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).

RECENT MAJOR CHANGES
Indications and Usage (1)…………………………03/2024
Dosing and Administration (2)………………07/2023
Warnings and Precaution, Hypoglycemia (5.4)…………03/2024

INDICATIONS AND USAGE
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 excess body weight and maintain weight reduction in adults and pediatric patients aged 12 years and older with obesity

• to reduce weight-related comorbidity condition (1).

DOSAGE AND ADMINISTRATION

• 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 (2.1).

• Inject subcutaneously in the abdomen, thigh or upper arm (2.1).

• Inject immediately after reconstitution of the prefilled single-dose pen (2.1).

• The maintenance dosage of WEGOVY® in adults is either 2.4 mg (recommended) or 1.7 mg once weekly (2.2).

• The maintenance dosage of WEGOVY® in pediatric patients aged 12 years and older is 2.4 mg once weekly (2.3).

DOSE FORMS AND STRENGTHS
Injection: prefilled 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 MTC or in patients with MEN2 (4).

WARNINGS AND PRECAUTIONS
• 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 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: 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 Reactions: 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
Most common adverse reactions (incidence ≥ 5%) in adults or pediatric patients aged 12 years and older are: nausea, diarrhea, vomiting, constipation, abdominal pain, headache, fatigue, dyspepsia, dizziness, abdominal distension, eructation, hypoglycemia in patients with type 2 diabetes, flatulence, heartburn, gastroenteritis, gastroesophageal reflux disease, and nasopharyngitis (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
Coadministration with other semaglutide-containing products or with any other GLP-1 receptor agonist is not recommended (1).

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: 03/2024

CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
12.2 Pharmacodynamics
12.3 Pharmacokinetics
12.6 Immuno genesis

NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

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 in Pediatric Patients Aged 12 Years and Older with Obesity

HOW SUPPLIED/STORAGE AND HANDLING

PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the full prescribing information are not listed.
2.3 Recommended Dosage in Pediatric Patients Aged 12 Years and Older

Dosage Initiation and Escalation
- Initiate WEGOVY® according to the dosage escalation schedule in Table 2 to minimize gastrointestinal adverse reactions [see Adverse Reactions (6.1)].
- If patients do not tolerate a dose during dosage escalation, consider delaying dosage escalation for 4 weeks.
- The 0.25 mg, 0.5 mg, and 1 mg once-weekly dosages are initiation and escalation dosages and are not approved as maintenance dosages.

Table 2. Recommended Dosage Regimen for Pediatric Patients Aged 12 Years and Older

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Weeks</th>
<th>Once weekly Subcutaneous Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initiation</td>
<td>1 through 4</td>
<td>0.25 mg&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Escalation</td>
<td>5 through 8</td>
<td>0.5 mg&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Maintenance</td>
<td>13 through 16</td>
<td>1.7 mg&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Maintenance</td>
<td>17 and onward</td>
<td>2.4 mg&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>Not approved as maintenance dosages.  <sup>b</sup>See Dosage Modifications for Adverse Reactions

Maintenance Dosage
- The maintenance dosage of WEGOVY® in adults is either 2.4 mg (recommenced) or 1.7 mg once weekly. Consider treatment response and tolerability when selecting the maintenance dosage [see Clinical Studies (14.2)].

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 persistent 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.

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®-treated pediatric patients aged 12 years and older than in WEGOVY®-treated adults. In randomized clinical trials in adult patients, cholelithiasis 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 adult patients and 0.2% of placebo-treated patients. In a clinical trial in pediatric patients aged 12 years and older, cholecystitis was reported by 3.8% of WEGOVY®-treated patients and 0% placebo-treated patients. Cholecystitis was reported by 0.8% of WEGOVY®-treated pediatric patients and 0% placebo-treated patients [see Adverse Reactions (6.3)].

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 adult patients with type 2 diabetes and body mass index (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 diabetes mellitus taking WEGOVY® in combination with insulin or an insulin secretagogue (e.g., sulfonylurea) may have an increased risk of hypoglycemia, including severe hypoglycemia. In adults, severe hypoglycemia was observed in 5% of patients treated with WEGOVY® who were concomitantly administered insulin or insulin secretagogue (such as sulfonylureas) 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.
Wegovy® (semaglutide) injection 2.4 mg

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 renal impairment or worsening renal function, leading to volume depletion [see Adverse Reactions (6)].

Monitor renal function when initiating or escalating doses of WEGOVY® in patients reporting severe adverse gastrointestinal reactions. Monitor renal function in patients with renal impairment reporting any adverse reactions that could lead to volume depletion.

5.6 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 WEGOVY® or an ingredient of the exipients 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®.

5.7 Diabetic Retinopathy Complications 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, diabetic retinopathy was reported by 4.0% of WEGOVY®-treated patients versus 1.1% of placebo-treated patients.

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 (3.0%) 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%).

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

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®-treated adult patients compared to placebo in clinical trials. More adult patients treated with WEGOVY® compared with placebo had maximum changes in heart rate 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® compared to placebo had maximum changes in heart rate of 20 bpm or more (54% versus 39%) [see Adverse Reactions (6.1)].

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. Discontinue WEGOVY® if heart rate increases by 20 bpm or more (≥2% and greater than placebo) in WEGOVY®-treated adults with obesity or overweight.

Table 3. Adverse Reactions (≥2% and Greater Than Placebo) in WEGOVY®-treated Adults with Obesity or Overweight

<table>
<thead>
<tr>
<th>Condition</th>
<th>Placebo N=2,161</th>
<th>WEGOVY® 2.4 mg N=2,116</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>Diarrhea</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>Dizziness</td>
<td>8</td>
<td>7</td>
</tr>
<tr>
<td>Abdominal Distension</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>Eructation</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>
<tr>
<td>Dysesthesia</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

Other Adverse Reactions in Adults and/or Pediatric Patients

Acute Pancreatitis

In WEGOVY® clinical trials in adults, 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.

