**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).

**SECTION CHANGES**

- **Recent Major Changes**
  - Indications and Usage (1)…………………..12/2022
  - Dosage and Administration (2.1, 2.3)…………………..12/2022
  - Warnings and Precautions (5.3, 5.6, 5.8)…………………..12/2022

- **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).
    - pediatric patients aged 12 years and older with an initial BMI at the 95th percentile or greater for age and sex (obesity) (1).

- **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).

- **Adverse Reactions**

- **Use in Specific Populations**

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

- **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).

- **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: 12/2022
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 a result of semaglutide-induced rodent thyroid C-cell tumors has not been determined (see Warnings and Precautions (5.1) and Nonclincial Toxicology (13.1)).
- WEGOVY® is contraindicated in patients with a personal or family history of MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2) (see Contraindications (4)). Counsel patients regarding the potential risk for MTC with the use of WEGOVY® and inform them of symptoms of thyroid tumors (e.g., a mass in the neck, dysphagia, dyspnea, persistent hoarseness), Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with WEGOVY® (see Contraindications (4) and Warnings and Precautions (5.1)).

Table 1. BMI Conversion Chart

<table>
<thead>
<tr>
<th>Weight (lb)</th>
<th>Height (in)</th>
</tr>
</thead>
<tbody>
<tr>
<td>125</td>
<td>58</td>
</tr>
<tr>
<td>130</td>
<td>60</td>
</tr>
<tr>
<td>135</td>
<td>61</td>
</tr>
<tr>
<td>140</td>
<td>62</td>
</tr>
<tr>
<td>145</td>
<td>63</td>
</tr>
<tr>
<td>150</td>
<td>64</td>
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<tr>
<td>155</td>
<td>65</td>
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<tr>
<td>160</td>
<td>66</td>
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<tr>
<td>165</td>
<td>67</td>
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<td>170</td>
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<tr>
<td>175</td>
<td>69</td>
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<tr>
<td>180</td>
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</tr>
<tr>
<td>185</td>
<td>71</td>
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<tr>
<td>190</td>
<td>72</td>
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<td>195</td>
<td>73</td>
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<tr>
<td>200</td>
<td>74</td>
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<tr>
<td>205</td>
<td>75</td>
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<tr>
<td>210</td>
<td>76</td>
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<tr>
<td>215</td>
<td>77</td>
</tr>
<tr>
<td>220</td>
<td>78</td>
</tr>
<tr>
<td>225</td>
<td>79</td>
</tr>
</tbody>
</table>

1 INDICATIONS AND USAGE

WEGOVY® is indicated as an adjunct to a reduced calorie diet and increased physical activity for chronic weight management in:

- adults with an initial body mass index (BMI) of [see Dosage and Administration (2.1)]:
  - ≥ 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)
- pediatric patients aged 12 years and older with an initial BMI at the 95th percentile or greater standardized for age and sex (obesity) [see Dosage and Administration (2.1)]

Limitation of Use

- WEGOVY® contains semaglutide and should not be coadministered with other semaglutide-containing products or with any other GLP-1 receptor agonist.
- The safety and effectiveness of WEGOVY® in combination with other products intended for weight loss, including prescription drugs, over-the-counter drugs, and herbal preparations, have not been established.
- WEGOVY® has not been studied in patients with a history of pancreatitis [see Warnings and Precautions (5.2)].

2 DOSAGE AND ADMINISTRATION

2.1 Patient Selection

Adult Patients

Select adult patients for WEGOVY® treatment as an adjunct to a reduced calorie diet and increased physical activity for chronic weight management based on the BMI values provided in Table 1. Table 1 presents a chart for determining BMI based on height and weight. BMI is calculated by dividing weight (in kilograms) by height (in meters) squared.

Table 1. BMI Conversion Chart

<table>
<thead>
<tr>
<th>Weight (lb)</th>
<th>Height (in)</th>
</tr>
</thead>
<tbody>
<tr>
<td>125</td>
<td>58</td>
</tr>
<tr>
<td>130</td>
<td>60</td>
</tr>
<tr>
<td>135</td>
<td>61</td>
</tr>
<tr>
<td>140</td>
<td>62</td>
</tr>
<tr>
<td>145</td>
<td>63</td>
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<tr>
<td>150</td>
<td>64</td>
</tr>
<tr>
<td>155</td>
<td>65</td>
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<tr>
<td>160</td>
<td>66</td>
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<tr>
<td>165</td>
<td>67</td>
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<tr>
<td>170</td>
<td>68</td>
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<tr>
<td>175</td>
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<td>180</td>
<td>70</td>
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<td>185</td>
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<td>73</td>
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<td>215</td>
<td>77</td>
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<tr>
<td>220</td>
<td>78</td>
</tr>
<tr>
<td>225</td>
<td>79</td>
</tr>
</tbody>
</table>

