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

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).

--- INDICATIONS AND USAGE ---

WEGOVY® is a glucagon-like peptide-1 (GLP-1) receptor agonist indicated as an adjunct to a reduced calorie diet and increased physical activity for chronic weight management in adult patients with an initial body mass index (BMI) of:

- ≥30 kg/m² or greater (obesity) or
- ≥27 kg/m² or greater (overweight) in the presence of at least one weight-related comorbid condition (e.g., hypertension, type 2 diabetes mellitus, or dyslipidemia) (1)

Limitations of Use:

- WEGOVY® should not be used in combination with other semaglutide-containing products or any other GLP-1 receptor agonist (1)
- The safety and efficacy of coadministration with other products for weight loss have not been established (1).
- WEGOVY® has not been studied in patients with a history of pancreatitis (1).

--- DOSAGE AND ADMINISTRATION ---

Administer WEGOVY® once weekly, on the same day each week, at any time of day, with or without meals (2.2).

Inject subcutaneously in the abdomen, thigh or upper arm (2.2).

Initiate at 0.25 mg once weekly for 4 weeks. In 4 week intervals, increase the dose until a dose of 2.4 mg is reached (2.3).

The maintenance dose of WEGOVY® is 2.4 mg once weekly (2.3).

In patients with type 2 diabetes, monitor blood glucose prior to starting and during WEGOVY® treatment.

--- DOSAGE FORMS AND STRENGTHS ---

Injection: pre-filled, single-dose pen that delivers doses of 0.25 mg, 0.5 mg, 1 mg, 1.7 mg or 2.4 mg (3).

--- CONTRAINDICATIONS ---

- Personal or family history of medullary thyroid carcinoma or in patients with Multiple Endocrine Neoplasia syndrome type 2 (4, 5.1).
- Known hypersensitivity to semaglutide or any of the excipients in WEGOVY® (4).

--- WARNINGS AND PRECAUTIONS ---

- Thyroid C-cell Tumors: See Boxed Warning (5.1).
- Acute Pancreatitis: Has occurred in clinical trials. Discontinue promptly if pancreatitis is suspected. Do not restart if pancreatitis is confirmed (5.2).
- Acute Gallbladder Disease: Has occurred in clinical trials. If cholecystitis is suspected, gallbladder studies and clinical follow-up are indicated (5.3).
- Hypoglycemia: Concomitant use with an insulin secretagogue or insulin may increase the risk of hypoglycemia, including severe hypoglycemia. Reducing the dose of insulin secretagogue or insulin may be necessary. Inform all patients of the risk of hypoglycemia and educate them on the signs and symptoms of hypoglycemia (5.4, 7.1).
- Acute Kidney Injury: Has occurred. Monitor renal function when initiating or escalating doses of WEGOVY® in patients reporting severe adverse gastrointestinal reactions or in those with renal impairment reporting severe adverse gastrointestinal reactions (5.5).
- Hypersensitivity: Anaphylactic reactions and angioedema have been reported postmarketing. Discontinue WEGOVY® if suspected and promptly seek medical advice (5.6).
- 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 (5.7).
- Heart Rate Increase: Monitor heart rate at regular intervals (5.8).
- Suicidal Behavior and Ideation: Monitor for depression or suicidal thoughts. Discontinue WEGOVY® if symptoms develop (5.9).

--- ADVERSE REACTIONS ---

The most common adverse reactions, reported in greater than or equal to 5% of patients treated with WEGOVY® are: nausea, diarrhea, vomiting, constipation, abdominal pain, headache, fatigue, dyspepsia, dizziness, abdominal distension, eructation, hypoglycemia in patients with type 2 diabetes, flatulence, gastroenteritis, and gastrointestinal reflux disease (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. Use with caution (7.2).

--- USE IN SPECIFIC POPULATIONS ---

- Pregnancy: May cause fetal harm. When pregnancy is recognized, discontinue WEGOVY® (8.1).
- Females and Males of Reproductive Potential: 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.

Revised: 06/2021

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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) and 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 hormones (e.g., a mass in the neck, dysphagia, 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) and Warnings and Precautions (5.1)).

Table 1. BMI Conversion Chart

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Height (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>45.4</td>
<td>170</td>
</tr>
<tr>
<td>51.1</td>
<td>175</td>
</tr>
<tr>
<td>56.9</td>
<td>180</td>
</tr>
<tr>
<td>62.6</td>
<td>185</td>
</tr>
<tr>
<td>68.4</td>
<td>190</td>
</tr>
</tbody>
</table>

Table 2. Dose Escalation Schedule

<table>
<thead>
<tr>
<th>Weeks</th>
<th>Weekly Dose</th>
<th>Dose Escalation</th>
<th>Maintenance Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 through 4</td>
<td>0.25 mg</td>
<td>Dose escalation</td>
<td>2.4 mg</td>
</tr>
<tr>
<td>5 through 8</td>
<td>0.5 mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9 through 12</td>
<td>1 mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13 through 16</td>
<td>1.7 mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 17 and onward</td>
<td>2.4 mg</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

4 CONTRAINDICATIONS
WEGOVY® is contraindicated in the following conditions:
• A personal or family history of medullary thyroid carcinoma (MTC) or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2) (see Warnings and Precautions (5.1)).
• A prior serious hypersensitivity reaction to semaglutide or to any of the excipients in WEGOVY®. Serious hypersensitivity reactions, including anaphylaxis and angioedema, have been reported with semaglutide (see Warnings and Precautions (5.6)).