Acute Gallbladder Disease

In WEGOVY® clinical trials in adults, cholelithiasis 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 adult patients and 0.2% of placebo-treated patients. In a clinical trial in pediatric patients aged 12 years and older [see Clinical Studies (14.3)], cholelithiasis was reported by 3.8% of WEGOVY®-treated patients and 0% placebo-treated patients. Cholecystitis was reported by 0.8% of WEGOVY®-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, clinically significant 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. A higher rate of clinically significant hypoglycemic episodes was reported with WEGOVY® (semaglutide 2.4 mg) versus placebo (1 mg) in a 1.2% versus 0.7% episodes per 100 patient years of exposure, respectively) 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®-treated patient versus none in placebo-treated patients. The risk of hypoglycemia was increased when WEGOVY® was used with a sulfonylurea.

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

Acute Kidney Injury
Acute kidney injury occurred in clinical trials 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 the episodes occurred more than 1 week post-dose. Rates of acute kidney injury were similar and 42% of placebo-treated patients reported gastrointestinal reactions related to WEGOVY® (30% vs. 16%). Other reactions that occurred at a higher incidence among patients receiving WEGOVY® were abdominal pain (44% vs. 16%), vomiting (25% vs. 6%), and diarrhea (14% vs. 6%) and were more frequent among patients receiving WEGOVY® (0.6%) than placebo (0.4%).

In a cardiovascular outcomes trial in adults, more fractures of the hip and pelvis were reported on WEGOVY® than on placebo in females (0.5 cases per 100 patient years vs. 0.2% or 5/2160, and in patients ages 75 years and older: 2.4% (17/703) vs. 0.6% (4/663), respectively.

Increase in Heart Rate
Mean increases in resting heart rate of 1 to 4 beats per minute (bpm) were observed and continuous clinical monitoring in WEGOVY®-treated adult patients compared to placebo in clinical trials. In trials in which adult patients were randomized prior to dose-escalation, more patients treated with WEGOVY® compared with placebo, and 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® compared to placebo had maximum changes in heart rate of 20 bpm or more (54% versus 39%).

Hypotension and Syncpe
Adverse reactions related to 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. Some reactions were related to gastrointestinal adverse reactions and were more frequent with WEGOVY® and placebo. Of patients with orthostatic hypotension were more frequently seen in patients on concomitant antihypertensive therapy. In a clinical trial in pediatric patients aged 12 years and older, 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.

Gastrointestinal Adverse Reactions
In clinical trials in adults, 73% of WEGOVY®-treated patients and 47% of patients receiving placebo reported gastrointestinal adverse reactions, including severe reactions that were reported more frequently among patients receiving WEGOVY® (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®-treated adult patients included dyspepsia, abdominal pain, constipation, diarrhea, eructation, flatulence, gastrointestinal reflux disease, gastritis, hemorrhoids, and hiccups. These reactions increased during dose escalation.

In the pediatric clinical trial, 62% of WEGOVY®-treated patients and 42% of placebo-treated patients reported gastrointestinal disorders. The most frequently reported reactions were nausea (44% versus 16%), vomiting (25% versus 6%), and diarrhea (30% versus 16%). Other gastrointestinal-related reactions that occurred at a higher incidence than placebo among WEGOVY®-treated pediatric patients included abdominal pain, constipation, eructation, gastrointestinal reflux disease, dyspepsia, and flatulence. Permanent discontinuation of treatment as a result of gastrointestinal adverse reactions occurred in 4.3% of WEGOVY®-treated adult patients versus 0.7% of placebo-treated patients. In a pediatric clinical trial, 2.3% of patients treated with WEGOVY® versus 1.5% of patients who received placebo discontinued treatment as a result of gastrointestinal adverse reactions.

Injection Site Reactions
In clinical trials in adults, 1.4% of WEGOVY®-treated patients and 1.0% 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, 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, allergic reactions including rash and urticaria occurred at a higher incidence than placebo among WEGOVY®-treated patients and 7% in 14% (1659) of WEGOVY®-treated patients who did not develop anti-semaglutide antibodies [see Clinical Pharmacology (12.6)].

Fractures
In the cardiovascular outcomes trial in adults, more fractures of the hip and pelvis were reported on WEGOVY® than on placebo in females (0.5 cases per 100 patient years vs. 0.2% or 5/2160, and in patients ages 75 years and older: 2.4% (17/703) vs. 0.6% (4/663), respectively.

Dysgeusia
Dysgeusia was increased in adult patients with baseline history of moderate or severe renal impairment at baseline), and older with normal baseline heart rate, more patients treated with WEGOVY® and older with normal baseline heart rate, more patients treated with WEGOVY® compared to placebo who did not develop anti-semaglutide antibodies and in 7% (114/1659) of WEGOVY®-treated patients who did not develop anti-semaglutide antibodies [see Clinical Pharmacology (12.6)].

Liver Enzymes
In a pediatric clinical trial, increases in alanine aminotransferase (ALT) greater than or equal to 5 times the upper limit of normal were observed in 4 (2%) 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 cardiovascular outcomes trial in adults, increases in total bilirubin greater than or equal to 3 times the upper limit of normal were observed in 9 (0.5%) WEGOVY®-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.

7 DRUG INTERACTIONS
7.1 Concomitant Use with an Insulin Secretagogue (e.g., Sulfonylurea)
WEGOVY® lowers blood glucose and can cause hypoglycemia. The risk of hypoglycemia is increased when WEGOVY® is used in combination with insulin or insulin secretagogues (e.g., sulfonylureas). The addition of WEGOVY® to patients with insulin has not been evaluated in clinical trials.

