correct imagery to text. For this specific reason, the IFU has been designed with an easy and direct column-based numbering. This approach has proven efficient to the highest degree, with 0 out of the almost 200 participants who interacted with the IFU in the formative and summative usability studies reporting any use errors or confusion regarding the flow of the eight figures in the steps 1-to-8 of the IFU."*
"While the general recommendations for Figure labelling in IFUs is reasonable for steps with multiple figures, for a single dose injection system, and in particular a simple one like the prefilled syringe, the handling steps are all sequential to each other, and without repeat steps. It is for this reason that the IFU did not include the Figure labels, also during the request for advice where this approach was shared with the Agency."
"Therefore, Novo Nordisk would like to present to the Agency that the column-based design already means that the sequential element are already in place in the design and that no further enhancement with Figure labels and cross-reference to the figures within the text below the figure are needed. Indeed, introducing new numbering might risk the introduction of use errors that were not apparent during the summative study."
 - **Review of response:** We determined that the rationale is acceptable, in this instance. Therefore, we have no additional recommendations for numbering and referencing the figures in the IFU at this time.

3 CONCLUSION

Novo Nordisk addressed all of our recommendations, and we have no additional recommendations at this time.

APPENDIX A. APPLICANT'S RESPONSE TO HF ADVICE RECEIVED ON MAY 5, 2026

The Applicant's response (updated IFU) for Ozempic dated May 5, 2026 is accessible in EDR via: <\\CDSESUB1\EVSPROD\nda209637\1582\m1\us\m1-14-2-3-s-039-ifu-5-5-26-final-ralo.pdf>

The Applicant's response (updated IFU) for Wegovy dated May 5, 2026 is accessible in EDR via: <\\CDSESUB1\EVSPROD\nda215256\1346\m1\us\m1-14-1-3-ifu-with-mpfs-final-agreed-04may2026.pdf>

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

AVINASH KONKANI
05/06/2026 09:42:54 AM

MATTHEW J BARLOW
05/06/2026 12:38:31 PM

Division of Diabetes, Lipid Disorders, and Obesity (DDLO)

and

Division of Regulatory Operations for Cardiology, Hematology, Endocrinology, and Nephrology (DRO-CHEN)

Labeling Review

Application Type and Number	NDA 215256 S-031 and NDA 218316 S-003
Date of Receipt	January 5, 2026
Applicant	Novo Nordisk Inc
Proprietary Name (nonproprietary name) dosage form	Wegovy (semaglutide) injection and Wegovy (semaglutide) tablets
DDLO Reviewers	Melinda Matheny, PharmD, MPH, BCPS, RAC Associate Director for Labeling, DDLO
DRO-CHEN Regulatory Project Manager (RPM)	Martin White, Senior Regulatory Project Manager
DRO-CHEN RPM Supervisory Concurrence	Elizabeth Solomon, MSHS, CCRP, RAC-Drugs, GWCPM

Labeling Reviewed

Background and Regulatory History of Application

Wegovy (semaglutide) injection under NDA 215256 was originally approved on June 4, 2021.

WEGOVY injection is indicated in combination with a reduced calorie diet and increased physical activity:

- To reduce the risk of major adverse cardiovascular (CV) events (CV death, non-fatal myocardial infarction, or non-fatal stroke) in adults with established CV disease and either obesity or overweight.
- To reduce excess body weight and maintain weight reduction long term in:
 - Adults and pediatric patients aged 12 years and older with obesity.
 - Adults with overweight in the presence of at least one weight-related comorbid condition.
- For the treatment of noncirrhotic metabolic dysfunction-associated steatohepatitis (MASH), formerly known as nonalcoholic steatohepatitis (NASH), with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis) in adults. This indication is approved under accelerated approval based on improvement of MASH and fibrosis [see *Clinical Studies (14.4)*]. Continued approval for this indication may be contingent upon the verification and description of clinical benefit in a confirmatory trial.

NDA 215256/S-031

- This Prior Approval sNDA provides for the addition of a new presentation of Wegovy injection in a single dose manual prefilled syringe (mPFS) for the approved doses (0.25 mg, 0.5 mg, 1.0 mg, 1.7 mg, and 2.4 mg). This

supplement provides for updates to the Prescribing Information (PI), as well as a new Instructions for Use (IFU) and carton and container labeling for the new single dose mPFS presentation.

Wegovy (semaglutide) tablets under NDA 218316 was originally approved December 19, 2025.

WEGOVY tablets are indicated in combination with a reduced calorie diet and increased physical activity:

- To reduce the risk of major adverse CV events (CV death, non-fatal myocardial infarction, or non-fatal stroke) in adults with established CV disease and either obesity or overweight.
- To reduce excess body weight and maintain weight reduction long term in adults with obesity, or in adults with overweight in the presence of at least one weight-related comorbid condition.

NDA 218316/S-003

This Prior Approval sNDA provides for alignment of the combined Wegovy injection and Wegovy tablets Prescribing Information based on the addition of a new presentation of Wegovy injection in a single dose mPFS.

Review

This labeling review compared the currently approved, March 19, 2026, PI for NDA 215256/S-029 (Wegovy injection) and NDA 218316/S-005 (Wegovy tablets) to the final agreed upon PI received on May 5, 2026.

A new IFU and Carton and Container labels for Wegovy injection single dose manual prefilled syringe (0.25 mg, 0.5 mg, 1.0 mg, 1.7 mg, and 2.4 mg) was introduced.

All final agreed upon labeling was received officially from the Applicant on May 5, 2026.

- Prescribing Information
- Instructions for Use for Wegovy injection single dose manual prefilled syringe (0.25 mg, 0.5 mg, 1.0 mg, 1.7 mg, and 2.4 mg)
- Carton Labels for Wegovy injection single dose manual prefilled syringe (0.25 mg, 0.5 mg, 1.0 mg, 1.7 mg, and 2.4 mg)
- Container Labels for Wegovy injection single dose manual prefilled syringe (0.25 mg, 0.5 mg, 1.0 mg, 1.7 mg, and 2.4 mg)

For a full list of recommendations, please see the following review in DARRTS:

- Clinical Pharmacology Reviews by Drs. Chongwoo Yu and Li Wang dated February 20, 2026, and April 23, 2026 (Referenced ID: 5749401, and 5786471, respectively)
- Division of Medication Error Prevention and Analysis 1 Label and Labeling Review by Sherly Abraham, R.Ph., and Damon Birkemeier, PharmD, FISMP dated March 6, 2026 (Reference ID: 5758524)
- Division of Medication Error Prevention and Analysis 1 Human Factors Study Results Report Review by Avinash Konkani, PhD, MS, BE., Matthew Barlow, RN, BSN, and Ariane O. Conrad, PharmD, BCACP, CDCES, FISMP dated April 3, 2026, 2026 (Reference ID: 5775328)
- Office of Prescription Drug Promotion (OPDP) Review by Ankur Kalola, PharmD dated April 28, 2026 (Reference ID: 5788620)
- Division of Medical Policy Programs (DMPP) Review by Kelly Jackson, PharmD, Ankur Kalola, PharmD and Marcia Williams, PhD dated April 29, 2026 (Reference ID: 5789268)
- Offices of Pharmaceutical Quality Assessment Review Sarah Zimmermann and Rohit Kolhatkar dated April 30, 2026)

Regulatory Recommendations

The labeling was reviewed and found acceptable. These supplements are ready for approval. The Agency should issue an approval letter for these supplements.

Attachments:

Final draft labeling, with revisions annotated.

See appended electronic signature page.

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

MARTIN L WHITE
05/05/2026 07:12:49 PM

**Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Medical Policy Initiatives
Division of Medical Policy Programs**

PATIENT LABELING MEMORANDUM

Date: April 29, 2026

To: Martin White, MS
Regulatory Project Manager
Division of Diabetes, Lipid Disorders, and Obesity (DDLO)

Through: Marcia Williams, PhD
Team Leader, Patient Labeling
Division of Medical Policy Programs (DMPP)

From: Kelly Jackson, PharmD
Patient Labeling Reviewer Position Title
Division of Medical Policy Programs (DMPP)

Ankur Kalola, PharmD
Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

Subject: DMPP and OPDP Concurrence with Submitted:
Instructions for Use (IFUs)

Drug Name (established name): WEGOVY (semaglutide)

Dosage Form and Route: injection, for subcutaneous use

Application
Type/Number/Supplement Number: NDA 215256 S-031
NDA 218316 S-003

Applicant: Novo Nordisk, Inc.

1 INTRODUCTION

On January 5, 2026, Novo Nordisk, Inc. submitted for the Agency's review a Prior Approval Supplement (PAS)- Chemistry, Manufacturing and Controls (CMC) to propose an additional presentation of WEGOVY (semaglutide) in a single dose manual prefilled syringe (mPFS) (b) (4)

(b) (4). On February 25, 2026, the Division of Diabetes, Lipid Disorders, and Obesity (DDLO) requested that the Division of Medical Policy Programs (DMPP) and the Office of Prescription Drug Promotion (OPDP) review the Applicant's proposed Instructions for Use (IFUs) for WEGOVY (semaglutide) injection, for subcutaneous use.

This memorandum documents the DMPP and OPDP review and concurrence with the Review Division's revisions to the proposed IFUs for WEGOVY (semaglutide).

2 MATERIAL REVIEWED

- Draft WEGOVY (semaglutide) Prescribing Information (PI) and IFUs received on January 5, 2026, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on April 27, 2026.

3 CONCLUSIONS

We concur with the Review Division's revisions to the proposed IFUs.

4 RECOMMENDATIONS

- Consult DMPP and OPDP regarding any additional revisions made to the PI to determine if corresponding revisions need to be made to the IFUs.

Please let us know if you have any questions.

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

KELLY D JACKSON
04/29/2026 11:35:30 AM

ANKUR S KALOLA
04/29/2026 01:39:46 PM

MARCIA B WILLIAMS
04/29/2026 01:44:18 PM

FOOD AND DRUG ADMINISTRATION
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion

******Pre-decisional Agency Information******

Memorandum

Date: April 28, 2026

To: Martin White, Regulatory Project Manager, Division of Diabetes, Lipid Disorders, and Obesity (DDLO)

Melinda Wilson, Associate Director for Labeling, DDLO

From: Ankur Kalola, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Sapna Shah, Team Leader, OPDP

Subject: OPDP Labeling Comments for
WEGOVY (semaglutide) injection, for subcutaneous use
WEGOVY (semaglutide) tablets, for oral use

NDA: 215256, S-31
218316, S-3

Background:

In response to DDLO's consult request dated February 25, 2026, OPDP has reviewed the proposed Prescribing Information (PI), Instructions for Use (IFU), and carton and container labeling for supplements 31 and 3, for Wegovy injection and Wegovy tablets, respectively. These supplements propose an additional presentation of Wegovy in a single dose manual prefilled syringe (mPFS) for all currently approved doses.

PI & IFU:

OPDP's review of the proposed PI is based on the draft labeling emailed to OPDP on April 27, 2026, and we do not have any comments at this time.

A combined OPDP and Division of Medical Policy Programs (DMPP) review will be completed for the proposed IFU, and comments will be sent under separate cover.

Carton and Container Labeling:

OPDP's review of the proposed carton and container labeling is based on the draft labeling emailed to OPDP on April 27, 2026, and we do not have any comments at this time.

Thank you for your consult. If you have any questions, please contact Ankur Kalola at 301-796-4530 or Ankur.Kalola@fda.hhs.gov.

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

ANKUR S KALOLA
04/28/2026 01:19:34 PM

HUMAN FACTORS STUDY RESULTS REPORT REVIEW

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

***** This document contains proprietary information that cannot be released to the public*****

Date of This Review:	April 03, 2026
Requesting Office or Division:	Division of Diabetes, Lipid Disorders, and Obesity (DDLO)
Application Type and Number:	NDA 209637/S-39 and NDA 215256/S-31
Product Type:	Combination Product (Drug-Device)
Product Name, Dosage Form and Strength:	Ozempic (semaglutide) injection, 0.25 mg/0.5 mL, 0.5 mg/0.5 mL, 1 mg/0.5 mL Wegovy (semaglutide) injection, 0.25 mg/0.5 mL, 0.5 mg/0.5 mL, 1 mg/0.5 mL, 1.7 mg/0.75 mL, 2.4 mg/0.75 mL
Device Constituent:	Pre-filled Syringe (PFS)
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Novo Nordisk Inc (Novo Nordisk)
FDA Received Date:	January 5, 2026; February 12, 2026; March 19, 2026
TTT ID #:	2026-18700; 2026-18467
DMEPA 1 Safety Evaluator:	Avinash Konkani, PhD, MS, BE
DMEPA 1 Team Leader:	Matthew Barlow, RN, BSN
DMEPA 1 Associate Director for Human Factors:	Ariane O. Conrad, PharmD, BCACP, CDCES, FISMP

1 REASON FOR REVIEW

This review evaluates the human factors (HF) validation study results report submitted under NDA 209637/S-39 and NDA 215256/S-31 for Ozempic and Wegovy (semaglutide) injection. These Chemistry, Manufacturing, and Controls (CMC) supplements are proposing the addition of a single-dose Pre-filled Syringe (PFS) presentation.

Ozempic is currently approved as three multiple dose single-patient use pens, and Wegovy is currently approved as a single-dose autoinjector (AI).

We considered the materials listed in Table 1 for this review.