Pediatric Patients Aged 12 Years and Older

Select pediatric patients aged 12 years and older for WEGOVY® treatment as an adjunct to a reduced calorie diet and increased physical activity for chronic weight management based on the BMI values provided in Table 1. Table 1 presents a chart for determining BMI based on height and weight. Table 2 presents BMI cut-offs for obesity in pediatric patients aged 12 years and older, determined based on the CDC age- and sex-specific growth charts.

Table 2. BMI Cut-offs for Obesity by Sex and Age for Pediatric Patients Aged 12 Years and Older (CDC Criteria)

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Body mass index (kg/m²)</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>24.2</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>12.5</td>
<td>24.7</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>25.1</td>
<td>20</td>
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</tr>
<tr>
<td>13.5</td>
<td>25.6</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>26.0</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>14.5</td>
<td>26.4</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>26.8</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>15.5</td>
<td>27.2</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>27.5</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>16.5</td>
<td>27.9</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>28.2</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>17.5</td>
<td>28.6</td>
<td>29</td>
<td></td>
</tr>
</tbody>
</table>

2.2 Important Monitoring and Administration Instructions

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

2.3 Recommended Dosage

Dosage Initiation and Escalation

In adults and pediatric patients aged 12 years and older, initiate WEGOVY® with a dosage of 0.25 mg injected subcutaneously once weekly. Then follow the dose escalation schedule in Table 3 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.

Table 3. Dosage Escalation Schedule

<table>
<thead>
<tr>
<th>Weeks</th>
<th>Weekly Dose</th>
<th>Dose escalation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.25 mg</td>
<td>maintenance dose</td>
</tr>
<tr>
<td>2</td>
<td>0.5 mg</td>
<td>maintenance dose</td>
</tr>
<tr>
<td>3</td>
<td>1 mg</td>
<td>maintenance dose</td>
</tr>
<tr>
<td>4</td>
<td>1.7 mg</td>
<td>maintenance dose</td>
</tr>
<tr>
<td>5</td>
<td>2.4 mg</td>
<td>maintenance dose</td>
</tr>
</tbody>
</table>

Maintenance Dosage

Adult Patients

- The maintenance dosage of WEGOVY® is 2.4 mg injected subcutaneously once weekly.
- If patients do not tolerate the maintenance 2.4 mg once-weekly dosage, the dosage can be temporarily decreased to 1.7 mg once weekly, for a maximum of 4 weeks. After 4 weeks, discontinue WEGOVY® to the maintenance 2.4 mg once-weekly dosage. Discontinue WEGOVY® if the patient cannot tolerate the 2.4 mg dosage.

Pediatric Patients Aged 12 Years and Older

- The recommended maintenance dosage of WEGOVY® is 2.4 mg injected subcutaneously once weekly.
- If patients do not tolerate the maintenance 2.4 mg once-weekly dosage, the maintenance dosage may be reduced to 1.7 mg once weekly. Discontinue WEGOVY® if the patient cannot tolerate the 1.7 mg dose.

2.4 Recommendations Regarding Missed Dose

If one dose is missed and the next scheduled dose is more than 2 days away (48 hours), administer WEGOVY® as soon as possible. If one dose is missed and the next scheduled dose is less than 2 days away (48 hours), do not administer the dose. Resume dosing on the regularly scheduled day of the week.

If 2 or more consecutive doses are missed, resume dosing as scheduled or, if needed, reinitate WEGOVY® and follow the dose escalation schedule, which may reduce the occurrence of gastrointestinal symptoms associated with reinitiation of treatment.

3 DOSAGE FORMS AND STRENGTHS

Injection: clear, colorless solution available in 5 pre-filled, disposable, single-dose pens:
- 0.25 mg/0.5 ml
- 0.5 mg/0.5 ml
- 1 mg/0.5 ml
- 1.7 mg/0.75 ml
- 2.4 mg/0.75 ml
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 medullary thyroid carcinoma (MTC) or in patients with MEN2. Counsel patients regarding the potential risk for MTC with the use of WEGOVY® and inform them of the risk of thyroid C-cell tumors (adenomas or carcinomas) in mice, rats, and dogs. These tumors have been observed in research animal species with high incidences of thyroid C-cell tumors (adenomas or carcinomas) in the neck, dysphagia, dyspnea, persistent hoarseness).