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 1-877-395-2760 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. Additionally, weight loss offers no benefit to a pregnant patient and may cause fetal harm. When a pregnancy is recognized, advise the patient to discontinue WEGOVY® and to continue using contraception. The risk associated with treatment in the second and third trimester of pregnancy has not been studied. In preclinical studies, 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®.

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 patient to discontinue WEGOVY® and to continue using contraception. The risk associated with treatment in the second and third trimester of pregnancy has not been studied. In preclinical studies, 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®.

There are no data on the presence of semaglutide or its metabolites in human milk, the effects on the breastfeeding infant, or the effects on milk production. Semaglutide was present in the milk of lactating women.
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 to 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

The safety and effectiveness of WEGOVY® as an adjunct to a reduced calorie diet and increased physical activity for weight reduction and long-term maintenance have been established in pediatric patients aged 12 years and older with obesity. Use of WEGOVY® for this indication is supported by a 68-week, double-blind, pivotal, randomized clinical trial in 201 pediatric patients aged 12 years and older with a BMI corresponding to ≥95th percentile for age and sex and from studies in adult patients with obesity (see Clinical Studies (14.3)).

Adverse reactions with WEGOVY® 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® had greater incidences of cholelithiasis, cholezystitis, hypotension, rash, and urticaria compared to adults treated with WEGOVY® (see Adverse Reactions (6.1)).

There are insufficient data in pediatric patients with type 2 diabetes treated with WEGOVY® for obesity to determine if there is an increased risk of hypoglycemia with WEGOVY® treatment similar to that reported in adults. Inform 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® and during WEGOVY® treatment. When initiating WEGOVY® in pediatric patients aged 12 years and older with type 2 diabetes, consider reducing the dose of concomitantly administered insulin secretagogue (such as sulfonylurea) or insulin to reduce the risk of hypoglycemia (see Warnings and Precautions (5.4)).

The safety and effectiveness of WEGOVY® have not been established in pediatric patients less than 12 years of age.

8.5 Geriatric Use

In the WEGOVY® clinical trials for weight reduction and long-term maintenance, 233 (9%) WEGOVY®-treated patients were aged 65 to 75 years and 23 (1%) WEGOVY®-treated patients were aged 75 years and older (see Clinical Studies (14.2)). In a cardiovascular outcomes trial, 2656 (30%) WEGOVY®-treated patients were aged 65 to 75 years and 703 (8%) WEGOVY®-treated patients were aged 75 years and older (see Clinical Studies (14.1)).

No overall difference in effectiveness was observed between patients aged 65 years or older and younger adult patients. In the cardiovascular outcomes trial, patients aged 75 years and older reported more fractures of the hip and pelvis on WEGOVY® than on placebo. Patients aged 75 years and older ( WEGOVY®-treated and placebo-treated) reported more serious adverse reactions overall compared to younger adult patients (see Adverse Reactions (6.1)).

8.6 Renal Impairment

No dose adjustment of WEGOVY® is recommended for patients with renal impairment. In a study in patients 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 patients 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. 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® (semaglutide) injection, for subcutaneous use, contains semaglutide, a human GLP-1 receptor agonist (or GLP-1 analog) (see CLINICAL PHARMACOLOGY (12.1)). The peptide backbone is produced by yeast fermentation. The main protraction mechanism of semaglutide is albinum 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 C104H157N122O122S 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.

The exact mechanism of cardiovascular risk reduction has not been established.

12.2 Pharmacodynamics

Semaglutide lowers body weight with greater fat mass loss than lean mass loss. Semaglutide decreases calorie 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. Semaglutide causes delays in 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 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.

Specific 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

<table>
<thead>
<tr>
<th>Intrinsic Factor</th>
<th>Relative Exposure (Cavg)</th>
<th>Ratio and 90% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Male</td>
<td></td>
</tr>
<tr>
<td>Age group</td>
<td>65–&lt;75 years</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;75 years</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td>Black or African American</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Asian</td>
<td></td>
</tr>
<tr>
<td></td>
<td>American Indian or Alaska Native</td>
<td></td>
</tr>
<tr>
<td>Ethnicity</td>
<td>Hispanic or Latino</td>
<td></td>
</tr>
<tr>
<td>Body weight</td>
<td>74 kg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>143 kg</td>
<td></td>
</tr>
<tr>
<td>Renal function</td>
<td>Mild</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td></td>
</tr>
<tr>
<td>Injection site</td>
<td>Thigh</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Upper arm</td>
<td></td>
</tr>
</tbody>
</table>

Data are steady-state dose-normalized average semaglutide exposures relative to a reference subject profile (non-Hispanic or Latino ethnicity, 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.

Patients with 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 0.6 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.
Patients with 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 Studies
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 co-administered 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.

Figure 3. Impact of semaglutide 1 mg on the pharmacokinetics of co-administered medications

Co-administered medication | Relative exposure | Ratio and 90% CI
--- | --- | ---
Methotrexate | AUC0-12h | 0.98 (0.96, 1.00)
 | Cmax | 1.00 (0.97, 1.03)
S-warfarin | AUC0-168h | 1.02 (0.99, 1.04)
 | Cmax | 1.00 (0.98, 1.02)
R-warfarin | AUC0-168h | 1.02 (0.99, 1.05)
 | Cmax | 1.00 (0.98, 1.03)
Digoxin | AUC0-12h | 0.99 (0.96, 1.01)
 | Cmax | 0.99 (0.96, 1.02)
Atravastatin | AUC0-72h | 1.00 (0.98, 1.02)
 | Cmax | 0.99 (0.97, 1.01)
Ethinylestradiol | AUC0-24h | 0.99 (0.97, 1.01)
 | Cmax | 1.00 (0.98, 1.02)
Levonorgestrel | AUC0-24h | 0.99 (0.97, 1.01)
 | Cmax | 1.00 (0.98, 1.02)

Relative exposure in terms of AUC and Cmax for each medication when given with semaglutide compared to without semaglutide. Metformin and oral contracolic drug (ethinylestradiol/levonorgestrel) were assessed at steady state. Warfarin (S-warfarin/R-warfarin), digoxin and atorvastatin were assessed after a single dose. Abbreviations: AUC: area under the curve, Cmax: maximum concentration, CI: confidence interval.