Table 1. Materials Considered for this Review	
Material Considered	Section/Appendix
Product Information	Section 1.1
Relevant Regulatory History Related to the Proposed Product's HF Development Program	Section 1.2
Human Factors (HF) Validation Study Report and HF-Related Supporting Documents	Appendix A
Information Requests Issued During the Review	Appendix B
Labels, Labeling, and Packaging	Appendix C
Tasks Involving Use Errors, Use Difficulties, and Close Calls for Section 3.1	Appendix D

1.1 PRODUCT INFORMATION

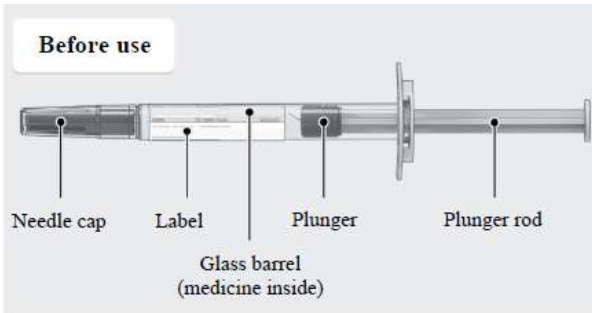
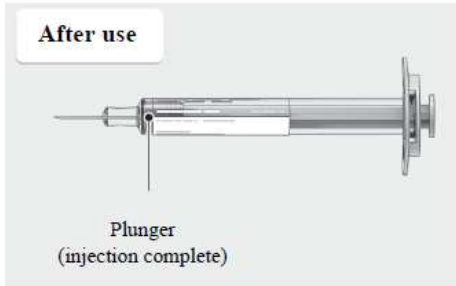
Table 2 presents product information for Ozempic and Wegovy that Novo Nordisk Inc submitted on January 5, 2026.

Table 2. Product Information for Ozempic and Wegovy		
Initial Approval Date	Ozempic: December 5, 2017	Wegovy: June, 4, 2021
Active Ingredient	Semaglutide	
Indication	Ozempic (approved): Ozempic is a glucagon-like peptide 1 (GLP-1) receptor agonist indicated: - as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. - to reduce the risk of major adverse cardiovascular events in adults with	Wegovy (approved): Wegovy is a glucagon-like peptide-1 (GLP-1) receptor agonist indicated in combination with a reduced calorie diet and increased physical activity: to reduce the risk of major adverse cardiovascular events (cardiovascular

	type 2 diabetes mellitus and established cardiovascular disease. to reduce the risk of sustained eGFR decline, end-stage kidney disease and cardiovascular death in adults with type 2 diabetes mellitus and chronic kidney disease.	death, non-fatal myocardial infarction, or non-fatal stroke) in adults with established cardiovascular disease and either obesity or overweight. - to reduce excess body weight and maintain weight reduction long term in: - Adults and pediatric patients aged 12 years and older with obesity - Adults with overweight in the presence of at least one weight-related comorbid condition. - for the treatment of noncirrhotic metabolic dysfunction-associated steatohepatitis (MASH), formerly known as nonalcoholic steatohepatitis (NASH), with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis) in adults.
Route of Administration	Subcutaneous	
Dosage Form	Approved: Multiple Dose Single Patient Use Pen Proposed: Single dose PFS	Approved: Single Dose Pen Proposed: Single dose PFS
Strength	Approved: 2 mg/3 mL (0.68 mg/mL), 4 mg/3 mL (1.34 mg/mL), 8 mg/3 mL (2.68 mg/mL) Proposed: 0.25 mg/0.5 mL, 0.5 mg/0.5 mL, 1 mg/0.5 mL	Approved: 0.25 mg/0.5 mL, 0.5 mg/0.5 mL, 1 mg/0.5 mL, 1.7 mg/0.75 mL, 2.4 mg/0.75 mL Proposed: 0.25 mg/0.5 mL, 0.5 mg/0.5 mL, 1 mg/0.5 mL, 1.7 mg/0.75 mL, 2.4 mg/0.75 mL

Dose and Frequency	Ozempic: Administer once weekly at any time of day, with or without meals. • Start at 0.25 mg once weekly. After 4 weeks, increase the dosage to 0.5 mg once weekly. • If additional glycemic control is needed, increase the dosage to 1 mg once weekly after at least 4 weeks on the 0.5 mg dose. • If additional glycemic control is needed, increase the dosage to 2 mg once weekly after at least 4 weeks on the 1 mg dosage. • To reduce the risk of sustained eGFR decline, end-stage kidney disease and cardiovascular death, increase the dosage to 1 mg once weekly after at least 4 weeks on the 0.5 mg dosage. • If a dose is missed, administer within 5 days of missed dose.	Wegovy: Administer Wegovy once weekly as an adjunct to diet and increased physical activity, on the same day each week, at any time of day, with or without meals. • Inject subcutaneously in the abdomen, thigh, or upper arm. • In patients with type 2 diabetes, monitor blood glucose prior to starting and during Wegovy treatment. • Initiate at 0.25 mg once weekly for 4 weeks. Then follow the dosage escalation schedule, titrating every 4 weeks to achieve the maintenance dosage. • (b) (4)																									
How Supplied	Approved: Multiple-dose Single Patient Use Pen in the following packaging configurations: <table><tr><th>Dose per Injection</th><th>Total Strength per Total Volume</th><th>Carton Contents</th></tr><tr><td>0.25 mg (Initiation)</td><td rowspan="2">2 mg/3 mL</td><td rowspan="2">One pen and Six NovoFine® Plus, needles</td></tr><tr><td>0.5 mg (Maintenance)</td></tr><tr><td>1 mg (Maintenance)</td><td>4 mg/3 mL</td><td>One pen and Four NovoFine® Plus, needles</td></tr><tr><td>2 mg (Maintenance)</td><td>8 mg/3 mL</td><td>One pen and Four NovoFine® Plus, needles</td></tr></table>	Dose per Injection	Total Strength per Total Volume	Carton Contents	0.25 mg (Initiation)	2 mg/3 mL	One pen and Six NovoFine® Plus, needles	0.5 mg (Maintenance)	1 mg (Maintenance)	4 mg/3 mL	One pen and Four NovoFine® Plus, needles	2 mg (Maintenance)	8 mg/3 mL	One pen and Four NovoFine® Plus, needles	Approved: Prefilled, disposable, Single-dose pen-injector with an integrated needle in the following packaging configurations: <table><tr><th>Total Strength per Total Volume</th><th>Carton Contents</th></tr><tr><td>0.25 mg/0.5 mL</td><td>Four Pen-injectors</td></tr><tr><td>0.5 mg/0.5 mL</td><td>Four Pen-injectors</td></tr><tr><td>1 mg/0.5 mL</td><td>Four Pen-injectors</td></tr><tr><td>1.7 mg/0.75 mL</td><td>Four Pen-injectors</td></tr><tr><td>2.4 mg/0.75 mL</td><td>Four Pen-injectors</td></tr></table>	Total Strength per Total Volume	Carton Contents	0.25 mg/0.5 mL	Four Pen-injectors	0.5 mg/0.5 mL	Four Pen-injectors	1 mg/0.5 mL	Four Pen-injectors	1.7 mg/0.75 mL	Four Pen-injectors	2.4 mg/0.75 mL	Four Pen-injectors
Dose per Injection	Total Strength per Total Volume	Carton Contents																									
0.25 mg (Initiation)	2 mg/3 mL	One pen and Six NovoFine® Plus, needles																									
0.5 mg (Maintenance)																											
1 mg (Maintenance)	4 mg/3 mL	One pen and Four NovoFine® Plus, needles																									
2 mg (Maintenance)	8 mg/3 mL	One pen and Four NovoFine® Plus, needles																									
Total Strength per Total Volume	Carton Contents																										
0.25 mg/0.5 mL	Four Pen-injectors																										
0.5 mg/0.5 mL	Four Pen-injectors																										
1 mg/0.5 mL	Four Pen-injectors																										
1.7 mg/0.75 mL	Four Pen-injectors																										
2.4 mg/0.75 mL	Four Pen-injectors																										

	Proposed: Disposable, single-dose pre-filled syringes in the following packaging configurations:	Proposed: Disposable, Single-dose pre-filled syringes in the following packaging configurations:																								
	<table><tr><th>Dose per Injection</th><th>Total Strength per Total Volume</th><th>Carton Contents</th></tr><tr><td>0.25 mg (Initiation)</td><td>0.25 mg/0.5 mL</td><td>Four Pre-filled Syringes</td></tr><tr><td>0.5 mg (Maintenance)</td><td>0.5 mg/0.5 mL</td><td>Four Pre-filled Syringes</td></tr><tr><td>1 mg (Maintenance)</td><td>1 mg/0.5 mL</td><td>Four Pre-filled Syringes</td></tr></table>	Dose per Injection	Total Strength per Total Volume	Carton Contents	0.25 mg (Initiation)	0.25 mg/0.5 mL	Four Pre-filled Syringes	0.5 mg (Maintenance)	0.5 mg/0.5 mL	Four Pre-filled Syringes	1 mg (Maintenance)	1 mg/0.5 mL	Four Pre-filled Syringes	<table><tr><th>Total Strength per Total Volume</th><th>Carton Contents</th></tr><tr><td>0.25 mg/0.5 mL</td><td>Four Pre-filled Syringes</td></tr><tr><td>0.5 mg/0.5 mL</td><td>Four Pre-filled Syringes</td></tr><tr><td>1 mg/0.5 mL</td><td>Four Pre-filled Syringes</td></tr><tr><td>1.7 mg/0.75 mL</td><td>Four Pre-filled Syringes</td></tr><tr><td>2.4 mg/0.75 mL</td><td>Four Pre-filled Syringes</td></tr></table>	Total Strength per Total Volume	Carton Contents	0.25 mg/0.5 mL	Four Pre-filled Syringes	0.5 mg/0.5 mL	Four Pre-filled Syringes	1 mg/0.5 mL	Four Pre-filled Syringes	1.7 mg/0.75 mL	Four Pre-filled Syringes	2.4 mg/0.75 mL	Four Pre-filled Syringes
Dose per Injection	Total Strength per Total Volume	Carton Contents																								
0.25 mg (Initiation)	0.25 mg/0.5 mL	Four Pre-filled Syringes																								
0.5 mg (Maintenance)	0.5 mg/0.5 mL	Four Pre-filled Syringes																								
1 mg (Maintenance)	1 mg/0.5 mL	Four Pre-filled Syringes																								
Total Strength per Total Volume	Carton Contents																									
0.25 mg/0.5 mL	Four Pre-filled Syringes																									
0.5 mg/0.5 mL	Four Pre-filled Syringes																									
1 mg/0.5 mL	Four Pre-filled Syringes																									
1.7 mg/0.75 mL	Four Pre-filled Syringes																									
2.4 mg/0.75 mL	Four Pre-filled Syringes																									
Storage	Recommended Storage Conditions for the Ozempic Pen: • Prior to first use, the Ozempic pen should be stored in a refrigerator between 36°F to 46°F (2°C to 8°C). • Do not store in the freezer or directly adjacent to the refrigerator cooling element. Do not freeze Ozempic and do not use Ozempic if it has been frozen. Ozempic must be kept in the original carton until time of administration. • After first use of the Ozempic pen, the pen can be stored for 56 days at controlled room temperature 59°F to 86°F (15°C to 30°C) or in a refrigerator 36°F to 46°F (2°C to 8°C). Do not freeze. Keep the pen cap on when not in use. Ozempic should be protected from excessive heat and sunlight. • Always remove and safely discard the needle after each injection and store the Ozempic pen without an injection needle attached. Always use a new needle for each injection.	• Store the Wegovy prefilled single-dose pen or syringe in the refrigerator from 36°F to 46°F (2°C to 8°C) . • If needed, prior to the pen or syringe cap removal, Wegovy can be kept from 46°F to 86°F (8°C to 30°C) up to 28 days. • Do not freeze. • Protect Wegovy from light. • Wegovy must be kept in the original carton until time of administration. • Discard the Wegovy pen or syringe after use.																								

	<table><tr><th>Prior to first use</th><th colspan="2">After first use</th></tr><tr><td>Refrigerated 36°F to 46°F (2°C to 8°C)</td><td>Room Temperature 59°F to 86°F (15°C to 30°C)</td><td>Refrigerated 36°F to 46°F (2°C to 8°C)</td></tr><tr><td>Until expiration date</td><td colspan="2">56 days</td></tr></table> Recommended Storage Conditions for the Ozempic Prefilled Syringe: • Store the Ozempic prefilled syringe refrigerated at 36°F to 46°F (2°C to 8°C). • If needed, the syringe can be kept from 46°F to 86°F (8°C to 30°C) up to 28 days. • Do not freeze Ozempic and do not use Ozempic if it has been frozen. Protect Ozempic from light. • Ozempic must be kept in the original carton until time of administration. • Discard the OZEMPIC syringe after use. <table><tr><td>Refrigerated 36°F to 46°F (2°C to 8°C)</td><td>Room Temperature 46°F to 86°F (8°C to 30°C)</td></tr><tr><td>Until expiration date</td><td>28 days</td></tr></table>	Prior to first use	After first use		Refrigerated 36°F to 46°F (2°C to 8°C)	Room Temperature 59°F to 86°F (15°C to 30°C)	Refrigerated 36°F to 46°F (2°C to 8°C)	Until expiration date	56 days		Refrigerated 36°F to 46°F (2°C to 8°C)	Room Temperature 46°F to 86°F (8°C to 30°C)	Until expiration date	28 days	
Prior to first use	After first use														
Refrigerated 36°F to 46°F (2°C to 8°C)	Room Temperature 59°F to 86°F (15°C to 30°C)	Refrigerated 36°F to 46°F (2°C to 8°C)													
Until expiration date	56 days														
Refrigerated 36°F to 46°F (2°C to 8°C)	Room Temperature 46°F to 86°F (8°C to 30°C)														
Until expiration date	28 days														
Container Closure/ Device Constituent (including figure)	Proposed: Pre-filled Syringe (PFS) Before use  Needle cap Label Plunger Plunger rod Glass barrel (medicine inside) After use  Plunger (injection complete)														

		
Intended Users	Adolescent patients (10–17 years old); Adult patients; Caregivers and Healthcare Professionals (HCPs)	
Intended Use Environment	Home and Healthcare facilities (e.g., a physician’s office, pharmacy, or hospital)	
Other important HF-related information relevant for this review	Ozempic: Novo Nordisk does not intend to market a 2 mg strength PFS presentation.	Wegovy: N/A

1.2 RELEVANT REGULATORY HISTORY RELATED TO THE PROPOSED PRODUCT’S HF DEVELOPMENT PROGRAM

On January 30, 2026, we searched for previous DMEPA reviews and FDA/Novo Nordisk Inc interactions relevant to this current review using the terms, “Ozempic”, “Wegovy”, “NDA 209637” and “NDA 215256”. The identified reviews and FDA/Novo Nordisk Inc interactions are provided below.