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

5.2 Acute Pancreatitis

Acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis, has been observed in patients treated with GLP-1 receptor agonists, including 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 re-started.

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 Glandular Disease

Treatment with WEGOVY® was associated with an increased occurrence of cholecystitis and cholelithiasis. The incidence of cholecystitis and cholelithiasis was higher in WEGOVY®-treated pediatric patients (mean age 12 years and older) than in other WEGOVY®-treated adults. In randomized clinical trials in adult patients, cholecystitis and cholelithiasis were reported by 1.6% of WEGOVY®-treated patients and 0.7% of placebo-treated patients. Cholecystitis was reported by 0.8% of WEGOVY®-treated adult patients and 0.5% 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% of placebo-treated patients. Cholecystitis was reported by 0.8% of WEGOVY®-treated pediatric patients and 0% placebo-treated patients (see Adverse Reactions [6.1]).

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, accounting for the increase in 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 adult 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 (e.g., 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 and symptoms of hypoglycemia, 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 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 semaglutide or to any of the excipients in WEGOVY® (see Adverse Reactions [6.2]).

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

5.7 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 and 2.7% placebo-treated patients (see Adverse Reactions [6.1]).

In a 2-year trial with semaglutide 0.5 mg and 1 mg once-weekly injection in adult patients with type 2 diabetes, the maximum changes from baseline at any visit of 10 to 19 bpm were greater in WEGOVY®-treated patients than in placebo-treated patients. In WEGOVY®-treated patients compared to placebo in clinical trials. More adult patients treated with WEGOVY® had maximum changes from baseline at any visit of 10 to 19 bpm compared to placebo (see Nonclinical Studies [10.1]).

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 5 bpm were reported in clinical trials in adult patients compared to placebo in clinical trials. More adult patients treated with WEGOVY® had maximum changes from baseline at any visit of 10 to 19 bpm compared to placebo (see Nonclinical Studies [10.1]).

Table 4. Adverse Reactions (≥2% and Greater Than Placebo) in WEGOVY®-Treated Adults with Obesity or Overweight for Chronic Weight Management

<table>
<thead>
<tr>
<th>Unwanted Effect</th>
<th>Placebo %</th>
<th>WEGOVY® %</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 1261</td>
<td>N = 2116</td>
<td></td>
</tr>
<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>8</td>
<td></td>
</tr>
<tr>
<td>Abdominal Distension</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Eructation</td>
<td>&lt;1</td>
<td>7</td>
</tr>
<tr>
<td>Hypoglycemia in 120Mg²</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>
</tbody>
</table>
Wegovy® (semaglutide) injection 2.4 mg

Adverse Reactions in a Clinical Trial of Pediatric Patients Aged 12 Years and Older with Obesity

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 obesity (see Clinical Studies [14,2]). Baseline characteristics included a mean age of 15.4 years, 58% of patients were male, 79% were White, 8% were Black or African American, 2% were Asian, and 11% were of other or unknown race; and 11% were of Hispanic or Latino ethnicity. The mean baseline body weight was 107.5 kg, and mean BMI was 37 kg/m².

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

Table 5. Adverse Reactions (≥ 3% and Greater than or Equal to 2%) in WEGOVY®-Treated Pediatric Patients Aged 12 Years and Older with Obesity for Chronic Weight Management

<table>
<thead>
<tr>
<th>Condition</th>
<th>Placebo N = 67</th>
<th>WEGOVY® N = 133</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>18%</td>
<td>42%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>10%</td>
<td>36%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>19%</td>
<td>22%</td>
</tr>
<tr>
<td>Headache</td>
<td>16%</td>
<td>17%</td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>16%</td>
<td>15%</td>
</tr>
<tr>
<td>Nausea or vomiting</td>
<td>10%</td>
<td>12%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>3%</td>
<td>8%</td>
</tr>
<tr>
<td>Gastroenteritis</td>
<td>3%</td>
<td>7%</td>
</tr>
<tr>
<td>Constipation</td>
<td>2%</td>
<td>6%</td>
</tr>
<tr>
<td>Gastroesophageal Reflux Disease</td>
<td>2%</td>
<td>4%</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>2%</td>
<td>4%</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>2%</td>
<td>4%</td>
</tr>
<tr>
<td>Limb pain</td>
<td>2%</td>
<td>4%</td>
</tr>
<tr>
<td>Anxiety</td>
<td>2%</td>
<td>4%</td>
</tr>
<tr>
<td>Hair Loss</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Cholelithiasis</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Eructation</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Influenza</td>
<td>0%</td>
<td>3%</td>
</tr>
<tr>
<td>Rash</td>
<td>0%</td>
<td>3%</td>
</tr>
<tr>
<td>Urticaria</td>
<td>0%</td>
<td>3%</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, 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

In WEGOVY®-treated pediatric patients aged 12 years and older with obesity who are taking insulin or insulin secretagogues, hypoglycemia was more frequent in WEGOVY®-treated patients compared with placebo.