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 other semaglutide products.

During the 68-week treatment periods in Studies 2 and 3 [see Clinical Studies (14.2), 50/1709 (3%) of WEGOVY®-treated patients developed anti-semaglutide antibodies. Of these 50 WEGOVY®-treated patients, 28 patients (2% of the total WEGOVY®-treated study population) developed antibodies that cross-reacted with native GLP-1. No identified clinically significant effect of anti-semaglutide antibodies on pharmacodynamics or effectiveness of semaglutide.

13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, 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/wk, 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) to the females. A statistically significant increase in thyroid C-cell adenomas was observed in mice at all dose levels 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 (0.04-, 0.1-, 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.

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® relative to placebo on major adverse cardiovascular 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). The primary endpoint, MACE, was the time to first occurrence of a three-part composite outcome which included cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke.
Table 6. Mean Changes in Anthropometry and Cardiometabolic Parameters at Week 104 in Study 1.2

<table>
<thead>
<tr>
<th>Parameter</th>
<th>PLACEO (Baseline)</th>
<th>WEGOVY® (Baseline)</th>
<th>WEGOVY® (Placebo)</th>
<th>% Difference from Baseline (Baseline)</th>
<th>% Difference from Placebo (Baseline)</th>
<th>% Difference from Baseline (LSMean)</th>
<th>% Difference from Placebo (LSMean)</th>
<th>Relative difference from placebo (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body Weight (kg)</td>
<td>96.8</td>
<td>-0.91</td>
<td>96.5</td>
<td>-9.41</td>
<td>-5.31</td>
<td>-9.21</td>
<td>-4.61</td>
<td>-0.33</td>
</tr>
<tr>
<td>Waist Circumference (cm)</td>
<td>111.4</td>
<td>-1.0</td>
<td>111.3</td>
<td>-7.6</td>
<td>-6.5</td>
<td>-7.6</td>
<td>-7.6</td>
<td>-0.39</td>
</tr>
<tr>
<td>Systolic Blood Pressure (mmHg)</td>
<td>131</td>
<td>-0.5</td>
<td>131</td>
<td>-3.8</td>
<td>-3.3</td>
<td>-3.8</td>
<td>-3.8</td>
<td>-0.38</td>
</tr>
<tr>
<td>Diastolic Blood Pressure (mmHg)</td>
<td>79</td>
<td>-0.5</td>
<td>79</td>
<td>-1.0</td>
<td>-0.5</td>
<td>-1.0</td>
<td>-1.0</td>
<td>-0.05</td>
</tr>
<tr>
<td>Heart Rate</td>
<td>69</td>
<td>0.7</td>
<td>69</td>
<td>3.8</td>
<td>3.1</td>
<td>3.8</td>
<td>3.8</td>
<td>0.37</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>5.8</td>
<td>0.0</td>
<td>5.8</td>
<td>-0.3</td>
<td>-0.3</td>
<td>-0.3</td>
<td>-0.3</td>
<td>-0.01</td>
</tr>
</tbody>
</table>

Baseline value is the geometric mean.

The reduction of MACE with WEGOVY® 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 Studies in Adults

The safety and efficacy of WEGOVY® 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; and one 68-week, randomized, double-blind trial that investigated two different doses of WEGOVY® versus placebo. In Study 2 (NCT03354965), 1,301 patients were randomized to receive WEGOVY® 1.7 mg, WEGOVY® 2.4 mg, or placebo, respectively. WEGOVY® was escalated to 1.7 mg or 2.4 mg subcutaneous weekly dosages or placebo 12 to 16 weeks followed by 52 weeks on either maintenance dose. In Studies 2, 3, and 5, all patients received instruction for a reduced calorie diet and increased physical activity throughout the trial. In Study 4, patients received an initial 8-week low-calorie diet (total energy intake 1,000 to 3,000 kcal/day deficit) and increased physical activity counseling (recommended to a minimum of 150 minutes/week). At baseline, the mean age was 46 years, 79% were White, 13% were Black or African American, and 2% were Asian. A total of 8% 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. At baseline, the mean age was 56 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.

The proportions of patients who discontinued study drug in Studies 2, 3, and 4 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 5, the proportions of patients who discontinued study drug were 5.8% and 11.6% for WEGOVY® and placebo, respectively. In Study 6, the proportions of patients who discontinued study drug were 7.9%, 6.5%, and 3.0% for WEGOVY® 1.7 mg, WEGOVY® 2.4 mg, and placebo, respectively.

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. For 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 7.

Table 7. Changes in Body Weight at Week 68 in Studies 2, 3, and 4

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients Losing Greater than or Equal to 5% Weight Loss (95% CI)</th>
<th>Patients Losing Greater than or Equal to 10% Weight Loss (95% CI)</th>
<th>Patients Losing Greater than or Equal to 15% Weight Loss (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Study 2</strong></td>
<td><strong>Obesity or overweight with comorbidity</strong></td>
<td><strong>Type 2 diabetes with obesity or overweight</strong></td>
<td><strong>Obesity or overweight with comorbidity undergoing intensive lifestyle therapy</strong></td>
</tr>
<tr>
<td>PLACEO (N=655)</td>
<td>31.1 (12.4; 48.1)</td>
<td>12.0 (5.4; 18.6)</td>
<td>4.8 (3.0; 6.5)</td>
</tr>
<tr>
<td>WEGOVY® (N=1306)</td>
<td>37.2 (28.9; 45.2)</td>
<td>27.1 (19.0; 35.3)</td>
<td>13.2 (10.3; 16.2)</td>
</tr>
<tr>
<td>PLACEBO (N=403)</td>
<td>27.2 (19.1; 35.2)</td>
<td>23.3 (15.2; 31.3)</td>
<td>10.3 (7.4; 13.2)</td>
</tr>
<tr>
<td>WEGOVY® (N=404)</td>
<td>11.9 (30.7; 43.8)</td>
<td>5.7 (10.8; 17.6)</td>
<td>4.5 (30.8; 53.7)</td>
</tr>
</tbody>
</table>