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 medullary thyroid carcinoma (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 hormones (e.g., a mass in the neck, dysphagia, 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.
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 semaglutide. Acute pancreatitis was observed in patients treated with WEGOVY® in clinical trials [see Adverse Reactions (6)]. After initiation of WEGOVY®, observe patients carefully for signs and symptoms of acute pancreatitis (including intermittent severe abdominal pain, sometimes radiating to the back, and which may or may not be accompanied by vomiting). If acute pancreatitis is suspected, WEGOVY® should promptly be discontinued and appropriate management should be initiated. If acute pancreatitis is confirmed, WEGOVY® should not be restarted.

WEGOVY® has not been studied in patients with a history of pancreatitis. It is unknown if patients with a history of pancreatitis are at higher risk for development of pancreatitis on WEGOVY®.

5.3 Acute Gallbladder Disease
In WEGOVY® randomized clinical trials, cholecystitis was reported by 1.6% of WEGOVY®-treated patients and 0.7% of placebo-treated patients. Cholecystitis was reported by 0.6% of WEGOVY®-treated patients and 0.2% of placebo-treated patients. Substantial or rapid weight loss can increase the risk of cholecystitis; 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 cholecystitis 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 patients with type 2 diabetes and BMI greater than or equal to 27 kg/m², hypoglycemia (defined as a plasma glucose less than 54 mg/dL) was reported in 6.2% of WEGOVY®-treated patients versus 2.5% of placebo-treated patients. One episode of severe hypoglycemia (requiring the assistance of another person) was reported in one WEGOVY®-treated patient versus no placebo-treated patients.

Patients with type 2 diabetes mellitus taking WEGOVY® in combination with an insulin secretagogue (such as sulfonylureas) or insulin may have an increased risk of hypoglycemia, including severe hypoglycemia [see Adverse Reactions (6.1)]. Hypoglycemia has been observed in patients treated with semaglutide at doses of 0.5 and 1 mg in combination with insulin. The addition of WEGOVY® in patients treated 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 type 2 diabetes, monitor blood glucose prior to starting WEGOVY® and during WEGOVY® treatment. When initiating WEGOVY®, consider reducing the dose of concomitantly administered insulin secretagogue (such as sulfonylureas) or insulin to reduce the risk of hypoglycemia [see Drug Interactions (7)].

5.5 Acute Kidney Injury
There have been postmarketing reports of acute kidney injury and worsening of chronic renal failure, which have in some cases required hemodialysis, in patients treated with semaglutide. Patients with renal impairment may be at greater risk of acute kidney injury, but some of these events have been reported in patients without known underlying renal disease. A majority of the reported events occurred in patients who had experienced nausea, vomiting, or diarrhea, leading to volume depletion [see Adverse Reactions (6)]. Monitor renal function when initiating or escalating doses of WEGOVY® in patients receiving several adverse gastrointestinal reactions. Monitor renal function in patients with renal impairment reporting any adverse reactions that could lead to volume depletion.

5.6 Hypersensitivity
Serious hypersensitivity reactions (e.g., anaphylaxis, angioedema) have been reported with semaglutide. If hypersensitivity reactions occur, discontinue use of WEGOVY®, treat promptly per standard of care, and monitor until signs and symptoms resolve. Do not use in patients with a previous hypersensitivity to semaglutide or any of the excipients in WEGOVY® [see Contraindications (4)].

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®.

5.7 Diabetic Retinopathy Complications in Patients with Type 2 Diabetes
In a trial of patients with type 2 diabetes and BMI greater than or equal to 27 kg/m², diabetic retinopathy was reported by 4.0% of WEGOVY®-treated patients and 2.7% placebo-treated patients.

In a 2-year trial with semaglutide 0.5 mg and 1 mg once-weekly injection in 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 (3.0%) compared to placebo (1.8%). The absolute risk increase for diabetic retinopathy was reported by 4.0% of WEGOVY®-treated patients and 0.7% of placebo-treated patients. Cholecystitis was reported by 0.6% of WEGOVY®-treated patients and 0.2% of placebo-treated patients. Substantial or rapid weight loss can increase the risk of cholecystitis; 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 cholecystitis is suspected, gallbladder studies and appropriate clinical follow-up are indicated.

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.

5.8 Heart Rate Increase
Mean increases in resting heart rate of 1 to 4 beats per minute (bpm) were observed in WEGOVY®, treated patients compared to placebo in clinical trials. 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). 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 heart beat while at rest during WEGOVY® treatment. If patients experience a sustained increase in resting heart rate, discontinue WEGOVY®.

5.9 Suicidal Behavior and Ideation
Suicidal behavior and ideation have been reported in clinical trials with other weight management products. Monitor patients treated with WEGOVY® for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior. Discontinue WEGOVY® in patients who experience suicidal thoughts or behaviors. Avoid WEGOVY® in patients with a history of suicidal attempts or active suicidal ideation.

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 [see Warnings and Precautions (5.5)]
- Hypersensitivity [see Warnings and Precautions (5.6)]
- Diabetic Retinopathy Complications in Patients with Type 2 Diabetes [see Warnings and Precautions (5.7)]
- Heart Rate Increase [see Warnings and Precautions (5.8)]
- Suicidal Behavior and Ideation [see Warnings and Precautions (5.9)]

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.