Hypoglycemia was increased during dose titration in clinical trials. The incidence among WEGOVY®-treated patients was 1.3% greater than or equal to 27 kg/m². In a pediatric clinical trial, rash was used with a 73% increase in 0.2% of patients receiving placebo 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 used with a 4.3% increase in 0.2% of patients receiving placebo treatment as a result of gastrointestinal adverse reactions.

Laboratory Abnormalities

Anemia and Leukopenia

Adult and pediatric patients treated with WEGOVY® had a mean increase from baseline in amylase of 15-16% and lipase of 39%. These changes were not observed in the placebo group. The clinical significance of elevations in lipase or amylase is unknown in the absence of other signs and symptoms of pancreatitis.

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 (3%) WEGOVY®-treated patients compared with 0% of placebo-treated patients. In some patients, increases in ALT and AST were associated with other confounding factors (such as gallstones).

6.2 Postmarketing Experience

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

Gastrointestinal Disorders: acute pancreatitis and necrotizing pancreatitis, sometimes resulting in death, ileus

Hyperglycemia: 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 has not been evaluated.

When initiating WEGOVY®, 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) 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 in adult patients, 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 their healthcare providers are encouraged to contact Nove 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 issues 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 16. 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 (0.4-, 2-, and 5-fold the MRHD) were administered throughout organogenesis from Gestation Day 6 to 16. Pharmacologically mediated reductions in maternal body weight gain and food consumption coincided with the occurrence of sporadic abnormalities (vertebra, sternebra, ribs) at greater than or equal to 0.075 mg/kg twice weekly (greater than or equal to 2 times human exposure).

In a pre- and postnatal development study in pregnant cynomolgus monkeys, subcutaneous doses of 0.015, 0.075, and 0.15 mg/kg twice weekly (0.2-, 1-, and 5-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 infant from WEGOVY® and the potential transfer of semaglutide to the breastfeeding infant. Discontinue the infant from WEGOVY® (see Data) and advise the mother of the risk to a fetus if the 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 (8.10)).

8.4 Pediatric Use

The safety and effectiveness of WEGOVY® as an adjunct to a reduced calorie diet and increased physical activity for chronic weight management have been established in pediatric patients aged 12 years and older with a BMI corresponding to ≥95th percentile standardized for age and sex. Use of WEGOVY® for this indication is supported by a 68-week, double-blind, placebo-controlled clinical trial in 201 pediatric patients aged 12 years and older with a BMI corresponding to 95th percentile for age and sex and from studies in adult patients with obesity (see Clinical Studies (14.2)).

Adverse reactions with WEGOVY® treatment in pediatric patients aged 12 years and older were similar to those reported in adults. Pediatric patients aged 12 years and older treated with WEGOVY® had greater incidences of cholecystitis, cholelithiasis, hypoglycemia, skin, and subcutaneous tissue 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 sulfonylureas) 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, 233 (9%) WEGOVY®-treated patients were between 65 and 75 years of age and 23 (1%) WEGOVY®-treated patients were 75 years of age and over (see Clinical Studies (14.1)). No overall differences in safety or effectiveness have been observed between patients 65 years of age and older and younger adult patients.

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 have included severe nausea, severe vomiting, and severe hypoglycemia. In the event of overdose, appropriate supportive treatment should be initiated according to the patient’s clinical signs and symptoms. 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_{51}H_{92}N_{30}O_{49} and the molecular weight is 1143.58 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, and 1 mg of semaglutide; and each 0.75 mL single-dose pen contains a solution of WEGOVY® containing 1.25 mg or 2 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 caloric intake. The effects are likely mediated by affecting appetite. Semaglutide stimulates insulin secretion and reduces glucagon secretion in a glucose-dependent manner. These effects can lead to a reduction of blood glucose.