LSMean = least squares mean; CI = confidence interval

The intent-to-treat population included all randomized patients. In Study 2, at week 68, the body weight was missing for 7.8% and 11.9% of patients randomized to WEGOVY® and placebo, respectively. In Study 3, at week 68, the body weight was missing for 4.0% and 6.7% of patients randomized to WEGOVY® and placebo, respectively. In Study 4, at week 68, the body weight was missing for 4.8% and 7.4% of patients randomized to WEGOVY® and placebo, respectively. Missing data were imputed from retrieved subjects of the same randomized treatment arm (RD-MI).

*p<0.0001 (adjusted 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® resulted in a statistically significant reduction in body weight compared with placebo (Table 8). Because patients who discontinued WEGOVY® 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®.
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 5 and Figure 6 for Studies 2 and 3. 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® and placebo curves at approximately 66%, and 12%, respectively, which correspond to the values shown in Table 7.

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% body weight loss from baseline to week 68. After 68 weeks, treatment with WEGOVY® 1.7 mg and 2.4 mg 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 9.

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 2.8% and 6.7% of patients randomized to WEGOVY® and placebo, respectively. Missing data were imputed from retrieved subjects of the same randomized treatment arm (RD-MI).

### Table 8. Changes in Body Weight at Week 68 in Study 5

<table>
<thead>
<tr>
<th>Body Weight (only randomized patients)</th>
<th>WEGOVY® 1.7 mg</th>
<th>WEGOVY® 2.4 mg</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean at week 0 (kg)</td>
<td>107.2</td>
<td></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>
<td></td>
</tr>
<tr>
<td>% change from week 20 at week 68 (LSMean)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% difference from placebo (LSMean)</td>
<td>-1.9 (16.0, -13.5)*</td>
<td>-4.8 (14.0, -13.5)*</td>
<td></td>
</tr>
</tbody>
</table>

LSMean = least squares mean; CI = confidence interval

### Table 9. Changes in Body Weight at Week 68 in Study 6 in East-Asian Patients (WEGOVY® 1.7 mg)

<table>
<thead>
<tr>
<th>Intention-to-treat1</th>
<th>Study 6 (BMI ≥35 kg/m² with at least one comorbidity or BMI 27-34.9 kg/m² with at least two comorbidities)</th>
<th>Placebo</th>
<th>WEGOVY® 1.7 mg</th>
<th>WEGOVY® 2.4 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body Weight</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline mean (kg)</td>
<td>90.2</td>
<td>86.1</td>
<td>86.9</td>
<td></td>
</tr>
<tr>
<td>% change from baseline (LSMean)</td>
<td></td>
<td>-2.1</td>
<td>-9.6</td>
<td>-13.2</td>
</tr>
<tr>
<td>% difference from placebo (LSMean) (95% CI)</td>
<td></td>
<td>-7.5</td>
<td>(-9.6, -5.4)*</td>
<td>-11.1 (12.9, -9.2)*</td>
</tr>
<tr>
<td>% of Patients losing greater than or equal to 5% body weight</td>
<td></td>
<td>18.4</td>
<td>72.8</td>
<td>84.0</td>
</tr>
<tr>
<td>% difference from placebo (LSMean) (95% CI)</td>
<td></td>
<td>53.3</td>
<td>(41.0, 65.6)*</td>
<td>64.5 (54.8, 74.3)*</td>
</tr>
<tr>
<td>% of Patients losing greater than or equal to 10% body weight</td>
<td></td>
<td>4.5</td>
<td>39.1</td>
<td>59.9</td>
</tr>
<tr>
<td>% difference from placebo (LSMean) (95% CI)</td>
<td></td>
<td>34.5</td>
<td>(23.9, 45.1)*</td>
<td>55.4 (47.3, 63.6)*</td>
</tr>
<tr>
<td>% of Patients losing greater than or equal to 15% body weight</td>
<td></td>
<td>2.6</td>
<td>20.8</td>
<td>38.2</td>
</tr>
<tr>
<td>% difference from placebo (LSMean) (95% CI)</td>
<td></td>
<td>18.2</td>
<td>(9.8, 26.7)*</td>
<td>35.6 (27.9, 43.3)*</td>
</tr>
</tbody>
</table>

LSMean = least squares mean; CI = confidence interval

1The intent-to-treat population includes all randomized patients. At baseline, 24.7% of patients had type 2 diabetes mellitus. The time courses of weight loss with WEGOVY® and placebo from baseline through week 68 are depicted in Figure 7, Figure 8 and Figure 9.

The observed values for patients completing each scheduled visit, and estimates with multiple imputations from retrieved dropouts (RD-MI) are presented in Table 9.
Effect of WEGOVY® on Anthropometry and Cardiometabolic Parameters in Adults

Changes in waist circumference and cardiometabolic parameters with WEGOVY® are shown in Table 10 for Studies 2, 3, and 4, in Table 11 for Study 5, and in Table 12 for Study 6.