- On June 14, 2024, Novo Nordisk submitted a Type C meeting request under NDA 209637 and cross-referenced this request for NDA 215256 *“to discuss with the Agency the proposal for introduction of the additional presentation of Wegovy and Ozempic as a prefilled syringe and the submission of a Prior Approval Supplement (PAS) for approval”*. They were seeking information related to differentiation study and Instructions for Use (IFUs) of other PFS formats.
 - On June 27, 2024, the meeting request was granted as written responses only.
 - In the Final Written Response dated August 29, 2024, the Agency informed Novo Nordisk that submission of differentiation study results was not required as part of the human factors (HF) validation study results report because the proposed prefilled syringes (PFSs) maintain identical strength coloring with existing Ozempic and Wegovy pens; however, these results could be retained in the design history file (DHF). Regarding the IFUs and leveraging strategies, the Agency indicated that it could not provide a definitive opinion and recommended that Novo Nordisk employ human factors engineering best practices to guide user interface design.^a
- On January 6, 2025, Novo Nordisk submitted identical HF validation study protocols under NDA 215256 and NDA 209637, as they propose to conduct a single study for both products. We reviewed the protocol and provided recommendations.
 - During the protocol review, we identified that Novo Nordisk did not propose a 2mg PFS for Ozempic. Therefore, we sent an IR on March 3, 2025 to clarify how Novo Nordisk intends to approach the lack of a 2 mg PFS for Ozempic. They responded on March 4, 2025 indicating that they were not pursuing a 2 mg PFS for Ozempic and that patients that use the 2 mg pen injector will continue to use that format.^b Of note, our review included a recommendation to revise their URRAs to analyze all tasks, including *“administration of two 1 mg injections for a complete 2 mg dose”*.^c
- On August 15, 2025, Novo Nordisk submitted their response^d to our HF validation study protocol advice dated May 14, 2025. This response was specific to our recommendation to revise their URRAs to analyze all tasks, including *“administration of two 1 mg injections for a complete 2 mg dose”*.

^a Kelly, L. Final Written Response for NDA 215256 and NDA 209637 Wegovy and Ozempic (semaglutide). Silver Spring (MD): FDA, CDER, OND; OCHEN; DDLO (US): 2024 AUG 29, Available from: <https://darrrts.fda.gov/darrrts/ViewDocument?documentId=090140af80765b9a&showAsPdf=true>

^b NDA 215256 and NDA 209637 Response to HF Information Request. Plainsboro (NJ): Novo Nordisk Inc. 2025 MAR 4. Available from: <\\CDSESUB1\EVSPROD\nda215256\0816\m5\53-clin-stud-rep\535-rep-effic-safety-stud\weight-management\5354-other-stud-rep\dv3484-ut342-2025\study-report-body.pdf>

^c Mathew, D. Human Factors Validation Study Protocol Advice for Ozempic and Wegovy injection (NDA 209637 & NDA 215256). Silver Spring (MD): FDA, CDER, OSE, PMS (US); 2025 MAY 14. Available from: <https://darrrts.fda.gov/darrrts/faces/ViewDocument?documentId=090140af807b8c50&sourceSys=DARRTS>

^d NDA 215256 and NDA 209637 Response to HF Advice. Plainsboro (NJ): Novo Nordisk Inc. 2025 AUG 15. Available from: <\\CDSESUB1\EVSPROD\nda215256\1020\m1\us\m1-11-3-clinical-information-amendment.pdf>

- On October 2, 2025, we finalized our review of Novo Nordisk’s response to HF validation study protocol advice. In this review we acknowledged their proposed labeling changes to the prescribing information (PI). However, we determined that these changes are inadequate to address the identified medication error risk of providers prescribing two 1 mg syringes for a 2 mg dose of semaglutide. Therefore, we recommended that they include a statement in the PI that clearly informs the prescriber that a 2 mg dose of Ozempic should only be administered with the multiple dose prefilled pen.^e
- On January 5, 2026, Novo Nordisk submitted identical HF validation study results reports for Ozempic and Wegovy (semaglutide) injection under NDA 209637/S-39 and NDA 215256/S-31 for addition of a single-dose PFS presentation, which is the subject of this review.

2 OVERALL ASSESSMENT OF HF STUDY DESIGN AND METHODOLOGY

This section provides a summary of the study design, and our evaluation of the study methodology to determine if the study has been appropriately designed to support the safe and effective use of the proposed product.

Table 3 presents a summary of the HF validation study (HFVS) design and our discussion of methodology concerns (as applicable). See Appendix A for more details on the study design.

Table 3. Study Methodology for Human Factors (HF) Validation Study																											
Study Design Elements				DMEPA Discussion of Methodology Concerns																							
User Group(s)																											
<table><tr><th rowspan="2"></th><th colspan="3">Distribution of Participants</th></tr><tr><th>Caregivers¹</th><th>Adult Patients²</th><th>Adolescent Patients</th></tr><tr><td>Current Wegovy Users</td><td>n = 7</td><td>n = 8</td><td>N/A</td></tr><tr><td>Current Ozempic Users</td><td>n = 9</td><td>n = 8</td><td>N/A</td></tr><tr><td>Other Products/ Insulin Experienced</td><td>n = 8</td><td>n = 8</td><td>N/A</td></tr><tr><td>Injection Naïve</td><td>n = 15</td><td>n = 15</td><td>n = 15</td></tr></table> • Total injection experienced patients: 24 • Total injection experienced caregivers: 24 • Total injection naïve patients: 15 • Total injection naïve caregivers: 15 • Total injection naïve adolescent patients: 15 Total study participants: 93					Distribution of Participants			Caregivers ¹	Adult Patients ²	Adolescent Patients	Current Wegovy Users	n = 7	n = 8	N/A	Current Ozempic Users	n = 9	n = 8	N/A	Other Products/ Insulin Experienced	n = 8	n = 8	N/A	Injection Naïve	n = 15	n = 15	n = 15	
	Distribution of Participants																										
	Caregivers ¹	Adult Patients ²	Adolescent Patients																								
Current Wegovy Users	n = 7	n = 8	N/A																								
Current Ozempic Users	n = 9	n = 8	N/A																								
Other Products/ Insulin Experienced	n = 8	n = 8	N/A																								
Injection Naïve	n = 15	n = 15	n = 15																								
Training																											

^e Christopher, K. Review of Response to HF Advice for Ozempic and Wegovy injection (NDA 209637 & NDA 215256). Silver Spring (MD): FDA, CDER, OSE, DMEPA1 (US); 2025 OCT 2. TTT No.: 2025-16005

Table 3. Study Methodology for Human Factors (HF) Validation Study															
Study Design Elements	DMEPA Discussion of Methodology Concerns														
None of the participants received any training.															
Moderator Script															
Novo Nordisk stated, “Per the FDA’s recommendation, the study protocol has been revised to remove any leading language in the test script.”															
Test Environment & Materials															
The test room was similar to a home living room or small office room. The test room was equipped with a table at which the test administrator, data analyst, and participant were seated. The room also included multiple video cameras to record the sessions. The test room was illuminated by overhead lights such as the lighting level in a home or in a physician’s office and it was relatively quiet, comparable to a physician’s office or home in which there is no major source of unwelcome noise. Study Materials: Novo Nordisk provided the following items for use during the usability test: • Production equivalent DV3484 PFS, water-filled (labelled as 0.25 mg strength of placeholder brand name “Ylecor”). • DV3484 PFS cartons (0.25 mg strength of “Ylecor”): Each carton contains one tray, four labelled PFSs and a printed, full-color IFU with placeholder name “Ylecor”. • Accessories: Injection cushion, Manikin, Sharps containers, Alcohol wipes, Paper towels/tissues etc. • Supporting equipment: Laptop computer, Digital video cameras, Digital still camera etc.															
Sequence of Study															
<table border="1"> <tr> <td>Use scenario 1</td><td>Simulated injection with IFU optional</td></tr> <tr> <td colspan="2">Subjective feedback and root cause analysis interview for Use Scenario 1</td></tr> <tr> <td>Use scenario 2</td><td>Knowledge-based assessment and labelling comprehension</td></tr> <tr> <td colspan="2">Subjective feedback and root cause analysis interview for Use Scenario 2</td></tr> <tr> <td>Use scenario 3</td><td>Simulated injection with prompted IFU use</td></tr> <tr> <td colspan="2">Subjective feedback and root cause analysis interview for Use Scenario 3</td></tr> <tr> <td colspan="2">Exit interview</td></tr> </table>	Use scenario 1	Simulated injection with IFU optional	Subjective feedback and root cause analysis interview for Use Scenario 1		Use scenario 2	Knowledge-based assessment and labelling comprehension	Subjective feedback and root cause analysis interview for Use Scenario 2		Use scenario 3	Simulated injection with prompted IFU use	Subjective feedback and root cause analysis interview for Use Scenario 3		Exit interview		
Use scenario 1	Simulated injection with IFU optional														
Subjective feedback and root cause analysis interview for Use Scenario 1															
Use scenario 2	Knowledge-based assessment and labelling comprehension														
Subjective feedback and root cause analysis interview for Use Scenario 2															
Use scenario 3	Simulated injection with prompted IFU use														
Subjective feedback and root cause analysis interview for Use Scenario 3															
Exit interview															

3 RESULTS AND ANALYSIS

In this section, we have carefully reviewed each reported event (i.e., use error, close call, use difficulty), Novo Nordisk’s URRAs, the participants’ subjective feedback, Novo Nordisk’s RCA, and Novo Nordisk’s comments and proposed mitigations (if applicable) to determine if the results indicate that the user interface has been appropriately designed to support the safe and

effective use of the proposed product. In Table 4 below, we provide a summary of the use-related events supplied by Novo Nordisk along with our detailed analysis of use-related events that resulted in recommendations and document our points of dissent with Novo Nordisk's findings.

Table 4. Detailed Analysis of Use Related Events and DMEPA’s Recommendations						
Legend: UE = use error; CC = close call; OD = operational difficulty (Novo Nordisk’s term for use difficulty); URR = use-related risk analysis; RCA = root cause analysis; HFVS = Human Factors Validation Study						
<u>Study participant identity (PID) codes provided by Novo Nordisk:</u> AN# Injection naïve adult patient participant; AO# Ozempic injection-experienced adult patient participant; AS# “Other” injection experienced adult patient participant; AW# Wegovy injection-experienced adult patient participant; CN# Injection naïve caregiver participant; CO# Ozempic injection-experienced caregiver participant; CS# “Other” injection experienced caregiver participant; CW# Wegovy injection-experienced caregiver participant; TN# Injection naïve adolescent participant.						
	Summary of Information Supplied by Applicant	DMEPA’s Identified Areas of Dissent and Recommendations				
1.	Scenario: Simulated Use (IFU Optional) Task: Pinch the skin <table><tr><th>Reported Issues:</th><th>Participant Type(s):</th></tr><tr><td>UE (n = 40)</td><td>AN = 6 AO = 4 AS = 4 AW = 6 CN = 7 CO = 2 CS = 1 CW = 1 TN = 9</td></tr></table>	Reported Issues:	Participant Type(s):	UE (n = 40)	AN = 6 AO = 4 AS = 4 AW = 6 CN = 7 CO = 2 CS = 1 CW = 1 TN = 9	
	Reported Issues:	Participant Type(s):				
	UE (n = 40)	AN = 6 AO = 4 AS = 4 AW = 6 CN = 7 CO = 2 CS = 1 CW = 1 TN = 9				
	Observed event(s): Did not pinch the skin					
	Potential harm associated with issues for this task: Per URR, Injection delivered by the wrong route (intra-muscular instead of subcutaneous) resulting in local discomfort with no systemic medical consequences.					
Relevant RCA/Subjective Feedback: Primary root causes included study artifact, negative transfer, memory lapse, and ambiguous labeling, with some participants stating the following: they thought the illustration under step 5 depicted holding or grabbing a natural skin fold rather than pinching or that the IFU’s						

Table 4. Detailed Analysis of Use Related Events and DMEPA's Recommendations

Legend: UE = use error; CC = close call; OD = operational difficulty (Novo Nordisk's term for use difficulty); URR = use-related risk analysis; RCA = root cause analysis; HFVS = Human Factors Validation Study

Study participant identity (PID) codes provided by Novo Nordisk: **AN#** Injection naïve adult patient participant; **AO#** Ozempic injection-experienced adult patient participant; **AS#** "Other" injection experienced adult patient participant; **AW#** Wegovy injection-experienced adult patient participant; **CN#** Injection naïve caregiver participant; **CO#** Ozempic injection-experienced caregiver participant; **CS#** "Other" injection experienced caregiver participant; **CW#** Wegovy injection-experienced caregiver participant; **TN#** Injection naïve adolescent participant.

	Summary of Information Supplied by Applicant	DMEPA's Identified Areas of Dissent and Recommendations
	illustrations under step 5-7 depicted pinching the abdomen and not the thigh it was unnecessary to pinch the thigh. • They overlooked the instruction to pinch the skin	
	Applicant's Comments and Proposed Post- HFVS Mitigations: Novo Nordisk stated, <i>"Mitigations have been implemented in the IFU to instruct the user to pinch their skin between the thumb and fingers to create a firm surface to inject into (RCM017)."</i> Further, Novo Nordisk stated, <i>"In the intended user population, patients with metabolic conditions such as overweight/obesity or T2D generally have thicker subcutaneous tissue, which further reduce this risk as these individuals can often achieve subcutaneous delivery without pinching the skin. The combination of (1) selecting an appropriate injection site, (2) pinching the skin, and (3) injecting at a 45° angle together maximize the likelihood of a subcutaneous injection. However, omitting one of these techniques does not necessarily cause an incorrect route (e.g., intradermal or intramuscular); if at least one technique is performed correctly, it is still probable that the injection will be subcutaneous for this patient population."</i> Additionally, Novo Nordisk stated <i>"Due to the low severity of this finding, Novo Nordisk considers the residual risk of this finding to be acceptable. Based on the analysis, it is evaluated that further mitigations or optimizations would not reduce the risk of this use error in a real-life setting."</i>	Some participants did not pinch the skin at the injection site when administering the injection. Some participants provided feedback indicating they misunderstood the illustrations or overlooked the instructions to pinch the skin under step 5-7. Therefore, we recommend revising the current instruction <i>"Pinch the skin and fully insert the prefilled syringe in a 45-degree angle"</i> by separating the statement into two distinct, sequential steps to improve prominence and emphasis. Further, the current figures under step 5, step 6, and step 7 could be revised to improve clarity regarding the instructions to pinch the skin. We provide our recommendation in Section 5.1 below. We have determined these changes can be implemented without submitting additional HF validation testing for Agency review.