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/m^2) or overweight (BMI greater than or equal to 27 kg/m^2). 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) Ratio and 90% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Male</td>
</tr>
<tr>
<td>Age-group</td>
<td>65−&lt;75 years</td>
</tr>
<tr>
<td></td>
<td>&gt;75 years</td>
</tr>
<tr>
<td>Race</td>
<td>Black or African American</td>
</tr>
<tr>
<td></td>
<td>Asian</td>
</tr>
<tr>
<td></td>
<td>American Indian or Alaska Native</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>Hispanic or Latino</td>
</tr>
<tr>
<td>Body weight</td>
<td>74 kg</td>
</tr>
<tr>
<td></td>
<td>143 kg</td>
</tr>
<tr>
<td>Renal function</td>
<td>Mild</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
</tr>
<tr>
<td>Injection site</td>
<td>Thigh</td>
</tr>
<tr>
<td></td>
<td>Upper arm</td>
</tr>
</tbody>
</table>

Data are steady-state dose-normalized average semaglutide exposures relative to a reference subject profile (non-Hispanic or Latino, while female aged 10 to less than 65 years, with a body weight of 150 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 0.5 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 patients 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 Interaction 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

<table>
<thead>
<tr>
<th>Co-administered medication</th>
<th>Relative exposure (Cavg) Ratio and 90% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin</td>
<td>AUC(0-12h) Cmax</td>
</tr>
<tr>
<td>AUC(0-16h) Cmax</td>
<td></td>
</tr>
<tr>
<td>S-warfarin</td>
<td>AUC(0-16h) Cmax</td>
</tr>
<tr>
<td>R-warfarin</td>
<td>AUC(0-16h) Cmax</td>
</tr>
<tr>
<td>Diovigox</td>
<td>AUC(0-12h) Cmax</td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>AUC(0-12h) Cmax</td>
</tr>
<tr>
<td>Ethinyelustradil</td>
<td>AUC(0-24h) Cmax</td>
</tr>
<tr>
<td>Levonorgestrel</td>
<td>AUC(0-24h) Cmax</td>
</tr>
</tbody>
</table>

Relative exposure in terms of AUC and Cmax for each medication when given with semaglutide compared to without semaglutide. Metformin and oral contraceptive drug (ethinyelustradil/levonorgestrel) were assessed at steady state. Warfarin (S-warfarin/R-warfarin), diovigox 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 other semaglutide products.

During the 68-week treatment periods in Studies 1 and 2, [see Clinical Studies (14.1)], 50/1790 (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 pharmacokinetics for WEGOVY® was observed. There is insufficient evidence to characterize the effects of anti-semaglutide antibodies on pharmacodynamics or effectiveness of semaglutide.

In the adult clinical trials (Studies 1 and 2), hypersensitivity reactions occurred in a higher percentage of WEGOVY®-treated patients who developed anti-semaglutide antibodies compared to those who did not develop anti-semaglutide antibodies [see Adverse Reactions (6.1)].

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 7-10% and were treated with either:

- WEGOVY® injection 2.4 mg
- Matching placebo

for each medication when given with semaglutide compared to without semaglutide. Metformin and oral contraceptive drug (ethinylestradiol/levonorgestrel) were assessed at steady state. Warfarin (S-warfarin/R-warfarin), diovigox and atorvastatin were assessed after a single dose.

Abbreviations: AUC = area under the curve, Cmax = maximum concentration, CI = confidence interval.

13.1.1 Carcinogenesis

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 at mating and throughout gestation. At 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.

13.2 Mutagenicity

Semaglutide did not induce chromosomal aberrations in Chinese hamster ovary cells treated with or without metabolism using S9. Semaglutide did not induce or inhibit the Ames assay or the mouse lymphoma assay with or without metabolism using S9. In vitro studies have shown very low potential for semaglutide to inhibit or induce human CYP enzymes, or to inhibit human drug transporters.

13.3 Impairment of Fertility

In an 18-month mating study using CD-1 mice administered semaglutide (0.01, 0.03, and 0.09 mg/kg/day), male fertility was not impaired. There was 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.

13.4 Teratology

Semaglutide was not teratogenic in rats or rabbits at doses up to 0.03 mg/kg/day (0.04-, 0.1-, and 0.4-fold the MRHD). No effects were observed on female 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.

13.5 Carcinogenesis

Semaglutide did not induce chromosomal aberrations in Chinese hamster ovary cells treated with or without metabolism using S9. Semaglutide did not induce or inhibit the Ames assay or the mouse lymphoma assay with or without metabolism using S9. In vitro studies have shown very low potential for semaglutide to inhibit or induce human CYP enzymes, or to inhibit human drug transporters.
Table 6. Changes in Body Weight at Week 68 in Studies 1, 2, and 3