### Table 10. Changes in Anthropometry and Cardiometabolic Parameters at Week 68 in Studies 2, 3, and 4

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Study 2 (Obesity or overweight with comorbidity)</th>
<th>Study 3 (Type 2 diabetes with obesity or overweight)</th>
<th>Study 4 (Obesity or overweight with comorbidity undergoing intensive lifestyle therapy)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo N=533</td>
<td>WEGOVY® N=1066</td>
<td>Placebo N=493</td>
</tr>
<tr>
<td>Waist Circumference (cm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>114.6</td>
<td>114.6</td>
<td>115.5</td>
</tr>
<tr>
<td>Changes from baseline (LSMean)</td>
<td>-4.1</td>
<td>-13.5</td>
<td>-4.5</td>
</tr>
<tr>
<td>Difference from placebo (LSMean)</td>
<td>-9.4</td>
<td></td>
<td>-4.9</td>
</tr>
<tr>
<td>Systolic Blood Pressure (mmHg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>127</td>
<td>126</td>
<td>130</td>
</tr>
<tr>
<td>Changes from baseline (LSMean)</td>
<td>-1.1</td>
<td>-6.2</td>
<td>-0.5</td>
</tr>
<tr>
<td>Difference from placebo (LSMean)</td>
<td>-5.1</td>
<td></td>
<td>-3.4</td>
</tr>
<tr>
<td>Diastolic Blood Pressure (mmHg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>80</td>
<td>80</td>
<td>80</td>
</tr>
<tr>
<td>Changes from baseline (LSMean)</td>
<td>-0.4</td>
<td>-2.8</td>
<td>-0.9</td>
</tr>
<tr>
<td>Difference from placebo (LSMean)</td>
<td>-2.4</td>
<td></td>
<td>-0.7</td>
</tr>
<tr>
<td>Heart Rate²,³</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>72</td>
<td>72</td>
<td>76</td>
</tr>
<tr>
<td>Changes from baseline (LSMean)</td>
<td>-0.7</td>
<td>3.5</td>
<td>-0.2</td>
</tr>
<tr>
<td>Difference from placebo (LSMean)</td>
<td>4.3</td>
<td></td>
<td>2.7</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>5.7</td>
<td>5.7</td>
<td>8.1</td>
</tr>
<tr>
<td>Changes from baseline (LSMean)</td>
<td>-0.2</td>
<td>-0.4</td>
<td>-0.4</td>
</tr>
<tr>
<td>Difference from placebo (LSMean)</td>
<td>-0.3</td>
<td></td>
<td>-1.2</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>192.1</td>
<td>189.6</td>
<td>170.8</td>
</tr>
<tr>
<td>Percent Change from baseline</td>
<td>0.1</td>
<td>-3.3</td>
<td>-0.5</td>
</tr>
<tr>
<td>Relative difference from placebo</td>
<td>-3.3</td>
<td></td>
<td>-0.9</td>
</tr>
<tr>
<td>LDL Cholesterol (mg/dL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>112.5</td>
<td>110.3</td>
<td>90.1</td>
</tr>
<tr>
<td>Percent Change from baseline</td>
<td>1.3</td>
<td>-2.5</td>
<td>0.1</td>
</tr>
<tr>
<td>Relative difference from placebo</td>
<td>-3.8</td>
<td></td>
<td>-0.4</td>
</tr>
<tr>
<td>HDL (mg/dL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>49.5</td>
<td>49.4</td>
<td>43.8</td>
</tr>
<tr>
<td>Percent Change from baseline</td>
<td>1.4</td>
<td>5.2</td>
<td>4.1</td>
</tr>
<tr>
<td>Relative difference from placebo</td>
<td>3.8</td>
<td></td>
<td>2.7</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>127.9</td>
<td>126.2</td>
<td>159.5</td>
</tr>
<tr>
<td>Percent Change from baseline</td>
<td>-7.3</td>
<td>-21.9</td>
<td>-9.4</td>
</tr>
<tr>
<td>Relative difference from placebo</td>
<td>-15.8</td>
<td></td>
<td>-13.9</td>
</tr>
</tbody>
</table>

1Missing data were imputed from retrieved subjects of the same randomized treatment arm (RD-MI)
2Model based estimates based on an analysis of covariance model including treatment and baseline value as a covariate
3Not included in the pre-specified hierarchical testing (except HbA1c for Study 3)
4Model based estimates based on a mixed model for repeated measures including treatment (and stratification factors for Study 3 only) as a factor and baseline value as a covariate
5Baseline value is the geometric mean

### Table 11. Mean Changes in Anthropometry and Cardiometabolic Parameters in Study 5 (Obesity or overweight with comorbidity after 20-week run-in)¹

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Placebo N=268</th>
<th>WEGOVY® N=535</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Randomization (week 20)</td>
<td>Change from Randomization (week 20) to week 68 (LSMean¹)</td>
</tr>
<tr>
<td>Waist Circumference (cm)</td>
<td>104.7</td>
<td>3.3</td>
</tr>
<tr>
<td>Systolic Blood Pressure (mmHg)</td>
<td>121</td>
<td>4.4</td>
</tr>
<tr>
<td>Diastolic Blood Pressure (mmHg)</td>
<td>78</td>
<td>0.9</td>
</tr>
<tr>
<td>Heart Rate²,³</td>
<td>76</td>
<td>-5.3</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>5.4</td>
<td>0.1</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dL)</td>
<td>175.1</td>
<td>11.4</td>
</tr>
<tr>
<td>LDL Cholesterol (mg/dL)</td>
<td>109.1</td>
<td>7.6</td>
</tr>
<tr>
<td>HDL Cholesterol (mg/dL)</td>
<td>43.6</td>
<td>17.8</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>95.3</td>
<td>14.8</td>
</tr>
</tbody>
</table>