3.1 ANALYSIS OF THE REMAINING IDENTIFIED ISSUES

The HF validation study results report showed use related events with the tasks evaluated by simulated use and knowledge task assessments listed in Appendix D. However, based on our review of the available assessment of these identified use related events, the available participants' subjective feedback (including when participants' subjective feedback did not indicate any potential issue with the user interface), Novo Nordisk's root cause analysis, and our evaluation of the residual risks and post-HFVS changes to the user interface, we have no additional recommendations to address the identified issues with the tasks in Appendix D.

4 LABELS AND LABELING

During our review of the proposed Instructions for Use (IFU), we found that the figures in the proposed IFU lack numbers/letters and are not referenced in the corresponding task instructions, therefore we are concerned that this creates potential user confusion. To minimize the user confusion regarding unlabeled and unreferenced figures in the proposed IFU, we have provided recommendations in section 5.1 for Novo Nordisk. These changes can be implemented without submitting additional HF validation testing data for Agency review.

We note that the DMEPA 1 nomenclature and labeling review team evaluated product specific label and labeling for Ozempic and Wegovy under separate covers and label and labeling comments have been sent to Novo Nordisk based on the outcome of those reviews.^{fg}

5 CONCLUSION AND RECOMMENDATIONS

The results of the HF validation study demonstrated several use errors, close calls, and use difficulties with critical tasks that may result in harm. Based on our review of the available participants' subjective feedback, and root cause analysis, we identified additional risk mitigations to address the use errors. We have provided recommendations in section 5.1 for Novo Nordisk. These changes can be implemented without submitting additional HF validation testing data for Agency review.

^f Shermock, S. Label and Labeling Review for Ozempic injection (NDA 209637/S-039). Silver Spring (MD): FDA, CDER, OSE, DMEPA1 (US); 2026 FEB 26. TTT ID: 2026-18859.

^g Abraham, S. Label and Labeling Review for Wegovy injection (NDA 215256/S-031). Silver Spring (MD): FDA, CDER, OSE, DMEPA1 (US); 2026 MAR 6. TTT ID: 2026-18233.

5.1 RECOMMENDATIONS FOR NOVO NORDISK INC

The results of the HF validation study demonstrated several use errors with critical tasks that may result in harm. Based on our review of the available participants' subjective feedback, and root cause analysis, we identified additional risk controls to address the use issues. We have determined that these revisions can be implemented without submitting additional HF validation testing data for Agency review.

1. Based on our overall assessment of the root cause analysis and subjective feedback for the task of "*Pinch the skin*", we note some participants misunderstood the illustrations under Steps 5-7 in the Instructions for Use (IFU). Therefore, to improve clarity and user comprehension of the task of "*Pinch the skin*", we recommend revising the current figure to clearly and prominently depict the skin pinching technique. For example, you could consider revising the figure to zoom in on the pinched skin and syringe, rather than displaying the anatomical (i.e., abdomen) location because some study participants interpreted these images to only apply to injections to the abdomen.
2. In addition, we note some participants overlooked the instructions to pinch the skin in the IFU. Therefore, we recommend revising the current instructional text "*Pinch the skin and fully insert the prefilled syringe in a 45-degree angle*" by separating the current statement into two distinct, sequential steps with enhanced formatting for emphasis. For example:
5 a: Gently pinch and hold a fold of skin at the injection site between your thumb and fingers. Hold the pinch throughout the injection.
5 b: Fully insert the needle into the pinched skin at a **45-degree angle** until it stops.
3. We note that the figures in your proposed IFU lack numbering and are not specifically referenced within the corresponding task instructions. This omission may create confusion for users attempting to correlate visual images with the written steps. To improve clarity and readability, we recommend assigning sequential lettering (e.g., Figure A, Figure B, Figure C) to all illustrations throughout the IFU. Additionally, incorporate references to these figures within the instructions, such as "See Figure X" or "(refer to Figure X)" at the appropriate point in each step to establish clear linkages between the written instructions and visual images.

APPENDICES:

APPENDIX A. HUMAN FACTORS (HF) VALIDATION STUDY REPORT AND HF-RELATED SUPPORTING DOCUMENTS

Documents for Ozempic received on January 5, 2026:

- The HF study results report and background information can be accessed in EDR via: <\\CDSESUB1\EVSPROD\nda209637\1476\m5\53-clin-stud-rep\535-rep-effic-safety-stud\type-2-diabetes\5354-other-stud-rep\dv3484-ut342-2025\study-report-body-ut342.pdf>
- The use-related risk analysis can be accessed in EDR via: Page#148 to 175 of the HF Study Results Report

Documents for Wegovy received on January 5, 2026:

- The HF study results report and background information can be accessed in EDR via: <\\CDSESUB1\EVSPROD\nda215256\1202\m5\53-clin-stud-rep\535-rep-effic-safety-stud\weight-management\5354-other-stud-rep\dv3484-ut342-2025\study-report-body-ut342.pdf>
- The use-related risk analysis can be accessed in EDR via: Page#148 to 175 of the HF Study Results Report

APPENDIX B. INFORMATION REQUESTS ISSUED DURING THE REVIEW

On February 9, 2026, we issued an Information Request (IR) to clarify whether the HF validation study results reports (UT342) submitted under NDA 209637/S-39 and NDA 215256/S-31, are identical. Further, we requested Novo Nordisk submit a definition for each participant identity code used in the HF validation study and the detailed individual participant demographics. On February 12, 2026, Novo Nordisk provided the same response for Ozempic and Wegovy, that can be accessed in EDR via:

For Ozempic: <\\CDSESUB1\EVSPROD\nda209637\1511\m5\53-clin-stud-rep\535-rep-effic-safety-stud\type-2-diabetes\5354-other-stud-rep\dv3484-ut342-2025\study-report-body.pdf>

For Wegovy: <\\CDSESUB1\EVSPROD\nda215256\1311\m5\53-clin-stud-rep\535-rep-effic-safety-stud\weight-management\5354-other-stud-rep\dv3484-ut342-2025\study-report-body-ir-resp-feb-9-26.pdf>

On March 17, 2026, we issued an Information Request (IR) to submit the detailed subjective feedback for all use issues, in tabular format, for all critical and non-critical tasks evaluated in the HF validation study. On March 19, 2026, Novo Nordisk provided the response for Ozempic and Wegovy, that can be accessed in EDR via:

For Ozempic: <\\CDSESUB1\EVSPROD\nda209637\1535\m5\53-clin-stud-rep\535-rep-effic-safety-stud\type-2-diabetes\5354-other-stud-rep\dv3484-ut342-2025\study-report-body.pdf>

For Wegovy: <\\CDSESUB1\EVSPROD\nda215256\1333\m5\53-clin-stud-rep\535-rep-effic-safety-stud\weight-management\5354-other-stud-rep\dv3484-ut342-2025\response-fda-ir-17mar2026.pdf>

APPENDIX C. LABELS, LABELING, AND PACKAGING

C.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,^h along with postmarket medication error experiences with similar products, we reviewed the following Ozempic and Wegovy labels and labeling submitted by Novo Nordisk Inc.

Labels and Labeling for Ozempic

- Container labels received on January 5, 2026.
- Carton labeling received on January 5, 2026.
- Instructions for Use (Image not shown) received on January 5, 2026, available from <\\CDSESUB1\EVSPROD\nda209637\1476\m1\us\m1-14-1-3-ozempic-dv3484-ifu-manuscript-mpfs-us-draft.pdf>
- Prescribing Information (Image not shown) received on January 5, 2026, available from <\\CDSESUB1\EVSPROD\nda209637\1476\m1\us\m1-14-1-3-ozempic-pi-draft-for-mpfs-final-clean.pdf>

Labels and Labeling for Wegovy

- Container labels received on January 5, 2026.
- Carton labeling received on January 5, 2026.
- Instructions for Use (Image not shown) received on January 5, 2026, available from <\\CDSESUB1\EVSPROD\nda215256\1202\m1\us\m1-14-1-3-wegovy-dv3484-ifu-manuscript-mpfs-us.pdf>
- Prescribing Information (Image not shown) received on January 5, 2026, available from <\\CDSESUB1\EVSPROD\nda215256\1202\m1\us\m1-14-1-3-215256-218316-pi-mpfs-draft-clean-22dec2025.docx>

^h Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

APPENDIX D. TASKS INVOLVING USE ERRORS, USE DIFFICULTIES, AND CLOSE CALLS FOR SECTION 3.1

PFS simulated use tasks:

- Open carton
- Remove seal from tray
- Inspect your Prefilled Syringe: There were two use errors observed for this task. Two participants primed the PFS prior to administering the injection with an intent to remove the air bubbles. The root cause analysis indicated that these use errors were due to negative transfer (*participant's previous experience of using other injection devices that require priming to remove air bubbles led them to think that the PFS also should be primed to remove air bubbles*). Based on our review of the subjective feedback, root cause analysis, and user interface, we did not identify any additional mitigations to address these use errors and have no recommendations at this time.
- Choose injection site: There were eight use errors observed for this task. Five participants selected their upper arm as the injection site and three participants selected their inner forearm as the injection site. The root cause analysis indicated that these use errors were due to "*Prior experience of receiving injections in the upper arm*" and "*Prior experience of receiving blood draws in the forearm*". Based on our review of the subjective feedback, root cause analysis, and user interface, we did not identify any additional mitigations to address these use errors and have no recommendations at this time.
- Clean injection site and allow to dry
- Pull the Rigid Needle Shield (Needle Cap) straight off while holding the barrel of the syringe: There were three different types of use errors, and one use difficulty (operational difficulty) observed for this task.
 - Plunger rod dislodgement (n=1): Participant held the syringe by the plunger rod during shield removal, unexpectedly dislodging it. Root cause: participants anticipated minimal force would be needed and did not expect the rod to dislodge.
 - Recapping the needle (n=6): Participants recapped the needle before injecting. Root causes: test artifact (recapping occurred when instructed to attach the injection cushion to the body) and perceived safety concerns about leaving the needle uncapped while attaching the injection cushion to the body.
 - Needle bending (n=1): Participant bent the needle while removing the needle shield at an angle. Root cause: fine-gauge needles are susceptible

to bending when the needle shield is removed at an angle rather than straight off.

- Difficulty recognizing need to remove needle shield (n=1): Participant had difficulty knowing to remove the needle shield before injecting. Root cause: the robust, thick plastic shield did not clearly indicate it must be removed prior to injection.

Based on our review of the subjective feedback, root cause analysis, and user interface, we did not identify any additional mitigations to address the aforementioned use errors and have no recommendations at this time.

- Put the Rigid Needle Shield into a sharps disposal container.
- Pick up the syringe with your other hand and insert needle to its full depth into your skin, at a 45° angle: There were 36 user errors observed for this task. 35 participants inserted the needle approximately at 90 degree angle and one participant pressed the plunger rod prior to inserting the needle into the injection cushion. The root cause analysis included:
 - Test artifacts: Simulated skin and participant nervousness affected performance
 - Negative transfer: Participants accustomed to inserting other injection devices (auto-injectors, pen-injectors, vial & syringe) at 90°
 - Difficulty judging angle: Challenging to accurately determine syringe angle when injecting into the injection cushion, causing inadvertent 90° insertion despite attempting 45°
 - Memory recall issues: Multi-step injection process required recall of numerous steps
 - IFU limitations: Lack of rationale explaining why 45° angle is necessary
 - Safety concerns: Perceived increased risk of needle damage (bending/breaking) and needle stick injury when injecting at 45° rather than perpendicular to skin
 - Angle literacy: Difficulty translating IFU figures into the actual degree of tilt needed to achieve 45°
 - Relatively low force required to expel medication: *“inadvertently expelled 5–10 drops of medication when they placed their thumb on the plunger prior to administering the injection.”*

Based on our review of the subjective feedback, root cause analysis, and user interface, we did not identify any additional mitigations to address these use errors and have no recommendations at this time.

- Push plunger rod all the way down using slow and constant pressure until the barrel is empty (until plunger stops): There was one use error observed for this

task. Participant *“removed the syringe from the injection cushion after injecting ~50% of the medication.”* The root cause analysis indicated that this use error was due to *“Test artefact – nervousness: participant indicated that they thought they injected a partial dose because they felt nervous and were rushing through the injection.”* And *“Temporary vision adjustment – bifocal contact lenses: participant reported recent changes to their bifocal contact lens prescription and noted an ongoing visual adjustment.”*

- Check the syringe to make sure the gray plunger stopper is in the position shown
- Pull the needle out of your skin at the same angle at which it entered
- Put the used prefilled syringe in a sharps disposal container after use

Knowledge task assessment:

- You have just come home from the pharmacy with your new medication. Where should you keep your medication before you use it for the first time? Answer: Store in the refrigerator or Store between 46° to 86° F (8°C to 30°C) for no longer than 28 days (4 weeks).
- What should you do if the medication has been frozen? Answer: Do not use the PFS if it has been frozen.
- Is there anything you should consider about how you store the syringes in between doses? Answer: Keep the syringes in the original carton.
- If you were to store the medication outside of the refrigerator, what should you consider? Answer: Keep the syringes away from direct heat and light.
- In what circumstances should you not use the syringe? Answer: Do not use the syringe if it appears to have been used, dropped, damaged or broken.
- What should you look for to confirm the medicine itself is safe and ready to use? Answer: Check the following: Expiration date and for clear and colorless to slightly yellow medicine.
- While inspecting the syringe, you see air bubbles. How should you proceed? Answer: Proceed with injection as normal and do not try to remove the air bubbles.
- What, if anything, should you do to prepare your skin for your injection? Answer: Clean the injection site with an alcohol wipe and allow to dry.
- Let's imagine you have just removed the cap, and you see a drop of liquid on the needle tip. How would you proceed? Answer: It is normal to see a drop. Continue with your injection right away.
- Imagine you've just given an injection, and a drop of blood appears on the site, what should you do? Answer: If blood appears at the injection site, lightly press with a cotton ball or gauze over it, without rubbing.