<table>
<thead>
<tr>
<th>Study</th>
<th>Placebo (N = 635)</th>
<th>WEGOVY® (N = 1306)</th>
<th>Placebo (N = 403)</th>
<th>WEGOVY® (N = 404)</th>
<th>Placebo (N = 204)</th>
<th>WEGOVY® (N = 407)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body Weight</td>
<td>Baseline (mean (kg))</td>
<td>105.2</td>
<td>105.4</td>
<td>101.5</td>
<td>99.9</td>
<td>103.7</td>
</tr>
<tr>
<td></td>
<td>% change from baseline (LSMean)</td>
<td>-2.4</td>
<td>-14.9</td>
<td>-3.4</td>
<td>-9.6</td>
<td>-5.7</td>
</tr>
<tr>
<td></td>
<td>% difference from placebo (LSMean) (95% CI)</td>
<td>-12.4 (-13.5, -11.6)*</td>
<td>-12.4 (-13.5, -11.6)*</td>
<td>-6.2 (-7.2, -5.2)*</td>
<td>-10.3 (-11.8, -8.7)*</td>
<td></td>
</tr>
<tr>
<td></td>
<td>% of Patients losing greater than or equal to 5% body weight</td>
<td>31.1</td>
<td>83.5</td>
<td>30.2</td>
<td>67.4</td>
<td>47.8</td>
</tr>
<tr>
<td></td>
<td>% difference from placebo (LSMean) (95% CI)</td>
<td>52.4 (48.1, 56.7)*</td>
<td>52.4 (48.1, 56.7)*</td>
<td>37.2 (30.7, 43.8)*</td>
<td>37.0 (28.9, 45.2)*</td>
<td></td>
</tr>
<tr>
<td></td>
<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>
<td>44.5</td>
<td>27.1</td>
</tr>
<tr>
<td></td>
<td>% difference from placebo (LSMean) (95% CI)</td>
<td>54.1 (50.4, 57.9)*</td>
<td>54.1 (50.4, 57.9)*</td>
<td>34.3 (28.6, 40.2)*</td>
<td>45.9 (38.0, 53.7)*</td>
<td></td>
</tr>
<tr>
<td></td>
<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>
<td>25.1</td>
<td>13.2</td>
</tr>
<tr>
<td></td>
<td>% difference from placebo (LSMean) (95% CI)</td>
<td>43.1 (39.8, 46.3)*</td>
<td>43.1 (39.8, 46.3)*</td>
<td>20.7 (15.7, 25.8)*</td>
<td>40.2 (33.1, 47.3)*</td>
<td></td>
</tr>
</tbody>
</table>

LSMean = least squares mean; CI = confidence interval

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.

Table 7. 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</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 803</td>
<td>N = 268</td>
</tr>
<tr>
<td>N = 535</td>
<td>N = 535</td>
</tr>
<tr>
<td>Body Weight (only randomized patients)</td>
<td>Mean at week 0 (kg)</td>
</tr>
<tr>
<td>% change from week 20 at week 68 (LSMean)</td>
<td>95.4 (22.7)</td>
</tr>
<tr>
<td>% difference from placebo (LSMean) (95% CI)</td>
<td>-14.8 (-16.0, -13.5)*</td>
</tr>
</tbody>
</table>

LSMean = least squares mean; CI = confidence interval

Of 902 patients (11%), the most common reason was adverse reactions (n=46, 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, 63.7% 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.

Results

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 6.

The time courses of weight loss with WEGOVY® and placebo from baseline through week 68 are observed data from in-trial period including imputed data for missing observations (RD-MI).

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 65%, and 12%, respectively, which correspond to the values shown in Table 6.
Figure 6. Change from Baseline (%) in Body Weight (Study 1 on Left and Study 2 on Right)

Figure 7. Change from Baseline (%) in Body Weight (Study 3 on Left and Study 4 on Right)

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 Adults
Changes in waist circumference and cardiometabolic parameters with WEGOVY® are shown in Table 8 for Studies 1, 2, and 3 and in Table 9 for Study 4, respectively.

Table 8. Changes in Anthropometry and Cardiometabolic Parameters 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 undergoing intensive 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 = 403</td>
</tr>
<tr>
<td>Waist Circumference (cm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>114.8</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 Rate (bpm)</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>
</tbody>
</table>
4.9

5.0

-0.5

51.6

-175.9

5.4

-0.3

4.1

2,4

-6.5

21.9

-0.2

8.1

50.9

5.2

108.7

95.3

98.1

127.9

0.3

5.7

43.6

112.5

1.3

110.3

-3.8

49.5

1.4

5.2

3.8

127.9

-7.3

-126.2

-15.8

175.1

43.8

159.5

1.3

125.2

2,4

1c

1c

2

2

Table 9. Mean Changes in Anthropometry and Cardiometabolic Parameters in Study 4 (Obesity or Overweight with Comorbidity after 20 Week Run-in)\(^*\)