1Missing data were imputed from retrieved subjects of the same randomized treatment arm (RD-MI)
²Model based estimates based on an analysis of covariance model including treatment as a factor and baseline value as a covariate
³Not included in the pre-specified hierarchical testing
⁴Model based estimates based on a mixed model for repeated measures including treatment as a factor and baseline values as a covariate
⁵Baseline value is the geometric mean
Table 12. Mean Changes in Anthropometry and Cardiometabolic Parameters at Week 68 in Study 6 in East-Asian Patients (WEGOVY® 1.7 mg)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Placebo N=101</th>
<th>WEGOVY® 1.7 mg N=101</th>
<th>WEGOVY® 2.4 mg N=199</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waist circumference (cm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>103.8</td>
<td>101.4</td>
<td>103.8</td>
</tr>
<tr>
<td>Change from baseline (LSMean)</td>
<td>-1.8</td>
<td>-7.1</td>
<td>-11.0</td>
</tr>
<tr>
<td>Difference from placebo (LSMean)</td>
<td></td>
<td>-5.9</td>
<td>-9.3</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>133</td>
<td>135</td>
<td>133</td>
</tr>
<tr>
<td>Change from baseline (LSMean)</td>
<td>-5.3</td>
<td>-10.8</td>
<td>-10.8</td>
</tr>
<tr>
<td>Difference from placebo (LSMean)</td>
<td></td>
<td>-5.4</td>
<td>-5.5</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>86</td>
<td>85</td>
<td>83</td>
</tr>
<tr>
<td>Change from baseline (LSMean)</td>
<td>-2.2</td>
<td>-4.6</td>
<td>-5.3</td>
</tr>
<tr>
<td>Difference from placebo (LSMean)</td>
<td></td>
<td>-2.4</td>
<td>-3.1</td>
</tr>
<tr>
<td>Heart Rate (bpm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>73</td>
<td>73</td>
<td>73</td>
</tr>
<tr>
<td>Change from baseline (LSMean)</td>
<td>2.4</td>
<td>4.4</td>
<td>6.3</td>
</tr>
<tr>
<td>Difference from placebo (LSMean)</td>
<td></td>
<td>2.0</td>
<td>3.9</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>6.4</td>
<td>6.4</td>
<td>6.4</td>
</tr>
<tr>
<td>Change from baseline (LSMean)</td>
<td>0.0</td>
<td>-0.9</td>
<td>-0.9</td>
</tr>
<tr>
<td>Difference from placebo (LSMean)</td>
<td></td>
<td>-0.9</td>
<td>-0.9</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>203.1</td>
<td>203.3</td>
<td>197.2</td>
</tr>
<tr>
<td>Percent change from baseline (LSMean)</td>
<td>0.8</td>
<td>-6.6</td>
<td>-8.7</td>
</tr>
<tr>
<td>Relative difference from placebo (LSMean)</td>
<td>-7.3</td>
<td>-9.4</td>
<td></td>
</tr>
<tr>
<td>LDL Cholesterol (mg/dL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>123.3</td>
<td>120.1</td>
<td>116.5</td>
</tr>
<tr>
<td>Percent change from baseline (LSMean)</td>
<td>-3.8</td>
<td>-10.1</td>
<td>-14.6</td>
</tr>
<tr>
<td>Relative difference from placebo (LSMean)</td>
<td>-6.6</td>
<td>-11.2</td>
<td></td>
</tr>
<tr>
<td>HDL Cholesterol (mg/dL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>48.7</td>
<td>50.2</td>
<td>50.8</td>
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<tr>
<td>Percent change from baseline (LSMean)</td>
<td>5.9</td>
<td>6.7</td>
<td>9.2</td>
</tr>
<tr>
<td>Relative difference from placebo (LSMean)</td>
<td>0.7</td>
<td>3.1</td>
<td></td>
</tr>
<tr>
<td>Triglyceride (mg/dL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>132.4</td>
<td>138.8</td>
<td>127.1</td>
</tr>
<tr>
<td>Percent change from baseline (LSMean)</td>
<td>5.5</td>
<td>-19.5</td>
<td>-21.2</td>
</tr>
<tr>
<td>Relative difference from placebo (LSMean)</td>
<td>-23.7</td>
<td>-25.3</td>
<td></td>
</tr>
</tbody>
</table>

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.
1Model based estimates based on an analysis of covariance model including treatment and type 2 diabetes status as factors and baseline value as a covariate
2Not included in the pre-specified hierarchical testing
3Model 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
4Baseline value is the geometric mean

14.3 Weight Reduction and Long-Term Maintenance Study in Pediatric Patients Aged 12 Years and Older with Obesity

Overview of Clinical Trial in Pediatric Patients
WEGOVY® 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 BMI ≥35 kg/m² corresponding to ≈95th percentile standardized for age and sex (study 7) (NCT04102189). After a 12-week lifestyle run-in period (including dietary recommendations and physical activity counseling), patients were randomized 2:1 to WEGOVY® once weekly or placebo once weekly. WEGOVY® 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®-treated patients who completed the trial, 86.7% were on the 2.4 mg dose at the end of the trial; for 5% of patients, 1.7 mg was the maximum tolerated dose.

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®-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® resulted in a statistically significant reduction in percent BMI compared with placebo. Greater proportions of patients treated with WEGOVY® achieved ≥5% reduction in baseline BMI than those treated with placebo as shown in Table 13.