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

MATTHEW J BARLOW on behalf of AVINASH KONKANI
04/03/2026 12:35:39 PM

MATTHEW J BARLOW
04/03/2026 12:35:59 PM

ARIANE O CONRAD
04/03/2026 01:15:17 PM

LABEL AND LABELING REVIEW

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

*** This document contains proprietary information that cannot be released to the public***

Date of This Review:	March 6, 2026
Requesting Office or Division:	Division of Diabetes, Lipid Disorders, and Obesity (DDLO)
Application Type and Number:	NDA 215256/S-031 and NDA 218316/S-003
Product Name, Dosage Form, and Strength:	Wegovy (semaglutide) Injection, Single-dose prefilled pens: 0.25 mg/0.5 mL, 0.5 mg/0.5 mL, 1 mg/0.5 mL, 1.7 mg/0.75 mL, 2.4 mg/0.75 mL Wegovy (semaglutide) tablets: 1.5 mg, 4 mg, 9 mg and 25 mg Proposed: Single-dose prefilled syringes: 0.25 mg/0.5 mL, 0.5 mg/0.5 mL, 1 mg/0.5 mL, 1.7 mg/0.75 mL, 2.4 mg/0.75 mL
Product Type:	Combination Product (Drug-Device)
Rx or OTC:	Prescription (Rx)
Applicant Name:	Novo Nordisk
FDA Received Date:	January 5, 2026; February 12, 2026
TTT ID #:	2026-18233
DMEPA 1 Safety Evaluator:	Sherly Abraham, R.Ph.
DMEPA 1 Team Leader:	Damon Birkemeier, PharmD, FISMP

1 INTRODUCTION

Novo Nordisk submitted a Chemistry Manufacturing and Controls (CMC) - Prior Approval Supplement (PAS) for Wegovy (semaglutide) Injection to propose an additional presentation of Wegovy in a single-dose prefilled syringe (b) (4).

Subsequently, the Division of Diabetes, Lipid Disorders, and Obesity (DDLO) requested that we review the proposed Wegovy Prescribing Information (PI), Instructions for Use (IFU), container labels, and carton labeling for areas of vulnerability that may lead to medication errors.

2 MATERIALS CONSIDERED

This section lists the materials considered for our review.

Table 1. Materials Considered for this Review	
Materials Considered	Appendix Section
Relevant Product Information	A
Labels and Labeling	B
Previous DMEPA Reviews	C

3 CONCLUSION

The proposed Wegovy Prescribing Information (PI), Instructions for Use (IFU), container labels, and carton labeling may be improved to promote safe use of this product from a medication error perspective. We provide the identified medication error issues, our rationale for concern, and our proposed recommendations to minimize the risk for medication error for the DDLO in Section 4 and for Novo Nordisk in Section 5.

Note that DMEPA 1 is evaluating the human factors validation study results under separate cover and, based on the outcome of that review, additional label and labeling comments may be forthcoming.

4 RECOMMENDATIONS FOR THE DIVISION OF DIABETES, LIPID DISORDERS, AND OBESITY (DDLO)

A. Prescribing Information

1. Highlights of Prescribing Information

- Recommendations to increase the readability of important product information for Description are noted in track changes below:

-----DOSAGE FORMS AND STRENGTHS----- - Injection: prefilled, single-dose pen or single-dose syringe that delivers doses of 0.25 mg, 0.5 mg, 1 mg, 1.7 mg or 2.4 mg (3) - Tablets: 1.5 mg, 4 mg, 9 mg and 25 mg (3)

2. Section 3 Dosage Forms and Strengths

- a. Recommendations to increase the readability of important product information for Description are noted in track changes below:

3 DOSAGE FORMS AND STRENGTHS

Injection: clear, colorless solution available in 5 prefilled, disposable, single-dose pens or single-dose syringes:

- 0.25 mg/0.5 mL
- 0.5 mg/0.5 mL
- 1 mg/0.5 mL
- 1.7 mg/0.75 mL
- 2.4 mg/0.75 mL

Tablet: white to light yellow, round shaped debossed with the strength on one side and "novo" on the other side:

- 1.5 mg
- 4 mg
- 9 mg

Tablet: white to light yellow, oval shaped debossed with the strength on one side and "novo" on the other side:

- 25 mg

3. Section 16 How Supplied/Storage and Handling

- a. Recommendations to increase the readability of important product information for Description are noted in track changes below:

16 HOW SUPPLIED/STORAGE AND HANDLING

WEGOVY Injection

How Supplied

WEGOVY injection is a clear, colorless solution in a prefilled, disposable, single-dose pen (b) (4) or single-dose syringe with an integrated needle. It is supplied in cartons containing 4 (b) (4) or 4 syringes in the following packaging configurations:

Device Type	Total Strength per Total Volume	NDC
Pen (b) (4)	0.25 mg/0.5 mL	0169-4525-14
Pen (b) (4)	0.5 mg/0.5 mL	0169-4505-14
Pen (b) (4)	1 mg/0.5 mL	0169-4501-14
Pen (b) (4)	1.7 mg/0.75 mL	0169-4517-14
Pen (b) (4)	2.4 mg/0.75 mL	0169-4524-14
Syringe	0.25 mg/0.5 mL	XXXX-XXXX-XX
Syringe	0.5 mg/0.5 mL	XXXX-XXXX-XX
Syringe	1 mg/0.5 mL	XXXX-XXXX-XX
Syringe	1.7 mg/0.75 mL	XXXX-XXXX-XX
Syringe	2.4 mg/0.75 mL	XXXX-XXXX-XX

Recommended Storage

Store the WEGOVY prefilled single-dose pen or single-dose syringe in the refrigerator from 36°F to 46°F (2°C to 8°C) (36°F to 46°F). If needed, prior to the pen or syringe cap removal, (b) (4) the pen can be kept from 46°F to 86°F (8°C to 30°C) (46°F to 86°F) up to 28 days. Do not freeze. (b) (4)

B. Instructions for Use (IFU)

1. The expiration date format that is shown in the picture to the right of numbered instruction 2 (Inspect your prefilled syringe) is inconsistent with the expiration date format on the proposed container label. Revise the image so the expiration date format is consistent across all labels and labeling.

2. The statement, (b) (4) in the IFU is inconsistent with the PI. Revise the labeling to ensure consistency across all labels and labeling.
3. The statement (b) (4). Images within the instructions for use should depict the prefilled syringe the end-user receives. Thus, we recommend deleting this statement from the IFU.

5 RECOMMENDATIONS FOR NOVO NORDISK

Table 2. Identified Issues and Recommendations for Novo Nordisk (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Container Labels And Carton Labeling			
1.	As currently presented, it is unclear if the month portion, "MM," of the expiration date format will use alphabetical or numerical characters.	A clearly defined expiration date will minimize confusion and risk for deteriorated drug medication errors. Presenting the month as two alphabetical characters does not clearly communicate, for example, whether 'MA' or 'JU' is for the months of March or May and June or July, respectively.	Clarify how you intend to express the month portion for the expiration date. FDA recommends using only numerical characters if only the year and 2-digit month is expressed. If using alphabetical characters, we recommend you revise the format for the month portion to three-letters (for example, "MAR" vs. "MA" to represent March) to prevent confusion.
Carton Labeling			
1.	It is not clear where the machine-readable product identifier is located on the label.	The Drug Supply Chain Security Act (DSCSA) requires, for certain prescription products, that the smallest saleable unit display a human-readable and machine-readable (2D data matrix barcode) product identifier.	The DSCSA guidance on product identifiers recommends a machine-readable (2D data matrix barcode) product identifier and a human-readable product identifier. Include the machine-readable data matrix barcode. The guidance also recommends the format of the human-readable portion be located

**Table 2. Identified Issues and Recommendations for Novo Nordisk
(entire table to be conveyed to Applicant)**

	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
			near the 2D data matrix barcode as the following: NDC: [insert NDC] SERIAL: [insert serial number] LOT: [insert lot number] EXP: [insert expiration date] We recommend that you review the draft guidance to determine if the product identifier requirements apply to your product's labeling. The draft guidance is available from: https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm621044.pdf
2.	The carton does not have a statement "dispense in this sealed carton".	The lack of this statement may result in dispensing and administration errors. Dispensing the device without the carton circumvents the safety features of the carton labeling and has led to medication errors and other safety concerns.	We recommend adding the statement "Dispense in this sealed carton" on the principal display panel of the carton.
3.	Regarding the "GTIN/Serial No./EXP/LOT" information associated with the black box on the side panel, we note that this information is	To reduce the risk of confusion.	Consider revising this information so that each abbreviation is located next to the appropriate information. For example: GTIN: 12345678901234 Serial No.: 0987654321

Table 2. Identified Issues and Recommendations for Novo Nordisk (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
	presented above the black box.		EXP: YYYY-MM-DD LOT: ABC1234

APPENDICES: MATERIALS CONSIDERED FOR THIS REVIEW

APPENDIX A. RELEVANT PRODUCT INFORMATION

Table 3 presents relevant product information for Wegovy received on February 12, 2026 from Novo Nordisk.

Table 3. Relevant Product Information for Wegovy	
Initial Approval Date	June 4, 2021
Active Ingredient	semaglutide
Indication	WEGOVY injection is indicated in combination with a reduced calorie diet and increased physical activity: To reduce the risk of major adverse cardiovascular (CV) events (CV death, non-fatal myocardial infarction, or non-fatal stroke) in adults with established CV disease and either obesity or overweight. To reduce excess body weight and maintain weight reduction long term in: ○ Adults and pediatric patients aged 12 years and older with obesity. ○ Adults with overweight in the presence of at least one weight-related comorbid condition. For the treatment of noncirrhotic metabolic dysfunction-associated steatohepatitis (MASH), formerly known as nonalcoholic steatohepatitis (NASH), with moderate to advanced liver fibrosis (consistent with stages F2 to F3 fibrosis) in adults. This indication is approved under accelerated approval based on improvement of MASH and fibrosis. WEGOVY tablets are indicated in combination with a reduced calorie diet and increased physical activity: • To reduce the risk of major adverse CV events (CV death, non-fatal myocardial infarction, or non-fatal stroke) in adults with established CV disease and either obesity or overweight. • To reduce excess body weight and maintain weight reduction long term in adults with obesity, or in adults with overweight in the presence of at least one weight-related comorbid condition.
Dosage Form	Injection Tablets

Table 3. Relevant Product Information for Wegovy

Strength	Prefilled, single-dose pen or syringe : 0.25 mg, 0.5 mg, 1 mg, 1.7 mg or 2.4 mg Tablets: 1.5 mg, 4 mg, 9 mg and 25 mg																															
Route of Administration	Subcutaneous injection and oral																															
Dose and Frequency	<u>Injection:</u> - Administer Wegovy once weekly as an adjunct to diet and increased physical activity, on the same day each week, at any time of day, with or without meals. - Inject subcutaneously in the abdomen, thigh, or upper arm. - In patients with type 2 diabetes, monitor blood glucose prior to starting and during Wegovy treatment. - Initiate at 0.25 mg once weekly for 4 weeks. Then follow the dosage escalation schedule (see table below), titrating every 4 weeks to achieve the maintenance dosage. (b) (4) - Take Wegovy tablets orally once-daily on an empty stomach <table border="1"> <thead> <tr> <th></th><th>Weeks</th><th>Once-weekly Subcutaneous Injection Dosage</th></tr> </thead> <tbody> <tr> <td>Starting Dosage</td><td>1 through 4</td><td>0.25 mg</td></tr> <tr> <td rowspan="3">Dosage Escalation</td><td>5 through 8</td><td>0.5 mg</td></tr> <tr> <td>9 through 12</td><td>1 mg</td></tr> <tr> <td>13 through 16</td><td>1.7 mg</td></tr> <tr> <td>Maintenance Dosage</td><td>17 and onward</td><td>See the indication below for the recommended maintenance dosage(s)</td></tr> </tbody> </table> <u>Tablet:</u> - Recommended starting dosage is 1.5 mg orally once daily. Follow dosage escalation table below to reduce the risk of gastrointestinal adverse reactions - In patients do not tolerate a dose during dose escalation, consider delaying dose escalation - Recommended maintenance dosage is 25 mg orally once daily - If patients do not tolerate the 25 mg orally once daily dosage, consider switching to Wegovy injection 1.7 mg once daily <table border="1"> <thead> <tr> <th></th><th>Days</th><th>Once Daily Tablet Dosage</th></tr> </thead> <tbody> <tr> <td>Starting Dosage</td><td>1 through 30</td><td>1.5 mg</td></tr> <tr> <td rowspan="2">Dosage Escalation</td><td>31 through 60</td><td>4 mg</td></tr> <tr> <td>61 through 90</td><td>9 mg</td></tr> <tr> <td>Maintenance Dosage</td><td>91 and onward</td><td>25 mg</td></tr> </tbody> </table>			Weeks	Once-weekly Subcutaneous Injection Dosage	Starting Dosage	1 through 4	0.25 mg	Dosage Escalation	5 through 8	0.5 mg	9 through 12	1 mg	13 through 16	1.7 mg	Maintenance Dosage	17 and onward	See the indication below for the recommended maintenance dosage(s)		Days	Once Daily Tablet Dosage	Starting Dosage	1 through 30	1.5 mg	Dosage Escalation	31 through 60	4 mg	61 through 90	9 mg	Maintenance Dosage	91 and onward	25 mg
	Weeks	Once-weekly Subcutaneous Injection Dosage																														
Starting Dosage	1 through 4	0.25 mg																														
Dosage Escalation	5 through 8	0.5 mg																														
	9 through 12	1 mg																														
	13 through 16	1.7 mg																														
Maintenance Dosage	17 and onward	See the indication below for the recommended maintenance dosage(s)																														
	Days	Once Daily Tablet Dosage																														
Starting Dosage	1 through 30	1.5 mg																														
Dosage Escalation	31 through 60	4 mg																														
	61 through 90	9 mg																														
Maintenance Dosage	91 and onward	25 mg																														

Table 3. Relevant Product Information for Wegovy	
How Supplied	• Injection is supplied in cartons containing 4 pen-injectors or 4 syringes in the following packaging configurations. • Tablets in bottles of 30.
Storage	<u>Injection:</u> Store the Wegovy prefilled single-dose pen or single-dose syringe in the refrigerator from 36°F to 46°F (2°C to 8°C). If needed, prior to the pen or syringe cap removal, Wegovy can be kept from 46°F to 86°F (8°C to 30°C) up to 28 days. Do not freeze. Protect Wegovy from light. Wegovy must be kept in the original carton until time of administration. Discard the Wegovy pen or syringe after use. <u>Tablets:</u> Store at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature]. Store and dispense Wegovy tablets in the original bottle. Store Wegovy tablet in the original bottle until use to protect tablets from moisture. Store Wegovy tablets in a dry place away from moisture.