<table>
<thead>
<tr>
<th>Intention-to-Treat</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 intensive lifestyle therapy)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PLACEBO N = 655</td>
<td>WEGOVY(^\circ) N = 1386</td>
<td>PLACEBO N = 403</td>
</tr>
<tr>
<td>HbA(_1c) (%)(^2)</td>
<td>Baseline</td>
<td>Changes from baseline (LSMean)(^1)</td>
<td>Relative difference from placebo (LSMean)(^1)</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dL)(^2)</td>
<td>Baseline</td>
<td>Percent Change from baseline (LSMean)(^1)</td>
<td>Relative difference from placebo (LSMean)(^1)</td>
</tr>
<tr>
<td>LDL Cholesterol (mg/dL)(^2)</td>
<td>Baseline</td>
<td>Percent Change from baseline (LSMean)(^1)</td>
<td>Relative difference from placebo (LSMean)(^1)</td>
</tr>
<tr>
<td>HDL (mg/dL)(^2)</td>
<td>Baseline</td>
<td>Percent Change from baseline (LSMean)(^1)</td>
<td>Relative difference from placebo (LSMean)(^1)</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)(^2)</td>
<td>Baseline</td>
<td>Percent Change from baseline (LSMean)(^1)</td>
<td>Relative difference from placebo (LSMean)(^1)</td>
</tr>
</tbody>
</table>

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

\(^1\)Model based estimates based on an analysis of covariance model including treatment (and stratification factors for Study 2 only) as a factor and baseline value as a covariate

\(^2\)Not included in the pre-specified hierarchical testing (except HbA\(_1c\) for Study 2)

\(^3\)Model based estimates based on a mixed model for repeated measures including treatment (and stratification factors for Study 2 only) as a factor and baseline values as a covariate

\(^4\)Baseline value is the geometric mean

14.2 Weight Management Study in Pediatric Patients Aged 12 Years and Older with Obesity

Overview of Clinical Trial in Pediatric Patients

WEGOVY\(^\circ\) was evaluated in a 68-week, double-blind, randomized, parallel group, placebo-controlled, multi-center trial in 201 pubertal pediatric patients aged 12 years and older with BMI corresponding to ≥95th percentile standardized for age and sex (see Dosage and Administration (2.1)). After a 12-week lifestyle run-in period (including dietary recommendations and physical activity counseling), patients were randomized 2:1 to WEGOVY\(^\circ\) once weekly or placebo once weekly. WEGOVY\(^\circ\) 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\(^\circ\)-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/m\(^2\).

The proportions of patients who discontinued study drug were 10% for the WEGOVY\(^\circ\)-treated group and 10% for the placebo-treated group.

Results

The primary endpoint was percent change in BMI from baseline to week 68. After 68 weeks, treatment with WEGOVY\(^\circ\) resulted in a statistically significant reduction in percent BMI compared with placebo. Greater proportions of patients treated with WEGOVY\(^\circ\) achieved ≥5% reduction in baseline BMI than those treated with placebo as shown in Table 10.
Table 10. Changes in Weight and BMI at Week 68 in Pediatric Patients with Obesity Aged 12 Years and Older in a Weight Management Trial

<table>
<thead>
<tr>
<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>
</tr>
<tr>
<td>Baseline (kg/m²)</td>
<td>35.7</td>
<td>37.7</td>
</tr>
<tr>
<td>% change from baseline (LSMean)</td>
<td>0.8</td>
<td>-1.9</td>
</tr>
<tr>
<td>% difference from placebo (LSMean)</td>
<td>-16.7</td>
<td>-12.7</td>
</tr>
<tr>
<td>% of Patients with greater than or equal to 5% reduction in baseline BMI</td>
<td>18.4</td>
<td>18.0</td>
</tr>
<tr>
<td>% difference from placebo (LSMean)</td>
<td>-18.0</td>
<td>-12.3</td>
</tr>
<tr>
<td>% of Patients with greater than or equal to 10% reduction in baseline BMI</td>
<td>7.7</td>
<td>16.1</td>
</tr>
<tr>
<td>% difference from placebo (LSMean)</td>
<td>-14.9</td>
<td>-12.1</td>
</tr>
<tr>
<td>% of Patients with greater than or equal to 15% reduction in baseline BMI</td>
<td>7.7</td>
<td>19.6</td>
</tr>
<tr>
<td>% difference from placebo (LSMean)</td>
<td>-15.7</td>
<td>-12.6</td>
</tr>
<tr>
<td>Body Weight</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline (kg)</td>
<td>102.6</td>
<td>109.9</td>
</tr>
<tr>
<td>% change from baseline (LSMean)</td>
<td>2.7</td>
<td>-14.7</td>
</tr>
<tr>
<td>% difference from placebo (LSMean)</td>
<td>-17.4</td>
<td>-12.4</td>
</tr>
</tbody>
</table>

LSMean = least squares mean; CI = confidence interval

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

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 11 for the study in pediatric patients aged 12 years and older.