Table 13. Changes in Weight and BMI at Week 68 in Pediatric Patients with Obesity Aged 12 Years and Older in Study 7

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Intention-To-Treat</th>
<th>Placebo N=67</th>
<th>WEGOVY® N=134</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline mean (kg/m²)</td>
<td>35.7</td>
<td>37.7</td>
<td></td>
</tr>
<tr>
<td>% change from baseline (LSMean)</td>
<td>0.6</td>
<td>-16.1</td>
<td></td>
</tr>
<tr>
<td>% difference from placebo (LSMean) (95% CI)</td>
<td>-16.7</td>
<td>(-20.3, -13.2)</td>
<td></td>
</tr>
<tr>
<td>% of Patients with greater than or equal to 5% reduction in baseline BMI</td>
<td>19.7</td>
<td>77.1</td>
<td></td>
</tr>
<tr>
<td>% difference from placebo (LSMean)</td>
<td>7.7</td>
<td>65.1</td>
<td></td>
</tr>
<tr>
<td>% of Patients with greater than or equal to 10% reduction in baseline BMI</td>
<td>4.0</td>
<td>57.8</td>
<td></td>
</tr>
<tr>
<td>% difference from placebo (LSMean)</td>
<td>53.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body Weight</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline mean (kg)</td>
<td>102.6</td>
<td>109.9</td>
<td></td>
</tr>
<tr>
<td>% change from baseline (LSMean)</td>
<td>2.7</td>
<td>-14.7</td>
<td></td>
</tr>
<tr>
<td>% difference from placebo (LSMean)</td>
<td>-17.4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

LSMean = least squares mean; CI = confidence interval
4The 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). After 68 weeks, the BMI was missing for 2.2% and 7.5% of patients randomized to WEGOVY® and placebo, respectively.
5Parameters 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® and placebo from baseline through week 68 is depicted in Figure 10. The cumulative frequency distribution of change in BMI is shown in Figure 11.

Figure 10. Change from Baseline (%) in BMI in Pediatric Patients with Obesity Aged 12 Years and Older in Study 7

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

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

Changes in waist circumference and cardiometabolic parameters with WEGOVY® are shown in Table 14 for the study in pediatric patients aged 12 years and older.
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 (5.6)].

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 (5.7)].

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 (5.8)].

Suicidal Behavior and Ideation
Advise patients to report emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior. Inform patients that if they experience suicidal thoughts or behaviors, they should stop taking WEGOVY® [see Warnings and Precautions (5.9)].

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)].

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. It is supplied in cartons containing 4 pen-injectors in the following packaging configurations:

<table>
<thead>
<tr>
<th>Total Strength per Total Volume</th>
<th>NDC</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.25 mg/0.5 mL</td>
<td>0169-4525-14</td>
</tr>
<tr>
<td>0.5 mg/0.5 mL</td>
<td>0169-4505-14</td>
</tr>
<tr>
<td>1 mg/0.5 mL</td>
<td>0169-4501-14</td>
</tr>
<tr>
<td>1.7 mg/0.75 mL</td>
<td>0169-4517-14</td>
</tr>
<tr>
<td>2.4 mg/0.75 mL</td>
<td>0169-4524-14</td>
</tr>
</tbody>
</table>

Recommended Storage
Store the 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.

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 and Warnings and Precautions (5.1)].

Acute Pancreatitis
Inform patients of the potential risk for acute pancreatitis. Instruct patients to discontinue WEGOVY® promptly and contact their physician if pancreatitis is suspected (severe abdominal pain that may radiate to the back, and which may or may not be accompanied by vomiting) [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 symptoms of hypoglycemia to their healthcare provider [see Warnings and Precautions (5.4)].

Dehydration and Renal Impairment
Advise patients treated with WEGOVY® of the potential risk of dehydration due to gastrointestinal adverse reactions and take precautions to avoid fluid depletion. Inform patients of the potential risk for worsening renal function and explain the associated signs and symptoms of renal impairment, as well as the possibility of dialysis as a medical intervention if renal failure occurs [see Warnings and Precautions (5.5)].
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 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® is an injectable 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.
  • that may help adults and children aged 12 years and older with obesity, or some adults with overweight who also have weight-related medical problems, to help them lose excess body 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® is safe and effective for use in children under 12 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®. See the end of this Medication Guide for a complete list of ingredients in WEGOVY®.

• Symptoms of a serious allergic reaction include:
  • swelling of your face, lips, tongue or throat
  • fainting or feeling dizzy
  • problems breathing or swelling
  • very rapid heartbeat
  • severe rash or itching

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.

• have or have had depression or suicidal thoughts, or mental health issues.

• 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.

• are breastfeeding or plan to breastfeed. It is not known if WEGOVY® 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®?

• Read the Instructions for Use that comes with WEGOVY®.

• Use WEGOVY® exactly as your healthcare provider tells you.

• 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. In the fifth month onwards, your healthcare provider may either maintain your dose at 1.7 mg weekly or increase your weekly dose to 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 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 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), especially those who also take medicines to treat diabetes mellitus such as insulin or sulfonylureas. Low blood sugar in patients with diabetes who receive WEGOVY® can be a serious 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
  • sweating
  • shakiness
  • blurred vision
  • slurred speech
  • weakness
  • anxiety
  • hunger
  • headache
  • irritability or mood changes
  • confusion or drowsiness
  • fast heartbeat
  • feeling jittery

• problems (kidney failure). In people who have kidney problems, diarrhea, 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
  • fainting or feeling dizzy

• 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.

• depression or thoughts of suicide. You should pay attention to any mental changes, especially sudden changes in your mood, behaviors, thoughts, or feelings. Call your healthcare provider right away if you have any mental changes that are new, worse, or worry you.

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

• nausea
• diarrhea
• vomiting
• weight loss
• change in vision
• upset stomach
• low blood sugar in people with type 2 diabetes

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.
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 symptoms 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: 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.

This Medication Guide has been approved by the U.S. Food and Drug Administration. Revised: 03/2024
**Instructions for Use**

**WEGOVY®**

(Wegovy®)

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.

**Important Information**

Read these 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**

**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:

- **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.

**Before use**

- **Pen window**
- **Needle cover**

**After use**

- **Needle cover** locks after use.

**Pen window**

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

**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.

**Click 1**
The injection starts.

**Click 2**
Keep applying pressure until the yellow bar has stopped moving.

Yellow bar has stopped moving. The injection is complete. Lift the pen slowly.

**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.

**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.

The injection takes about 5-10 seconds.