WEGOVY® was evaluated for safety in 3 randomized, double-blind, placebo-controlled trials that included 2116 patients with overweight or obesity treated with WEGOVY® for up to 68 weeks and a 7 week off drug follow-up period. Baseline characteristics included a mean age of 48 years, 71% women, 72% White, 42% with hypertension, 19% with type 2 diabetes, 43% with dyslipidemia, 28% with a BMI greater than 40 kg/m², and 4% with cardiovascular disease.

In clinical trials, 6.8% of patients treated with WEGOVY® 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 0.0%), and diarrhea (0.7% versus 0.1%) for WEGOVY® and placebo, respectively.

Adverse reactions reported in greater than or equal to 2% of WEGOVY®-treated patients and more frequently than in placebo-treated patients are shown in Table 3.

Table 3. Adverse Reactions Occurring in ≥2% of WEGOVY®-treated Patients and More Frequently than with Placebo

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Placebo N=1261</th>
<th>WEGOVY® N=2116</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>16</td>
<td>44</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>16</td>
<td>30</td>
</tr>
<tr>
<td>Vomiting</td>
<td>6</td>
<td>24</td>
</tr>
<tr>
<td>Constipation</td>
<td>11</td>
<td>24</td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>10</td>
<td>20</td>
</tr>
<tr>
<td>Headache</td>
<td>10</td>
<td>14</td>
</tr>
<tr>
<td>Fatigue</td>
<td>5</td>
<td>11</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>Dizziness</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>Abdominal Distension</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Eruption</td>
<td>&lt;1</td>
<td>7</td>
</tr>
<tr>
<td>Hypoglycemia in T2DM</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Flatulence</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Gastroenteritis</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Gastroesophageal Reflux Disease</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Gastritis</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Gastroenteritis Viral</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Hair Loss</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>

*Includes abdominal pain, abdominal pain upper, abdominal pain lower, gastrointestinal pain, abdominal tenderness, abdominal discomfort and epigastric discomfort

*Includes fatigue and aethesia

*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 2, WEGOVY® N=403, PLoAR N=462). See text below for further information regarding hypoglycemia in patients with and without type 2 diabetes. T2DM = type 2 diabetes mellitus

*Includes chronic gastritis, gastritis, gastritis erosive, and reflux gastritis

Acute Pancreatitis
In WEGOVY® clinical trials, acute pancreatitis was confirmed by adjudication in 4 WEGOVY®-treated patients (0.2 cases per 100 patient years) versus 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.

WEGOVY® (semaglutide) injection 2.4 mg
Wegovy® (semaglutide) injection 2.4 mg

6.3 Postmarketing Experience

The following adverse reactions have been reported during post-approval use of semaglutide. 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

Hypersensitivity: anaphylaxis, angioedema, rash, urticaria

Renal and Urinary Disorders: acute kidney injury

7 DRUG INTERACTIONS

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

Wegovy® lowers blood glucose and can cause hypoglycemia. The risk of hypoglycemia is increased when Wegovy® is used in combination with insulin secretagogues (e.g., sulfonylureas) or insulin. The addition of Wegovy® in patients treated with insulin should only be undertaken after careful consideration. When initiating Wegovy®, consider reducing the dose of concomitantly administered insulin secretagogue (such as sulfonylureas) or insulin to reduce the risk of hypoglycemia [see Warnings and Precautions (5.4) and 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, semaglutide did not affect the absorption of orally administered medications [see Clinical Pharmacology (12.3)]. Nonetheless, monitor the effects of oral medications concomitantly administered with Wegovy®.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Exposure Registry

There will be a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to semaglutide during pregnancy. Pregnant women exposed to Wegovy® and healthcare providers are encouraged to contact Novo Nordisk at 1-800-727-6500.

Risk Summary

Based on animal reproduction studies, there may be potential risks to the fetus from exposure to semaglutide during pregnancy. Additionally, 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, and discontinue Wegovy® [see Clinical Considerations]. 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.

In pregnant rats administered semaglutide during organogenesis, embryofetal mortality, structural abnormalities and alterations to growth occurred at maternal exposures below the maximum recommended human dose (MRHD) based on AUC. In rabbits and cynomolgus monkeys administered semaglutide during organogenesis, early pregnancy losses and structural abnormalities were observed at below the MRHD (rabbit) and greater than or equal to 2-fold the MRHD (monkey). These findings coincided with a marked maternal body weight loss in both animal species [see Data]. The estimated background risk of major birth defects and miscarriage for the indicated population are unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, 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.

Data

Animal Data

In a combined fertility and embryofetal development study in rats, subcutaneous doses of 0.01, 0.03 and 0.09 mg/kg/day (0.04-, 0.1-, and 0.4-fold the MRHD) were administered to males for 4 weeks prior to and throughout mating and to females for 2 weeks prior to mating, and throughout organogenesis to Gestation Day 17. In parental animals, 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 the human exposure.

In an embryofetal development study in pregnant rabbits, subcutaneous doses of 0.0010, 0.0025 or 0.0075 mg/kg/day (0.01-, 0.1-, and 0.9-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 (sternebra) fetal abnormalities were observed at greater than or equal to 0.0025 mg/kg/day, at clinically relevant exposures.

In an embryofetal development study in pregnant cynomolgus monkeys, subcutaneous doses of 0.015, 0.075, and 0.15 mg/kg twice weekly (0.2-, 1-, and 3-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 (greater than or equal to 1 time human exposure).
8.2 Lactation

Risk Summary

There are no data on the presence of semaglutide or its metabolites in human milk, the effects on the breastfed infant, or the effects on milk production. Semaglutide was present in the milk of lactating rats. When a drug is present in animal milk, it is likely that the drug will be present in human milk (see Data). 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.