Table 11. Mean Changes in Anthropometry and Cardiometabolic Parameters in Pediatric Patients with Obesity Aged 12 Years and Older

<table>
<thead>
<tr>
<th>PLACEBO N = 67</th>
<th>WEGOVY® N = 134</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waist Circumference (cm²)</td>
<td>107.3</td>
</tr>
<tr>
<td>Systolic Blood Pressure (mmHg)</td>
<td>120.0</td>
</tr>
<tr>
<td>Diastolic Blood Pressure (mmHg)</td>
<td>73.8</td>
</tr>
<tr>
<td>Heart Rate per minute</td>
<td>76.0</td>
</tr>
<tr>
<td>HbA1C (%)</td>
<td>5.4</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dL)²,³</td>
<td>160.1</td>
</tr>
<tr>
<td>LDL Cholesterol (mg/dL)²,³</td>
<td>91.7</td>
</tr>
<tr>
<td>HDL Cholesterol (mg/dL)²</td>
<td>43.3</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)²,³</td>
<td>100.0</td>
</tr>
</tbody>
</table>

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

Figure 8. Change from Baseline (%) in BMI in Pediatric Patients with Obesity Aged 12 Years and Older in a Weight Management Trial

Figure 9. Change in BMI (%) from Baseline to Week 68 in Pediatric Patients with Obesity Aged 12 Years and Older in a Weight Management Trial

17 PATIENT COUNSELING INFORMATION

Adopt 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 type 2 diabetes mellitus on glycemic lowering therapy that they may have an increased risk of hypoglycemia when using WEGOVY® and to report signs and/or symptoms of hypoglycemia to their healthcare provider (see Warnings and Precautions (5.4)).

Dehydration and Renal Impairment

Advise patients to treat 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)).

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 1-800-727-6500 [see Use in Specific Populations (8.1)].
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 that may help adults and children aged 12 years and older with obesity, or some adults with excess weight (overweight) who also have weight-related medical problems to help them lose weight and keep the weight off.
- WEGOVY® should be used with a reduced calorie meal plan and increased physical activity.
- WEGOVY® contains semaglutide and should not be used with other semaglutide-containing products or other GLP-1 receptor agonists.
- It is not known if WEGOVY® is safe and effective when taken with other prescription, over-the-counter, or herbal weight loss products.
- It is not known if WEGOVY® can be used safely in people with a history of pancreatitis.
- 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 swallowing; 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 1-800-727-6500.
- 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 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 dose to 0.5 mg. If 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 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 may 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 sulfonylureas 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
  - irritability or mood changes
  - fast heartbeat
  - feeling jittery
  - kidney 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
- 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 and children aged 12 years and older may include:
- nausea
- diarrhea
- vomiting
- constipation
- stomach (abdomen) pain
- headache
- tiredness (fatigue)
- upset stomach
- dizziness
- feeling bloated
- belching
- gas
- heartburn
- runny nose or sore throat

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, sodium chloride, and water for injection

This Medication Guide has been approved by the U.S. Food and Drug Administration.
Issued: 12/2022
Instructions for Use

WEGOVY® (semaglutide) injection

WEGOVY® comes in five strengths:

- 0.25 mg / 0.5 mL
- 0.5 mg / 0.5 mL
- 1 mg / 0.5 mL
- 1.7 mg / 0.75 mL
- 2.4 mg / 0.75 mL

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

Important information

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

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

How do I store WEGOVY®?

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

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

WEGOVY® pen parts

Expiration date
(Ex: 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.

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

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.

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.

- Suppliers 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. 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.

- What if blood appears after injection?
  If blood appears at the injection site, press the site lightly with a gauze pad or cotton ball.

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

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.

Manufactured by:
Novo Nordisk A/S
Novo Allé
DK-2880 Bagsvaerd, Denmark
For information about WEGOVY®, go to startWegovy.com or contact:
Novo Nordisk Inc.
800 Scudders Mill Road
Plainsboro, NJ 08536
1-833-WEGOVY®-1
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This Instructions for Use has been approved by the U.S. Food and Drug Administration.
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