APPENDIX B. LABELS AND LABELING

B.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,^a along with postmarket medication error data, we reviewed the following Wegovy labels and labeling submitted by Novo Nordisk.

- Prescribing Information received on February 12, 2026, available from <\\CDSESUB1\EVSPROD\nda215256\1312\m1\us\m1-14-1-3-wegovy-215256-218316-pi-with-mpfs-tc.docx>
- Instructions for Use received on January 5, 2026, available from <\\CDSESUB1\EVSPROD\nda215256\1202\m1\us\m1-14-1-3-wegovy-dv3484-ifu-manuscript-mpfs-us.pdf>
- Container label received on January 5, 2026
- Carton labeling received on January 5, 2026

6 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

^a Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

APPENDIX C. PREVIOUS DMEPA REVIEWS

On February 17, 2026, we searched for previous DMEPA reviews relevant to this current review using the term, NDA 215256 and Wegovy. Our search identified two previous reviews^{b,c} since the date of our last search on May 29, 2025, applicable for this current review.

^b Vee S. Label and Labeling Review for Wegovy (NDA 215256/S-025). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2025 JUN 10 TTT ID No.: 2025-14168

^c Topper C. Label and Labeling Review for Wegovy (NDA 215256/S-023). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2025 AUG 20. TTT ID No.: 2025-13506

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

SHERLY ABRAHAM
03/06/2026 02:22:56 PM

DAMON A BIRKEMEIER
03/06/2026 02:27:03 PM

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

215256Orig1s031

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS

From: White, Martin
Sent: Fri 01 May 2026 05:10:37 PM -0400 UTC
To: 'CIVT (Christina Talley)'
Cc: DJCH (Devraj Chakravarty)
Subject: RE: [EXTERNAL] RE: NDA 215256 S-031 and NDA 218316 S-003 Wegovy Labeling Negotiations
Attachments: NDA 215256 S-031 Wegovy IFU to Novo Nordisk 5.1.2026.docx, NDA 215256 S-031 Wegovy US PI to Novo Nordisk 5.1.2026.docx

Hello,

Reference is made to NDA 215256 supplement 031 and to NDA 218316 supplement 003 submitted on January 5, 2026.

FDA has compiled the attached comments for your draft labeling submitted for the above-mentioned sNDAs. We request that you accept all proposed changes that you agree with, make additional revisions as requested. All of your proposed changes from this version should be marked via tracked changes. If there are no changes, please submit the **final agreed upon label to me via email**.

Complete a final Selected Requirements for Prescribing Information (SRPI) checklist of important format elements of the Prescribing Information (PI) based on regulations (21 CFR 201.56 and 201.57) and guidances. The SRPI checklist can be found [here](#). Additional labeling resources are available on the [Prescribing Information Resources](#) website.

Provide a response by noon on **May 4, 2026**.

Regards,
Martin

Martin White, M.S.
Phone 240.402.6018
Martin.White@fda.hhs.gov

From: CIVT (Christina Talley) <civt@novonordisk.com>
Sent: Thursday, April 30, 2026 2:46 PM
To: White, Martin <Martin.White@fda.hhs.gov>
Cc: CIVT (Christina Talley) <civt@novonordisk.com>; DJCH (Devraj Chakravarty) <djch@novonordisk.com>
Subject: RE: [EXTERNAL] RE: NDA 215256 S-031 and NDA 218316 S-003 Wegovy Labeling Negotiations

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear Martin,

Please see the attached updated US PI, IFU, and representative carton labeling for 215256/S-031 and NDA 218316/S-003.

Best regards,
Christina

Christina Talley
Associate Director Reg Affairs TA
40014540 CMR - REG AFFAIRS (2)

Novo Nordisk Inc. | +1-3463392618 (mobile) | civt@novonordisk.com

From: White, Martin <Martin.White@fda.hhs.gov>
Sent: Tuesday, April 28, 2026 5:26 PM
To: CIVT (Christina Talley) <civt@novonordisk.com>
Cc: DJCH (Devraj Chakravarty) <djch@novonordisk.com>
Subject: RE: [EXTERNAL] RE: NDA 215256 S-031 and NDA 218316 S-003 Wegovy Labeling Negotiations

Caution: This email is from outside Novo Nordisk's system. Think before clicking links or opening attachments. Use Report Phishing to report suspicious emails.

Hello,

Reference is made to NDA 215256 supplement 031 and to NDA 218316 supplement 003 submitted on January 5, 2026.

FDA has compiled the attached comments for your draft labeling submitted for the above-mentioned sNDAs. We request that you accept all proposed changes that you agree with, make additional revisions as requested. All of your proposed changes from this version should be marked via tracked changes. If there are no changes, please submit the final agreed upon label to me via email.

Complete a final Selected Requirements for Prescribing Information (SRPI) checklist of important format elements of the Prescribing Information (PI) based on regulations (21 CFR 201.56 and 201.57) and guidances. The SRPI checklist can be found [here](#). Additional labeling resources are available on the [Prescribing Information Resources](#) website.

In addition, we have the following comments for the Carton and Container Labeling:

"The temperature storage conditions have not been revised to the recommended 2°C to 8°C (36°F to 46°F) format. Please update."

Provide a response by **April 30, 2026**.

Regards,
Martin

Martin White, M.S.
Phone 240.402.6018
Martin.White@fda.hhs.gov

From: CIVT (Christina Talley) <civt@novonordisk.com>
Sent: Tuesday, April 21, 2026 2:11 PM
To: White, Martin <Martin.White@fda.hhs.gov>
Cc: CIVT (Christina Talley) <civt@novonordisk.com>; DJCH (Devraj Chakravarty) <djch@novonordisk.com>
Subject: [EXTERNAL] RE: NDA 215256 S-031 and NDA 218316 S-003 Wegovy Labeling Negotiations

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear Martin,

Please see attached the revised US PI, IFU, and representative carton labeling for 215256/S-031 and NDA 218316/S-003.

Best regards,
Christina

Christina Talley
Associate Director Reg Affairs TA
40014540 CMR - REG AFFAIRS (2)

Novo Nordisk Inc. | +1-3463392618 (mobile) | civt@novonordisk.com

From: White, Martin <Martin.White@fda.hhs.gov>
Sent: Tuesday, April 14, 2026 7:50 PM
To: DJCH (Devraj Chakravarty) <djch@novonordisk.com>; CIVT (Christina Talley) <civt@novonordisk.com>
Subject: NDA 215256 S-031 and NDA 218316 S-003 Wegovy Labeling Negotiations

Caution: This email is from outside Novo Nordisk's system. Think before clicking links or opening attachments. Use Report Phishing to report suspicious emails.

Hello,

Reference is made to NDA 215256 supplement 031 and to NDA 218316 supplement 003 submitted on January 5, 2026.

FDA has compiled the attached comments for your draft labeling submitted for the above-mentioned sNDAs. We request that you accept all proposed changes that you agree with, make additional revisions as requested. All of your proposed changes from this version should be marked via tracked changes. If there are no changes, please submit the final agreed upon label to me via email.

Complete a final Selected Requirements for Prescribing Information (SRPI) checklist of important format elements of the Prescribing Information (PI) based on regulations (21 CFR 201.56 and 201.57) and guidances. The SRPI checklist can be found [here](#). Additional labeling resources are available on the [Prescribing Information Resources](#) website.

In addition, we have the following comments for the Carton and Container Labeling:

- Revise storage condition temperatures in alignment with the recommendations provided for the Prescribing Information, e.g. “Store in the refrigerator from 2°C to 8°C (36°F to 46°F)....”

	Identified Issue	Rationale for Concern	Recommendation
Container Labels And Carton Labeling			
1.	As currently presented, it is unclear if the month portion, “MM,” of the expiration date format will use alphabetical or numerical characters.	A clearly defined expiration date will minimize confusion and risk for deteriorated drug medication errors. Presenting the month as two alphabetical characters does not clearly communicate, for example, whether ‘MA’ or ‘JU’ is for the months of March or May and June or July, respectively.	Clarify how you intend to express the month portion for the expiration date. FDA recommends using only numerical characters if only the year and 2-digit month is expressed. If using alphabetical characters, we recommend you revise the format for the month portion to three-letters (for example, “MAR” vs. “MA” to represent March) to prevent confusion.
Carton Labeling			
	It is not clear where the machine-readable product identifier is located on the label.	The Drug Supply Chain Security Act (DSCSA) requires, for certain prescription products, that the smallest saleable unit display a human-readable and machine-readable (2D data matrix barcode) product identifier.	The DSCSA guidance on product identifiers recommends a machine-readable (2D data matrix barcode) product identifier and a human-readable product identifier. Include the machine-readable data matrix barcode. The guidance also recommends the format of the human-readable portion be located near the 2D data matrix barcode as the following: NDC: [insert NDC] SERIAL: [insert serial number] LOT: [insert lot number] EXP: [insert expiration date] We recommend that you review the draft guidance to determine if the product identifier requirements apply to your

	Identified Issue	Rationale for Concern	Recommendation
			product's labeling. The draft guidance is available from: https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm621044.pdf
1.	The carton does not have a statement "dispense in this sealed carton".	The lack of this statement may result in dispensing and administration errors. Dispensing the device without the carton circumvents the safety features of the carton labeling and has led to medication errors and other safety concerns.	We recommend adding the statement "Dispense in this sealed carton" on the principal display panel of the carton.
2.	Regarding the "GTIN/Serial No./EXP/LOT" information associated with the black box on the side panel, we note that this information is presented above the black box.	To reduce the risk of confusion.	Consider revising this information so that each abbreviation is located next to the appropriate information. For example: GTIN: 12345678901234 Serial No.: 0987654321 EXP: YYYY-MM-DD LOT: ABC1234

Provide a response by **April 21, 2026**.

Regards,
Martin

Martin White, MS
Regulatory Project Manager
Diabetes, Lipid Disorders, and Obesity
Division of Regulatory Operations for Cardiology, Hematology, Endocrinology, and Nephrology
Office of Regulatory Operations
Center for Drug Evaluation and Research
WO22 - Room 3389
10903 New Hampshire Avenue
Silver Spring, MD 20903

Phone 240.402.6018
Fax 301.595.2123
Martin.White@fda.hhs.gov

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

MARTIN L WHITE
05/04/2026 01:29:10 PM

From: White, Martin
Sent: Tue 28 Apr 2026 06:25:46 PM -0400 UTC
To: 'CIVT (Christina Talley)'
Cc: DJCH (Devraj Chakravarty)
Subject: RE: [EXTERNAL] RE: NDA 215256 S-031 and NDA 218316 S-003 Wegovy Labeling Negotiations
Attachments: NDA 215256 S-031 Wegovy US PI to Novo Nordisk 4.28.2026.docx, NDA 215256 S-031 Wegovy Trade Carton 0.25 mg Novo Nordisk to FDA 21APR2026.pdf, NDA 215256 S-031 Wegovy IFU to Novo Nordisk 4.28.2026.docx

Hello,

Reference is made to NDA 215256 supplement 031 and to NDA 218316 supplement 003 submitted on January 5, 2026.

FDA has compiled the attached comments for your draft labeling submitted for the above-mentioned sNDAs. We request that you accept all proposed changes that you agree with, make additional revisions as requested. All of your proposed changes from this version should be marked via tracked changes. If there are no changes, please submit the **final agreed upon label to me via email**.

Complete a final Selected Requirements for Prescribing Information (SRPI) checklist of important format elements of the Prescribing Information (PI) based on regulations (21 CFR 201.56 and 201.57) and guidances. The SRPI checklist can be found [here](#). Additional labeling resources are available on the [Prescribing Information Resources](#) website.

In addition, we have the following comments for the Carton and Container Labeling:

"The temperature storage conditions have not been revised to the recommended 2°C to 8°C (36°F to 46°F) format. Please update."

Provide a response by **April 30, 2026**.

Regards,
Martin

Martin White, M.S.
Phone 240.402.6018
Martin.White@fda.hhs.gov

From: CIVT (Christina Talley) <civt@novonordisk.com>
Sent: Tuesday, April 21, 2026 2:11 PM
To: White, Martin <Martin.White@fda.hhs.gov>
Cc: CIVT (Christina Talley) <civt@novonordisk.com>; DJCH (Devraj Chakravarty) <djch@novonordisk.com>
Subject: [EXTERNAL] RE: NDA 215256 S-031 and NDA 218316 S-003 Wegovy Labeling Negotiations

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear Martin,

Please see attached the revised US PI, IFU, and representative carton labeling for 215256/S-031 and NDA 218316/S-003.