Data

In lactating rats, semaglutide was detected in milk at levels 3-12 fold lower than in maternal plasma.

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

Safety and efficacy of WEGOVY® have not been established in pediatric patients.

8.5 Geriatric Use

In the WEGOVY® clinical trials, 233 (8.8%) WEGOVY®-treated patients were between 65 and 75 years of age and 23 (0.9%) WEGOVY®-treated patients were 75 years of age or over. No overall differences in safety or efficacy were detected between these patients and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

8.6 Renal Impairment

No dose adjustment of WEGOVY® is recommended for patients with renal impairment. In a study in subjects with renal impairment, including end-stage renal disease, no clinically relevant change in semaglutide pharmacokinetics was observed (see Clinical Pharmacology (12.3)).

8.7 Hepatic Impairment

No dose adjustment of WEGOVY® is recommended for patients with hepatic impairment. In a study in subjects with different degrees of hepatic impairment, no clinically relevant change in semaglutide pharmacokinetics was observed (see Clinical Pharmacology (12.3)).

10 OVERDOSAGE

Overdoses have been reported with other GLP-1 receptor agonists. Effects include 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. 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® (semaglutide) injection, for subcutaneous use, 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_{320}N_{41}O_{93}S and the molecular weight is 4113.58 g/mol.

Figure 1. Structural Formula of semaglutide

WEGOVY® 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 or 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.

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.

12.2 Pharmacodynamics

Semaglutide lowers body weight through decreased calorie intake. The effects are likely mediated by affecting appetite. As with other GLP-1 receptor agonists, semaglutide stimulates insulin secretion and reduces glucagon secretion in a glucose-dependent manner. These effects can lead to a reduction of blood glucose.

Cardiac electrophysiology (QTc)

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

12.3 Pharmacokinetics

Absorption

Absolute bioavailability of semaglutide is 89%. 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® was approximately 75 nmol/L in patients with either obesity (BMI greater than or equal to 30 kg/m²) or overweight (BMI greater than or equal to 27 kg/m²). The steady state exposure of WEGOVY® increased proportionally with doses up to 2.4 mg once-weekly.

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 obesity or overweight 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 dose of 2.4 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.

Special Populations

The effects of intrinsic factors on the pharmacokinetics of semaglutide are shown in Figure 2.

Figure 2. Impact of intrinsic factors on semaglutide exposure

Intrinsic factor Relative exposure (Cavg) Ratio and 90% CI

| Sex | Male | | |
| Age group | 65—< 75 years | >75 years | | |
| Race | Black or African American | Asian | American Indian or Alaska Native | | |
| Ethnicity | Hispanic or Latino | | |
| Body weight | 74 kg | 143 kg | | |
| Renal function | Mild | Moderate | | |
| Injection site | Thigh | Upper arm | | |

Data are steady-state dose-normalized average semaglutide exposures relative to a reference subject profile (non-Hispanic or Latino, white female aged 18 to less than 65 years, with a body weight of 110 kg and normal renal function, who injected in the abdomen). Body weight categories (74 and 143 kg) represent the 5% and 95% percentiles in the dataset.

Renal Impairment

Renal impairment did not impact the exposure of semaglutide in a clinically relevant manner. The pharmacokinetics of semaglutide were evaluated following a single dose of 0.5 mg semaglutide in a study of patients with different degrees of renal impairment (mild, moderate, severe, or ESRD) compared with subjects with normal renal function. The pharmacokinetics were also assessed in subjects with overweight (BMI 27-29.9 kg/m²) or obesity (BMI greater than or equal to 30 kg/m²) and mild to moderate renal impairment, based on data from clinical trials.

Hepatic Impairment

Hepatic impairment did not impact the exposure of semaglutide. The pharmacokinetics of semaglutide were evaluated following a single dose of 0.5 mg semaglutide in a study of patients with different degrees of hepatic impairment (mild, moderate, severe) compared with subjects with normal hepatic function.

Drug Interactions

In vitro studies have shown very low potential for semaglutide to inhibit or induce CYP enzymes, or to inhibit drug transporters.

The delay of gastric emptying with semaglutide may influence the absorption of concomitantly administered oral medications (see Drug Interactions (7.2)). The potential effect of semaglutide on the absorption of coadministered oral medications was studied in trials at semaglutide 1 mg steady-state exposure. No clinically relevant drug-drug interactions with semaglutide (Figure 3) were observed based on the evaluated medications. In a separate study, no apparent effect on the rate of gastric emptying was observed with semaglutide 2.4 mg.
The intent-to-treat population includes all randomized patients. In Study 1, at week 68, the body weight was missing for 44.5% of patients randomized to WEGOVY® and placebo, respectively. Among the 803 randomized patients, the mean age was 46 years, 79% were women, 83.7% were White, 13% were Black or African American, and 2.4% Asian. A total of 7.8% were Hispanic or Latino. Mean body weight at randomization (week 20) was 96.1 kg and mean BMI at randomization (week 20) was 34.4 kg/m².

The proportions of patients who discontinued study drug in Studies 1, 2, and 3 was 16.0% for the WEGOVY®-treated group and 19.1% for the placebo-treated group, and 6.8% of patients treated with WEGOVY® and 3.2% of patients treated with placebo discontinued treatment due to an adverse reaction [see Adverse Reactions (6.1)]. In Study 4, the proportions of patients who discontinued study drug were 5.8% and 11.6% for WEGOVY® and placebo, respectively.

14.1 Weight Management Studies in Adults with Overweight or Obesity

For Studies 1, 2, and 3, 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® resulted in a statistically significant reduction in body weight compared with placebo. Greater proportions of patients treated with WEGOVY® achieved 5%, 10%, and 15% weight loss than those treated with placebo as shown in Table 4.

### Table 4. Changes in Body Weight at Week 68 in Studies 1, 2 and 3

<table>
<thead>
<tr>
<th></th>
<th>Study 1 (Obesity or overweight with comorbidity)</th>
<th>Study 2 (Type 2 diabetes with obesity or overweight)</th>
<th>Study 3 (Obesity or overweight with comorbidity undergoing intense lifestyle therapy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intention-to-Treat</td>
<td>PLACEBO N = 655</td>
<td>WEGOVY® N = 1306</td>
<td>PLACEBO N = 204</td>
</tr>
<tr>
<td></td>
<td>N = 654</td>
<td>N = 403</td>
<td>N = 204</td>
</tr>
<tr>
<td>Body Weight</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline mean (kg)</td>
<td>105.2</td>
<td>105.4</td>
<td>100.5</td>
</tr>
<tr>
<td>% change from baseline (LSMean)</td>
<td>-2.4</td>
<td>-14.9</td>
<td>-3.4</td>
</tr>
<tr>
<td>% difference from placebo (LSMean) (95% CI)</td>
<td>-12.4</td>
<td>(-13.3; -11.6)*</td>
<td>-6.2</td>
</tr>
<tr>
<td>% of Patients losing greater than or equal to 5% weight body weight</td>
<td>31.1</td>
<td>83.5</td>
<td>30.2</td>
</tr>
<tr>
<td>% difference from placebo (LSMean) (95% CI)</td>
<td>52.4</td>
<td>(48.1; 56.7)*</td>
<td>37.2</td>
</tr>
<tr>
<td>% of Patients losing greater than or equal to 10% body weight</td>
<td>12.0</td>
<td>66.1</td>
<td>10.2</td>
</tr>
<tr>
<td>% difference from placebo (LSMean) (95% CI)</td>
<td>54.1</td>
<td>(50.4; 57.9)*</td>
<td>34.3</td>
</tr>
<tr>
<td>% of Patients losing greater than or equal to 15% body weight</td>
<td>4.8</td>
<td>47.9</td>
<td>4.3</td>
</tr>
<tr>
<td>% difference from placebo (LSMean) (95% CI)</td>
<td>43.1</td>
<td>(39.8; 46.3)*</td>
<td>20.7</td>
</tr>
</tbody>
</table>

**Placebo:** 5%; 10% and 15% weight loss than those treated with placebo as shown in Table 4.

### 14 CLINICAL STUDIES

**Overview of Clinical Studies**

The safety and efficacy of WEGOVY® for chronic weight management (weight loss and maintenance) in conjunction with a reduced calorie diet and increased physical activity were studied in three 68-week, randomized, double-blind, placebo-controlled trials and one 68-week, randomized, double-blind, placebo withdrawal trial. In Studies 1, 2, and 3, WEGOVY® or matching placebo was escalated to 2.4 mg subcutaneous weekly during a 16-week period followed by 52 weeks on maintenance dose. In Study 4, WEGOVY® was escalated during a 20-week run-in period, and patients who reached WEGOVY® 2.4 mg after the run-in period were randomized to either continued treatment with WEGOVY® or placebo for 48 weeks.

In Studies 1, 2, and 4, all patients received instruction for a reduced calorie meal diet (approximately 500 kcal/day defic, 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 3, patients received an initial 8-week low-calorie diet (total energy intake 1000 to 1200 kcal/day) followed by 60 weeks of a reduced calorie diet (1200-1800 kcal/day) and increased physical activity (100 mins/week with gradual increase to 200 mins/week).

**Study 1**

Study 1 was a 68-week trial that enrolled 1961 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. Mean body weight at randomization was 106.8 kg and mean BMI was 38.3 kg/m². All patients received WEGOVY® 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 and were then randomized in a 2:1 ratio to either continue on WEGOVY® or receive placebo. Among the 803 randomized patients, the mean age was 46 years, 79% were women, 83.7% were White, 13% were Black or African American, and 2.4% Asian. A total of 7.8% were Hispanic or Latino. Mean body weight at randomization (week 20) was 96.1 kg and mean BMI at randomization (week 20) was 34.4 kg/m².

The safety and efficacy of WEGOVY® was assessed after a single dose. Abbreviations: AUC: area under the curve, Cmax: maximum concentration, CI: confidence interval.

### 13 NONCLINICAL TOXICOLOGY

#### 13.1 Carcinogenesis, Impairment of Fertility

In a 2-year carcinogenicity study in CD-1 mice, subcutaneous doses of 0.3, 1, and 3 mg/kg/day (2-, 8-, and 22-fold the maximum recommended human dose [MRHD] of 2.4 mg/week based on AUC) were administered to the males, and 0.1, 0.3 and 1 mg/kg/day (0.6-, 2-, and 5-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 (greater than or equal to 0.6 times human exposure).