Best regards,
Christina

Christina Talley
Associate Director Reg Affairs TA
40014540 CMR - REG AFFAIRS (2)

Novo Nordisk Inc. | +1-3463392618 (mobile) | civt@novonordisk.com

From: White, Martin <Martin.White@fda.hhs.gov>
Sent: Tuesday, April 14, 2026 7:50 PM
To: DJCH (Devraj Chakravarty) <djch@novonordisk.com>; CIVT (Christina Talley) <civt@novonordisk.com>
Subject: NDA 215256 S-031 and NDA 218316 S-003 Wegovy Labeling Negotiations

Caution: This email is from outside Novo Nordisk's system. Think before clicking links or opening attachments. Use Report Phishing to report suspicious emails.

Hello,

Reference is made to NDA 215256 supplement 031 and to NDA 218316 supplement 003 submitted on January 5, 2026.

FDA has compiled the attached comments for your draft labeling submitted for the above-mentioned sNDAs. We request that you accept all proposed changes that you agree with, make additional revisions as requested. All of your proposed changes from this version should be marked via tracked changes. If there are no changes, please submit the **final agreed upon label to me via email**.

Complete a final Selected Requirements for Prescribing Information (SRPI) checklist of important format elements of the Prescribing Information (PI) based on regulations (21 CFR 201.56 and 201.57) and guidances. The SRPI checklist can be found [here](#). Additional labeling resources are available on the [Prescribing Information Resources](#) website.

In addition, we have the following comments for the Carton and Container Labeling:

- Revise storage condition temperatures in alignment with the recommendations provided for the Prescribing Information, e.g. "Store in the refrigerator from 2°C to 8°C (36°F to 46°F)..."

	Identified Issue	Rationale for Concern	Recommendation
Container Labels And Carton Labeling			
1.	As currently presented, it is unclear if the month portion, "MM," of the expiration date format will use alphabetical or numerical characters.	A clearly defined expiration date will minimize confusion and risk for deteriorated drug medication errors. Presenting the month as two alphabetical characters does not clearly communicate, for example, whether 'MA' or 'JU' is for the months of March or May and June or July, respectively.	Clarify how you intend to express the month portion for the expiration date. FDA recommends using only numerical characters if only the year and 2-digit month is expressed. If using alphabetical characters, we recommend you revise the format for the month portion to three-letters (for example, "MAR" vs. "MA" to represent March) to prevent confusion.
Carton Labeling			
	It is not clear where the machine-readable product identifier is located on the label.	The Drug Supply Chain Security Act (DSCSA) requires, for certain prescription products, that the smallest saleable unit display a human-readable and machine-readable (2D data matrix barcode) product identifier.	The DSCSA guidance on product identifiers recommends a machine-readable (2D data matrix barcode) product identifier and a human-readable product identifier. Include the machine-readable data matrix barcode. The guidance also recommends the format of the human-readable portion be located near the 2D data matrix barcode as the following: NDC: [insert NDC] SERIAL: [insert serial number] LOT: [insert lot number] EXP: [insert expiration date] We recommend that you review the draft guidance to determine if the product identifier requirements apply to your product's labeling. The draft guidance is available from: https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm621044.pdf
1.	The carton does not have a statement "dispense in	The lack of this statement may result in dispensing and administration errors. Dispensing the device	We recommend adding the statement "Dispense in this sealed carton" on the principal display panel of the carton.

	Identified Issue	Rationale for Concern	Recommendation
	this sealed carton”.	without the carton circumvents the safety features of the carton labeling and has led to medication errors and other safety concerns.	
2.	Regarding the “GTIN/Serial No./EXP/LOT” information associated with the black box on the side panel, we note that this information is presented above the black box.	To reduce the risk of confusion.	Consider revising this information so that each abbreviation is located next to the appropriate information. For example: GTIN: 12345678901234 Serial No.: 0987654321 EXP: YYYY-MM-DD LOT: ABC1234

Provide a response by **April 21, 2026**.

Regards,
Martin

Martin White, MS
Regulatory Project Manager
Diabetes, Lipid Disorders, and Obesity
Division of Regulatory Operations for Cardiology, Hematology, Endocrinology, and Nephrology
Office of Regulatory Operations
Center for Drug Evaluation and Research
WO22 - Room 3389
10903 New Hampshire Avenue
Silver Spring, MD 20903
Phone 240.402.6018
Fax 301.595.2123
Martin.White@fda.hhs.gov

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

MARTIN L WHITE
04/29/2026 07:37:36 AM

From: White, Martin
Sent: Tue 14 Apr 2026 08:49:43 PM -0400 UTC
To: DJCH (Devraj Chakravarty); CIVT (Christina Talley)
Subject: NDA 215256 S-031 and NDA 218316 S-003 Wegovy Labeling Negotiations
Attachments: NDA 215256 S-031 Wegovy tracked to firm on 4.14.2026.docx, NDA 215256 S-031 Wegovy_DV3484_IFU_tracked to firm on 4.14.2026.docx

Hello,

Reference is made to NDA 215256 supplement 031 and to NDA 218316 supplement 003 submitted on January 5, 2026.

FDA has compiled the attached comments for your draft labeling submitted for the above-mentioned sNDAs. We request that you accept all proposed changes that you agree with, make additional revisions as requested. All of your proposed changes from this version should be marked via tracked changes. If there are no changes, please submit the **final agreed upon label to me via email**.

Complete a final Selected Requirements for Prescribing Information (SRPI) checklist of important format elements of the Prescribing Information (PI) based on regulations (21 CFR 201.56 and 201.57) and guidances. The SRPI checklist can be found [here](#). Additional labeling resources are available on the [Prescribing Information Resources](#) website.

In addition, we have the following comments for the Carton and Container Labeling:

- Revise storage condition temperatures in alignment with the recommendations provided for the Prescribing Information, e.g. "Store in the refrigerator from 2°C to 8°C (36°F to 46°F)...."

	Identified Issue	Rationale for Concern	Recommendation
Container Labels And Carton Labeling			
1.	As currently presented, it is unclear if the month portion, "MM," of the expiration date format will use alphabetical or numerical characters.	A clearly defined expiration date will minimize confusion and risk for deteriorated drug medication errors. Presenting the month as two alphabetical characters does not clearly communicate, for example, whether 'MA' or 'JU' is for the months of March or May and June or July, respectively.	Clarify how you intend to express the month portion for the expiration date. FDA recommends using only numerical characters if only the year and 2-digit month is expressed. If using alphabetical characters, we recommend you revise the format for the month portion to three-letters (for example, "MAR" vs. "MA" to represent March) to prevent confusion.
Carton Labeling			

	Identified Issue	Rationale for Concern	Recommendation
	It is not clear where the machine-readable product identifier is located on the label.	The Drug Supply Chain Security Act (DSCSA) requires, for certain prescription products, that the smallest saleable unit display a human-readable and machine-readable (2D data matrix barcode) product identifier.	The DSCSA guidance on product identifiers recommends a machine-readable (2D data matrix barcode) product identifier and a human-readable product identifier. Include the machine-readable data matrix barcode. The guidance also recommends the format of the human-readable portion be located near the 2D data matrix barcode as the following: NDC: [insert NDC] SERIAL: [insert serial number] LOT: [insert lot number] EXP: [insert expiration date] We recommend that you review the draft guidance to determine if the product identifier requirements apply to your product's labeling. The draft guidance is available from: https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm621044.pdf
1.	The carton does not have a statement "dispense in this sealed carton".	The lack of this statement may result in dispensing and administration errors. Dispensing the device without the carton circumvents the safety features of the carton labeling and has led to medication errors and other safety concerns.	We recommend adding the statement "Dispense in this sealed carton" on the principal display panel of the carton.
2.	Regarding the "GTIN/Serial No./EXP/LOT" information associated with the black box on the side panel, we note that this information is presented	To reduce the risk of confusion.	Consider revising this information so that each abbreviation is located next to the appropriate information. For example: GTIN: 12345678901234 Serial No.: 0987654321 EXP: YYYY-MM-DD LOT: ABC1234

	Identified Issue	Rationale for Concern	Recommendation
	above the black box.		

Provide a response by **April 21, 2026**.

Regards,
Martin

Martin White, MS
Regulatory Project Manager
Diabetes, Lipid Disorders, and Obesity
Division of Regulatory Operations for Cardiology, Hematology, Endocrinology, and Nephrology
Office of Regulatory Operations
Center for Drug Evaluation and Research
WO22 - Room 3389
10903 New Hampshire Avenue
Silver Spring, MD 20903
Phone 240.402.6018
Fax 301.595.2123
Martin.White@fda.hhs.gov

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

MARTIN L WHITE
04/20/2026 12:15:43 PM

Mathew, Davis

From: Mathew, Davis
Sent: Tuesday, March 17, 2026 4:15 PM
To: 'ptrb@novonordisk.com'; 'civt@novonordisk.com'
Cc: Rashid, Nichelle E; Kelly, Lindsey
Subject: NDA 215256/S-031 & NDA 209637/S-039 Wegovy and Ozempic Human Factors Information Request

Dear Patricia Robson and Christina Talley,

Please refer to your supplemental new drug application (NDA) dated and received January 05, 2026, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for NDA 209637/S-39 and NDA 215256/S-31 for Ozempic and Wegovy (semaglutide) injection, which propose the addition of a single-dose Pre-filled Syringe (PFS) presentation.

We also refer to:

- Your January 05, 2026 submission, containing Human Factors study report.
- Your submission, dated and received February 12, 2026, in response to our February 09, 2026, information request.

We are reviewing your submission and have the following information requests. We request a prompt response by **COB Thursday, March 19, 2026**, in order to continue our evaluation of your submission.

Your January 5, 2026 submissions under NDA 209637/S-39 and NDA 215256/S-31 included the document "*DV3484 Human Factors Engineering Report (UT342)*." While your UT342 report contains root cause analyses for each critical and non-critical task evaluated in Use Scenario 1 (Simulated injection with IFU optional) and Use Scenario 2 (Knowledge-based assessment and labeling comprehension), it lacks detailed subjective feedback for these tasks. Detailed subjective feedback is necessary to allow for a comprehensive analysis of your human factors (HF) engineering report (HF validation study results report).

As such we are unable to adequately review your HF engineering report UT342.

Therefore, please provide the detailed subjective feedback for all use issues, in tabular format, for all critical and non-critical tasks evaluated in both use scenarios. Additionally, include, in the table, the respective participant identity codes highlighting which participant provided the specific feedback.

Place your response in eCTD Section 5.3.5.4 – Other Study reports and related information.

Include the following statement “**RESPONSE TO HF INFORMATION REQUEST**” in bold capital letters at the top of your cover letter, and at the top of the first page of the main submission document.

Please submit a courtesy copy of your response via email followed by an official submission to your application.

Please confirm receipt of this communication.

If you have any questions regarding the contents of this letter or any other aspects of the Human Factors review process, contact me at (240)-402-4559

Thanks,

Davis Mathew, PharmD, RPh

Safety Regulatory Project Manager

Center for Drug Evaluation and Research (CDER)

Office of Surveillance and Epidemiology (OSE)

Ph: 240-402-4559

E: davis.mathew@fda.hhs.gov



This e-mail message may contain information that is protected, privileged, or confidential, and it should not be disseminated, distributed, or copied to persons not authorized to receive such information. If you are not the intended recipient, any dissemination, distribution or copying is strictly prohibited. If you think you have received this e-mail message in error, please e-mail the sender immediately at davis.mathew@fda.hhs.gov.

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

DAVIS MATHEW
03/17/2026 04:23:43 PM

From: DJCH (Devraj Chakravarty) <djch@novonordisk.com>
Sent: Fri 06 Mar 2026 03:53:02 PM -0500 UTC
To: White, Martin
Subject: [EXTERNAL] RE: NDA 215256 Wegovy S-031

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and know the content is safe.

Dear Martin

I confirm receipt of the Agency's request for S-931.

Best regards

Devraj Chakravarty
DIRECTOR - REG AFFAIRS - TA
40014540 CMR - REG AFFAIRS

Novo Nordisk Inc. | +1-6093735398 (mobile) | +1-6093735398 (direct) | djch@novonordisk.com

From: White, Martin <Martin.White@fda.hhs.gov>
Sent: Friday, March 6, 2026 3:14 PM
To: DJCH (Devraj Chakravarty) <djch@novonordisk.com>
Subject: NDA 215256 Wegovy S-031

Caution: This email is from outside Novo Nordisk's system. Think before clicking links or opening attachments. Use Report Phishing to report suspicious emails.

Devraj,

When supplement 31 was submitted, we received a pdf copy of the IFU. Will you send a word version so that we can make edits to the document?