In a 2-year carcinogenicity study in Sprague Dawley rats, subcutaneous doses of 0.0025, 0.01, 0.025 and 0.1 mg/kg/day were administered (below quantification, 0.2-, 0.4-, and 2-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 Boxed Warning and Warnings and Precautions (5.1)]. Semaglutide was not mutagenic or clastogenic in a standard battery of genotoxicity tests (bacterial mutagenicity Ames human lymphocyte chromosome aberration, rat bone marrow micronucleus).

In a combined fertility and embryo-fetal development study in rats, subcutaneous doses of 0.01, 0.03 and 0.09 mg/kg/day (0.4-, 1-, and 0.4-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. These effects were likely an adaptive response secondary to the pharmacological effect of semaglutide on food consumption and body weight.

**PLACEBO**

### 14.2 Levonorgestrel and Ethinyl estradiol

**Levonorgestrel**

**Ethinyl estradiol**
### Table 5. Changes in Body Weight at Week 68 - Study 4 (Obesity or overweight with comorbidity after 20 week run-in)

<table>
<thead>
<tr>
<th>WEGOVY®</th>
<th>PLACEBO N = 268</th>
<th>WEGOVY® N = 535</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body Weight (only randomized patients)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean at week 0 (kg)</td>
<td>107.2</td>
<td></td>
</tr>
<tr>
<td>Mean at week 20 (SD) (kg)</td>
<td>95.4 (22.7)</td>
<td>96.5 (22.5)</td>
</tr>
<tr>
<td>% change from week 20 at week 68 (LSMean)</td>
<td>6.9</td>
<td>-7.9</td>
</tr>
<tr>
<td>% difference from placebo (LSMean) (95% CI)</td>
<td>-14.8 (-16.0; -13.5)*</td>
<td></td>
</tr>
</tbody>
</table>

LSMean = least squares mean; CI = confidence interval
*p<0.001 (unadjusted 2-sided) for superiority, controlled for multiplicity.

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 4 and Figure 5 for Studies 1 and 2. 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 1 intersects the WEGOVY® and placebo curves at approximately 66%, and 12%, respectively, which correspond to the values shown in Table 4.

### Figure 4. Change in body weight (%) from baseline to week 68 (Study 1)

### Figure 5. Change in body weight (%) from baseline to week 68 (Study 2)

### Table 6. Changes in Anthropometry and Cardiometabolic Parameters at Week 68 in Studies 1, 2 and 3

<table>
<thead>
<tr>
<th>Study 1 (Obesity or overweight with comorbidity)</th>
<th>Study 2 (Type 2 diabetes with obesity)</th>
<th>Study 3 (Obesity or overweight with comorbidity undergoing intensive lifestyle therapy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intention-to-Treat</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waist Circumference (cm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>114.8</td>
<td>115.5</td>
</tr>
<tr>
<td>Changes from baseline (LSMean)</td>
<td>-4.1</td>
<td>-4.5</td>
</tr>
<tr>
<td>Difference from placebo (LSMean)</td>
<td>-9.4</td>
<td>-9.4</td>
</tr>
<tr>
<td>Systolic Blood Pressure (mmHg)</td>
<td>127</td>
<td>130</td>
</tr>
<tr>
<td>Baseline</td>
<td>-1.1</td>
<td>-0.5</td>
</tr>
<tr>
<td>Changes from baseline (LSMean)</td>
<td>-6.2</td>
<td>-3.9</td>
</tr>
<tr>
<td>Difference from placebo (LSMean)</td>
<td>-5.1</td>
<td>-3.4</td>
</tr>
<tr>
<td>Diastolic Blood Pressure (mmHg)</td>
<td>80</td>
<td>80</td>
</tr>
<tr>
<td>Baseline</td>
<td>-0.4</td>
<td>-0.9</td>
</tr>
<tr>
<td>Changes from baseline (LSMean)</td>
<td>-2.8</td>
<td>-1.6</td>
</tr>
<tr>
<td>Difference from placebo (LSMean)</td>
<td>-2.4</td>
<td>-0.8</td>
</tr>
<tr>
<td>Heart Rate (%)</td>
<td>72</td>
<td>76</td>
</tr>
<tr>
<td>Baseline</td>
<td>-0.7</td>
<td>-0.2</td>
</tr>
<tr>
<td>Changes from baseline (LSMean)</td>
<td>3.5</td>
<td>2.5</td>
</tr>
<tr>
<td>Difference from placebo (LSMean)</td>
<td>4.3</td>
<td>2.7</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>5.7</td>
<td>5.7</td>
</tr>
<tr>
<td>Baseline</td>
<td>0.2</td>
<td>0.4</td>
</tr>
<tr>
<td>Changes from baseline (LSMean)</td>
<td>-0.4</td>
<td>-1.6</td>
</tr>
<tr>
<td>Difference from placebo (LSMean)</td>
<td>-0.3</td>
<td>-0.3</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dL)</td>
<td>192.1</td>
<td>170.8</td>
</tr>
<tr>
<td>Baseline</td>
<td>0.1</td>
<td>-0.5</td>
</tr>
<tr>
<td>Percent Change from baseline (LSMean)</td>
<td>-3.3</td>
<td>-1.4</td>
</tr>
<tr>
<td>Relative difference from placebo (LSMean)</td>
<td>-3.3</td>
<td>-0.9</td>
</tr>
<tr>
<td>LDL Cholesterol (mg/dL)</td>
<td>112.5</td>
<td>90.1</td>
</tr>
<tr>
<td>Baseline</td>
<td>1.3</td>
<td>-2.5</td>
</tr>
<tr>
<td>Percent Change from baseline (LSMean)</td>
<td>0.1</td>
<td>0.5</td>
</tr>
<tr>
<td>Relative difference from placebo (LSMean)</td>
<td>-3.8</td>
<td>0.4</td>
</tr>
</tbody>
</table>