Regards,
Martin

Martin White, MS
Regulatory Project Manager
Diabetes, Lipid Disorders, and Obesity
Division of Regulatory Operations for Cardiology, Hematology, Endocrinology, and Nephrology
Office of Regulatory Operations
Center for Drug Evaluation and Research
WO22 - Room 3389
10903 New Hampshire Avenue
Silver Spring, MD 20903

Phone 240.402.6018
Fax 301.595.2123
Martin.White@fda.hhs.gov

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

MARTIN L WHITE
03/06/2026 04:29:28 PM

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR OPDP (previously DDMAC) LABELING REVIEW CONSULTATION **Please send immediately following the Filing/Planning meeting**					
TO: CDER-OPDP-RPM		FROM: (Name/Title, Office/Division/Phone number of requestor) Martin White 2404026018					
REQUEST DATE: 2.25.2026	IND NO.	NDA/BLA NO. NDA 215256 S-031 NDA 218316 S-003	TYPE OF DOCUMENTS (PLEASE CHECK OFF BELOW)				
NAME OF DRUG: Wegovy injection Wegovy tablets	PRIORITY CONSIDERATION: Priority		CLASSIFICATION OF DRUG GLP-1	DESIRED COMPLETION DATE (Generally 1 week before the wrap-up meeting)			
NAME OF FIRM: Novo Nordisk			PDUFA Date: May 5, 2026				
TYPE OF LABEL TO REVIEW							
<table style="width: 100%; border: none;"> <tr> <td style="width: 33%; vertical-align: top;"> TYPE OF LABELING: (Check all that apply) ☒ PRESCRIBING INFORMATION (PI) ☐ PATIENT PACKAGE INSERT (PPI) ☐ CARTON/CONTAINER LABELING ☐ MEDICATION GUIDE ☒ INSTRUCTIONS FOR USE (IFU) </td> <td style="width: 33%; vertical-align: top;"> TYPE OF APPLICATION/SUBMISSION ☐ ORIGINAL NDA/BLA ☐ IND ☐ EFFICACY SUPPLEMENT ☐ SAFETY SUPPLEMENT ☐ LABELING SUPPLEMENT ☐ PLR CONVERSION CMC supplement </td> <td style="width: 33%; vertical-align: top;"> REASON FOR LABELING CONSULT ☐ INITIAL PROPOSED LABELING ☒ LABELING REVISION For OSE USE ONLY ☐ REMS </td> </tr> </table>					TYPE OF LABELING: (Check all that apply) ☒ PRESCRIBING INFORMATION (PI) ☐ PATIENT PACKAGE INSERT (PPI) ☐ CARTON/CONTAINER LABELING ☐ MEDICATION GUIDE ☒ INSTRUCTIONS FOR USE (IFU)	TYPE OF APPLICATION/SUBMISSION ☐ ORIGINAL NDA/BLA ☐ IND ☐ EFFICACY SUPPLEMENT ☐ SAFETY SUPPLEMENT ☐ LABELING SUPPLEMENT ☐ PLR CONVERSION CMC supplement	REASON FOR LABELING CONSULT ☐ INITIAL PROPOSED LABELING ☒ LABELING REVISION For OSE USE ONLY ☐ REMS
TYPE OF LABELING: (Check all that apply) ☒ PRESCRIBING INFORMATION (PI) ☐ PATIENT PACKAGE INSERT (PPI) ☐ CARTON/CONTAINER LABELING ☐ MEDICATION GUIDE ☒ INSTRUCTIONS FOR USE (IFU)	TYPE OF APPLICATION/SUBMISSION ☐ ORIGINAL NDA/BLA ☐ IND ☐ EFFICACY SUPPLEMENT ☐ SAFETY SUPPLEMENT ☐ LABELING SUPPLEMENT ☐ PLR CONVERSION CMC supplement	REASON FOR LABELING CONSULT ☐ INITIAL PROPOSED LABELING ☒ LABELING REVISION For OSE USE ONLY ☐ REMS					
EDR link to submission: EDR Location: \\CDSESUB1\evsprod\NDA215256\1202							
Please Note: There is no need to send labeling at this time. OPDP reviews substantially complete labeling, which has already been marked up by the CDER Review Team. After the disciplines have completed their sections of the labeling, a full review team labeling meeting can be held to go over all of the revisions. Within a week after this meeting, "substantially complete" labeling should be sent to OPDP. Once the substantially complete labeling is received, OPDP will complete its review within 14 calendar days. OSE/DRISK ONLY: For REMS consults to OPDP, send a word copy of all REMS materials and the most recent labeling to CDER DDMAC RPM. List out all materials included in the consult, broken down by audience (consumer vs provider), in the comments section below.							
COMMENTS/SPECIAL INSTRUCTIONS: This supplemental application proposes an additional presentation of Wegovy in a single dose manual prefilled syringe (mPFS) for all currently approved doses (0.25 mg, 0.5 mg, 1.0 mg, 1.7 mg, and 2.4 mg). The sNDA contains draft labeling for the physician insert (in Word), an IFU, and carton and container labels. Labeling will be sent to Applicant approximately April 5, 2026. The user fee goal date will be May 5, 2026.:							
SIGNATURE OF REQUESTER							
SIGNATURE OF RECEIVER			METHOD OF DELIVERY (Check one)				

06/14/2018

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

MARTIN L WHITE
02/25/2026 11:27:33 AM

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		REQUEST FOR PATIENT LABELING REVIEW CONSULTATION	
TO: CDER-DMPP-PatientLabelingTeam		FROM: (Name/Title, Office/Division/Phone number of requestor) Martin White/RPM/DDLO/240-402-6018	
REQUEST DATE: 2.25.2026	NDA/BLA NO.: NDA 215256 S-031 NDA 218316 S-003	TYPE OF DOCUMENTS: (PLEASE CHECK OFF BELOW)	
NAME OF DRUG: Wegovy injection Wegovy tablets	PRIORITY CONSIDERATION: Priority	CLASSIFICATION OF DRUG: GLP-1	DESIRED COMPLETION DATE (Generally 2 Weeks after receiving substantially complete labeling)
SPONSOR: Novo Nordisk		PDUFA Date: May 5, 2026	
TYPE OF LABEL TO REVIEW			
TYPE OF LABELING: (Check all that apply) ☐ PATIENT PACKAGE INSERT (PPI) ☐ MEDICATION GUIDE ☒ INSTRUCTIONS FOR USE(IFU)		TYPE OF APPLICATION/SUBMISSION ☐ ORIGINAL NDA/BLA/ANDA ☐ EFFICACY SUPPLEMENT ☐ SAFETY SUPPLEMENT ☐ LABELING SUPPLEMENT ☒ MANUFACTURING (CMC) SUPPLEMENT ☐ PLR CONVERSION	
		REASON FOR LABELING CONSULT ☐ INITIAL PROPOSED LABELING ☒ LABELING REVISION	
EDR link to submission: EDR Location: \\CDSESUB1\evsprod\NDA215256\1202			
Please Note: DMPP uses substantially complete labeling, which has already been marked up by the CDER Review Team, when reviewing MedGuides, IFUs, and PPIs. Once the substantially complete labeling is received, DMPP will complete its review within 14 calendar days. Please provide a copy of the sponsor's proposed patient labeling in Word format.			
COMMENTS/SPECIAL INSTRUCTIONS: This supplemental application proposes an additional presentation of Wegovy in a single dose manual prefilled syringe (mPFS) for all currently approved doses (0.25 mg, 0.5 mg, 1.0 mg, 1.7 mg, and 2.4 mg). The sNDA contains draft labeling for the physician insert (in Word), an IFU, and carton and container labels. Labeling will be sent to Applicant approximately April 5, 2026. The user fee goal date will be May 5, 2026.			
SIGNATURE OF REQUESTER			
SIGNATURE OF RECEIVER			

Version: 06/06/2016

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

MARTIN L WHITE
02/25/2026 11:38:12 AM

Mathew, Davis

From: Mathew, Davis
Sent: Monday, February 9, 2026 10:40 AM
To: 'ptrb@novonordisk.com'
Cc: Rashid, Nichelle E; Joshi, Ameet; Kelly, Lindsey
Subject: NDA 215256/S-031 & NDA 209637/S-039 Wegovy and Ozempic Human Factors Information Request

Dear Patricia Robson,

Please refer to your supplemental new drug application (NDA) dated and received January 05, 2026, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for NDA 209637/S-39 and NDA 215256/S-31 for Ozempic and Wegovy (semaglutide) injection, which propose the addition of a single-dose Pre-filled Syringe (PFS) presentation.

We also refer to your January 05, 2026 submission, containing Human Factors study report.

We are reviewing your submission and have the following information requests. We request a prompt response by **COB Wednesday, February 11, 2026**, in order to continue our evaluation of your submission.

In your January 5, 2026 submissions, under NDA 209637/S-39 and NDA 215256/S-31 respectively, you included the document "*DV3484 Human Factors Engineering Report (UT342)*". However, it is not clear if the HF engineering reports (UT342) submitted under each supplemental NDA are identical.

Further, our preliminary review identified that you did not define the participant identity (PID) codes (e.g., AN01, TN01, CW01, etc.) used in the HF engineering report *UT342*. Additionally, you did not include individual participant demographics. The definition of each participant identity code and the individual participant demographics are necessary to allow for an efficient and robust analysis of your human factors (HF) validation study results.

As such we are unable to adequately review your HF engineering report *UT342* (HF validation study results report). Therefore, please provide the following:

- 1) Clarify whether the "*DV3484 Human Factors Engineering Report (UT342)*" documents submitted under NDA 209637/S-39 and NDA 215256/S-31, respectively, are identical. If the reports are not identical, please provide a summary table highlighting the key differences between the two reports.

- 2) A definition for each participant identity code used in the HF validation study related to each distinct user group.
- 3) Detailed individual participant demographics.

Place your response in eCTD Section 5.3.5.4 – Other Study reports and related information.

Include the following statement “**RESPONSE TO HF INFORMATION REQUEST**” in bold capital letters at the top of your cover letter, and at the top of the first page of the main submission document.

Please submit a courtesy copy of your response via email followed by an official submission to your application.

Please confirm receipt of this communication.

If you have any questions regarding the contents of this letter or any other aspects of the Human Factors review process, contact me at (240)-402-4559.

Thanks,

Davis Mathew, PharmD, RPh

Safety Regulatory Project Manager

Center for Drug Evaluation and Research (CDER)

Office of Surveillance and Epidemiology (OSE)

Ph: 240-402-4559

E: davis.mathew@fda.hhs.gov



This e-mail message may contain information that is protected, privileged, or confidential, and it should not be disseminated, distributed, or copied to persons not authorized to receive such information. If you are not the intended recipient, any dissemination, distribution or copying is strictly prohibited. If you think you have received this e-mail message in error, please e-mail the sender immediately at davis.mathew@fda.hhs.gov.

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

DAVIS MATHEW
02/09/2026 10:45:25 AM

NDA 215256/S-031

**ACKNOWLEDGMENT --
PRIOR APPROVAL SUPPLEMENT**

Novo Nordisk Inc.
Attention: Devraj Chakravarty
Director, Regulatory Affairs
800 Scudders Mill Road
P.O. Box 846
Plainsboro, NJ 08536

Dear Devraj Chakravarty:

We have received your supplemental new drug application (sNDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA or the Act) for the following:

NDA NUMBER:	215256
SUPPLEMENT NUMBER:	031
PRODUCT NAME:	Wegovy (semaglutide) injection
DATE OF SUBMISSION:	January 5, 2026
DATE OF RECEIPT:	January 5, 2026

This supplemental application proposes an additional presentation of Wegovy in a single dose manual prefilled syringe (mPFS) for all currently approved doses (0.25 mg, 0.5 mg, 1.0 mg, 1.7 mg, and 2.4 mg). The proposed changes to the combined labeling are being submitted to both NDA 215256 and NDA 218316.

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on March 6, 2026, in accordance with 21 CFR 314.101(a).

If the application is filed, the user fee goal date will be May 5, 2026.

If you have not already done so, promptly submit the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at FDA.gov.¹

¹ <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

Failure to submit the content of labeling in SPL format may result in a refusal-to-file action.

If you have any questions, call me at 240-402-6018.

Sincerely,

{See appended electronic signature page}

Martin White, M.S.
Regulatory Project Manager
Diabetes, Lipid Disorders, and Obesity
Division of Regulatory Operations for Cardiology,
Hematology, Endocrinology, and Nephrology
Office of Regulatory Operations
Office of New Drugs
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

MARTIN L WHITE
01/23/2026 10:49:11 AM

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION			REQUEST FOR CONSULTATION	
TO (Division/Office): Mail: OSE			FROM: Martin White DDLO	
DATE 1.7.2026	IND NO. 126360	NDA NO. 215256	TYPE OF DOCUMENT CMC supplement	DATE OF DOCUMENT 1.5.2026
NAME OF DRUG Wegovy injection		PRIORITY CONSIDERATION Priority	CLASSIFICATION OF DRUG GLP-1	DESIRED COMPLETION DATE 4/3/2026
NAME OF FIRM: Novo Nordisk				
REASON FOR REQUEST				
I. GENERAL				
☐ NEW PROTOCOL ☐ PROGRESS REPORT ☐ NEW CORRESPONDENCE ☐ DRUG ADVERTISING ☐ ADVERSE REACTION REPORT ☐ MANUFACTURING CHANGE/ADDITION ☐ MEETING PLANNED BY ☐ PRE-NDA MEETING ☐ END OF PHASE II MEETING ☐ RESUBMISSION ☐ SAFETY/EFFICACY ☐ CONTROL SUPPLEMENT ☐ RESPONSE TO DEFICIENCY LETTER ☐ FINAL PRINTED LABELING ☒ LABELING REVISION ☐ ORIGINAL NEW CORRESPONDENCE ☐ FORMULATIVE REVIEW ☐ MEDICATION ERRORS ☐ OTHER (SPECIFY BELOW):				
II. BIOMETRICS				
STATISTICAL EVALUATION BRANCH			STATISTICAL APPLICATION BRANCH	
☐ TYPE A OR B NDA REVIEW ☐ END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER (SPECIFY BELOW):			☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER (SPECIFY BELOW):	
III. BIOPHARMACEUTICS				
☐ DISSOLUTION ☐ BIOAVAILABILITY STUDIES ☐ PHASE IV STUDIES			☐ DEFICIENCY LETTER RESPONSE ☐ PROTOCOL-BIOPHARMACEUTICS ☐ IN-VIVO WAIVER REQUEST	
IV. DRUG EXPERIENCE				
☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below) ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP			☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY ☐ SUMMARY OF ADVERSE EXPERIENCE ☐ POISON RISK ANALYSIS	
V. SCIENTIFIC INVESTIGATIONS				
☐ CLINICAL			☐ PRECLINICAL	
COMMENTS/SPECIAL INSTRUCTIONS: DDLO received a supplement for Wegovy (NDA 215256) on January 5, 2026. This supplemental application proposes the addition of a new presentation of Wegovy in a manual prefilled syringe (mPFS) for all currently approved doses (0.25 mg, 0.5 mg, 1.0 mg, 1.7 mg, and 2.4 mg). The link to the submission is below EDR Location: \\CDSESUB1\evsprod\NDA215256\1202 The submission includes the proposed carton and container labeling, SPL labeling content, proposed mPFS Instructions for Use (IFU), and a revised Prescribing Information in both tracked/clean MS Word versions of the combined Wegovy® PI that reflect all proposed changes. I will provide dates for meetings once review assignments have been made. The submission includes Human Factors data. The goal date for this submission is 5/5/2026.				
SIGNATURE OF REQUESTER			METHOD OF DELIVERY (Check all that apply)	

	☐ MAIL ☐ DARRTS ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

06/18/2013

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

MARTIN L WHITE
01/07/2026 02:10:48 PM