The time courses of weight loss with WEGOVY® and placebo from baseline through week 68 are depicted in Figures 6 and Figure 7.
WEGOVY® (semaglutide) injection 2.4 mg

Table 7. Mean Changes in Anthropometry and Cardiometabolic Parameters in Study 4 (Obesity or overweight with comorbidity after 20 week run-in)

<table>
<thead>
<tr>
<th></th>
<th>PLACEBO N = 268</th>
<th>WEGOVY® N = 535</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Randomization</strong> (week 20)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Change from Randomization (week 20) to week 68 (LSMean)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waist Circumference (cm)</td>
<td>104.7</td>
<td>105.5</td>
</tr>
<tr>
<td>Systolic Blood Pressure (mmHg)</td>
<td>121</td>
<td>121</td>
</tr>
<tr>
<td>Diastolic Blood Pressure (mmHg)</td>
<td>78</td>
<td>78</td>
</tr>
<tr>
<td>Heart Rate</td>
<td>76</td>
<td>76</td>
</tr>
<tr>
<td>Fasting Blood Glucose (mg/dL)</td>
<td>121</td>
<td>121</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dL)</td>
<td>109.1</td>
<td>109.1</td>
</tr>
<tr>
<td>LDL Cholesterol (mg/dL)</td>
<td>90.1</td>
<td>90.1</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>95.3</td>
<td>95.3</td>
</tr>
<tr>
<td><strong>Relative difference from placebo (LSMean)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waist Circumference (cm)</td>
<td>3.3</td>
<td>3.3</td>
</tr>
<tr>
<td>Systolic Blood Pressure (mmHg)</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Diastolic Blood Pressure (mmHg)</td>
<td>0.3</td>
<td>0.3</td>
</tr>
<tr>
<td>Heart Rate</td>
<td>-2.0</td>
<td>-2.0</td>
</tr>
<tr>
<td>Fasting Blood Glucose (mg/dL)</td>
<td>-0.1</td>
<td>-0.1</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dL)</td>
<td>-5.8</td>
<td>-5.8</td>
</tr>
<tr>
<td>LDL Cholesterol (mg/dL)</td>
<td>-6.1</td>
<td>-6.1</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>-17.8</td>
<td>-17.8</td>
</tr>
</tbody>
</table>

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

| **Model based estimates based on an analysis of covariance model including treatment and baseline values as a covariate** |                 |                 |
| **Not included in the pre-specified hierarchical testing** |                 |                 |
| **Model based estimates based on a mixed model with repeated measures including treatment and baseline values as a covariate** |                 |                 |
| **Baseline value is the geometric mean** |                 |                 |

**14.3 Cardiovascular Outcomes Trial of Semaglutide 0.5 mg and 1 mg in Patients with Type 2 Diabetes and Cardiovascular Disease**

Semaglutide 0.5 mg and 1 mg (OZEMPIC®) are used in the treatment of type 2 diabetes mellitus in adults. The efficacy of semaglutide at doses of 0.5 mg and 1 mg have not been established for chronic weight management.

SUSTAIN 6 was a 104-week, double-blind trial in which 3297 patients with type 2 diabetes and atherosclerotic cardiovascular disease were randomized to semaglutide 0.5 mg once-weekly, semaglutide 1 mg once-weekly, or placebo in addition to standard-of-care for a median study observation time of 2.1 years. In total, 2,735 (83%) of the patients had a history of cardiovascular disease and 582 (17%) were at high risk but without known cardiovascular disease. The mean age at baseline was 65 years, and 61% were men. Overall, 83% were White, 7% were Black or African American, and 8% were Asian. A total of 16% were identified as Hispanic or Latino. In total, 98.0% of the patients completed the trial and the vital status was known at the end of the trial for 99.6%. The primary composite endpoint was the time from randomization to first occurrence of a major adverse cardiovascular event (MACE): cardiovascular death, non-fatal myocardial infarction or non-fatal stroke. The total number of primary component MACE endpoints was 254 (108 [6.6%] with semaglutide and 146 [8.9%] with placebo). No increased risk for MACE was observed with semaglutide 0.5 mg and 1 mg.

**16 HOW SUPPLIED/STORAGE AND HANDLING**

**How Supplied**

WEGOVY® injection is a clear, colorless solution in a pre-filled, disposable, single-dose pen-injector with an integrated needle in the following packaging configurations:

<table>
<thead>
<tr>
<th>Total Strength per Total Volume</th>
<th>Dose per Pen</th>
<th>Carton Contents</th>
<th>NDC</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.25 mg/0.5 mL</td>
<td>1 dose of 0.25 mg</td>
<td>4 pens</td>
<td>0169-4525-14</td>
</tr>
<tr>
<td>0.5 mg/0.5 mL</td>
<td>1 dose of 0.5 mg</td>
<td>4 pens</td>
<td>0169-4505-14</td>
</tr>
<tr>
<td>1 mg/0.5 mL</td>
<td>1 dose of 1 mg</td>
<td>4 pens</td>
<td>0169-4501-14</td>
</tr>
<tr>
<td>1.7 mg/0.75 mL</td>
<td>1 dose of 1.7 mg</td>
<td>4 pens</td>
<td>0169-4517-14</td>
</tr>
<tr>
<td>2.4 mg/0.75 mL</td>
<td>1 dose of 2.4 mg</td>
<td>4 pens</td>
<td>0169-4524-14</td>
</tr>
</tbody>
</table>

**Recommended Storage**

Store WEGOVY® single-dose pen in the refrigerator from 2°C to 8°C (36°F to 46°F). If needed, prior to cap removal, the pen can be kept from 8°C to 30°C (46°F to 86°F) 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 after use.
There is a pregnancy exposure registry for women who 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), talk to your healthcare provider about how you can use WEGOVY® safely and for use in children 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 medullary thyroid carcinoma (MTC) or if you have an endocrine system condition called Multiple Endocrine Neoplasia syndrome type 2 (MEN 2).
- you have had a serious allergic reaction to semaglutide or any of the ingredients in 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 how 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 insulins. 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®?
- Read the Instructions for Use that comes with WEGOVY®.
- Use WEGOVY® exactly as your healthcare provider tells you to.

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.

Start WEGOVY® with 0.25 mg per week in your first month. In your second month, increase your weekly dose to 0.5 mg. In the third month, increase your weekly dose to 1 mg. In the fourth month, increase your weekly dose to 1.7 mg and in the fifth month onwards, increase your weekly dose to the full dose of 2.4 mg. 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 scheduled 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 more than 2 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.

If you take too much WEGOVY®, you may have severe nausea, severe vomiting and severe low blood sugar. Call your healthcare provider or go to the nearest hospital emergency room right away if you experience any of these symptoms.

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 vomiting. 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)
  - yellowing of skin or eyes (jaundice)
  - fever
  - 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 sulphonylureas or insulin. 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
  - fast heartbeat
  - feeling jittery
  - kidney problems (kidney failure), in people who have kidney problems, diabetes, nausea, and vomiting may cause a loss of fluids (dehydration) which may cause kidney problems to get worse. It is important for you to drink fluids to help reduce your chance of dehydration.
- 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
  - severe rash or itching
  - problems breathing or swallowing
  - very rapid heartbeat
  - severe or life-threatening allergic reaction (anaphylaxis)

See the end of this Medication Guide for a complete list of ingredients in WEGOVY®.
Instructions for Use

WEGOVY® (semaglutide) injection

WEGOVY® comes in five strengths:

<table>
<thead>
<tr>
<th>Strength</th>
<th>Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.25 mg/0.5 mL</td>
<td>1 mL</td>
</tr>
<tr>
<td>0.5 mg/0.5 mL</td>
<td>1 mL</td>
</tr>
<tr>
<td>1 mg/0.5 mL</td>
<td>1 mL</td>
</tr>
<tr>
<td>1.7 mg/0.75 mL</td>
<td>2 mL</td>
</tr>
<tr>
<td>2.4 mg/0.75 mL</td>
<td>2 mL</td>
</tr>
</tbody>
</table>

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.

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 it 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

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

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

<table>
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<td>2.4 mg/0.75 mL</td>
<td>2 mL</td>
</tr>
</tbody>
</table>

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.

Pen window

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

Pen cap

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 thigh), 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. Choose your injection site.
- No one area should be used more than once a week.
- You may use the same site each week, as long as you use the site that is best for you.
- After the injection, keep the pen in the refrigerator or at room temperature. Do not freeze.
- You may inject into your upper leg (front of the thigh), 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.

Step 5. Inject WEGOVY®.
- 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.
- How to use your WEGOVY® pen.
- Check your WEGOVY® pen.
- Choose your injection site.
- Remove pen cap.
- How to inject WEGOVY®:
  - Use the front of your upper leg (front of the thigh), 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.
  - Do not inject into the same area each week.
  - Do not use the same injection site more than once a week.
  - You may inject into your upper leg (front of the thigh), 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.

Step 6. Throw away pen.
- Do not use your WEGOVY® pen without receiving training from your healthcare provider.
- Contact Novo Nordisk at 1-833-934-6891 if your WEGOVY® pen fails any of these checks.
- Check your WEGOVY® pen.
- Choose your injection site.
- Remove pen cap.
- How to inject WEGOVY®.
- Throw away the 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 7. Record your dose.
- Do not use your WEGOVY® pen without receiving training from your healthcare provider.
- Contact Novo Nordisk at 1-833-934-6891 if your WEGOVY® pen fails any of these checks.
- Check your WEGOVY® pen.
- Choose your injection site.
- Remove pen cap.
- How to inject WEGOVY®.
- Throw away the 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 8. Dispose of used pens.
- Do not use your WEGOVY® pen without receiving training from your healthcare provider.
- Contact Novo Nordisk at 1-833-934-6891 if your WEGOVY® pen fails any of these checks.
- Check your WEGOVY® pen.
- Choose your injection site.
- Remove pen cap.
- How to inject WEGOVY®.
- Throw away the 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 9. Take care of yourself.
- Do not use your WEGOVY® pen without receiving training from your healthcare provider.
- Contact Novo Nordisk at 1-833-934-6891 if your WEGOVY® pen fails any of these checks.
- Check your WEGOVY® pen.
- Choose your injection site.
- Remove pen cap.
- How to inject WEGOVY®.
- Throw away the 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.

Pen window

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

Pen cap

Locks after use.
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.

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