HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use SAXENDA® safely and effectively. See full prescribing information for SAXENDA®. SAXENDA® (liraglutide) injection, solution for subcutaneous use Initial U.S. Approval: 2010

WARNING: RISK OF THYROID C-CELL TUMORS

See full prescribing information for complete boxed warning.

- Liraglutide causes thyroid C-cell tumors at clinically relevant exposures in both genders of rats and mice. It is unknown whether Saxenda® causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as the human relevance of liraglutide-induced rodent thyroid C-cell tumors has not been determined (5.1).
- Saxenda® 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 the symptoms of thyroid tumors (4, 5.1, 13.1).

— Recent Major Changes ——
Boxed Warning 9/2016
Warnings and Precautions, Risk of Thyroid C-cell Tumors (5.1) 9/2016

— Indications and Usage ——
Saxenda® 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 (obese) (1) or
- 27 kg/m² or greater (overweight) in the presence of at least one weight-related comorbid condition (e.g. hypertension, type 2 diabetes mellitus, or dyslipidemia) (1).

Limitations of Use:
- Saxenda® is not indicated for the treatment of type 2 diabetes (1).
- Saxenda® should not be used in combination with any other GLP-1 receptor agonist (1).
- Saxenda® should not be used with insulin (1, 5.4).
- The effects of Saxenda® on cardiovascular morbidity and mortality have not been established (1).
- The safety and efficacy of coadministration with other products for weight loss have not been established (1).
- Saxenda® has not been studied in patients with a history of pancreatitis (1, 5.2).

DOSAGE AND ADMINISTRATION

- Recommended dose of Saxenda® is 3 mg daily. Administer at any time of day, without regard to the timing of meals (2). Initiate at 0.6 mg per day for one week. In weekly intervals, increase the dose until a dose of 3 mg is reached (2).
- Inject subcutaneously in the abdomen, thigh or upper arm (2).
- The injection site and timing can be changed without dose adjustment (2).

DOSAGE FORMS AND STRENGTHS

- Solution for subcutaneous injection, pre-filled, multi-dose pen that delivers doses of 0.6 mg, 1.2 mg, 1.8 mg, 2.4 mg or 3 mg (6 mg/mL, 3 mL) (3).

CONTRAINDICATIONS

- Personal or family history of medullary thyroid carcinoma or Multiple Endocrine Neoplasia syndrome type 2 (4, 5.1).
- Hypersensitivity to liraglutide or any product components (4, 5.7).
- Pregnancy (4, 8.1).

WARNINGS AND PRECAUTIONS

- Thyroid C-cell Tumors: See Boxed Warning (5.1).
- Acute Pancreatitis: Discontinue promptly if pancreatitis is suspected. Do not restart if pancreatitis is confirmed (5.2).
- Acute Gallbladder Disease: If cholelithiasis or cholecystitis are suspected, gallbladder studies are indicated (5.3).
- Serious Hypoglycemia: Can occur when Saxenda® is used with an insulin secretagogue (e.g. a sulfonylurea). Consider lowering the dose of anti-diabetic drugs to reduce the risk of hypoglycemia (2, 5.4).
- Heart Rate Increase: Monitor heart rate at regular intervals (5.5).
- Renal Impairment: Has been reported postmarketing, usually in association with nausea, vomiting, diarrhea, or dehydration which may sometimes require hemodialysis. Use caution when initiating or escalating doses of Saxenda® in patients with renal impairment (5.6).
- Hypersensitivity Reactions: Postmarketing reports of serious hypersensitivity reactions (e.g., anaphylactic reactions and angioedema). Discontinue Saxenda® and other suspect medications and promptly seek medical advice (5.7).
- Suicidal Behavior and Ideation: Monitor for depression or suicidal thoughts. Discontinue Saxenda® if symptoms develop (5.8).

ADVERSE REACTIONS

- Most common adverse reactions, reported in greater than or equal to 5% are: nausea, hypoglycemia, diarrhea, constipation, vomiting, headache, decreased appetite, dyspepsia, fatigue, dizziness, abdominal pain, and increased lipase (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact Novo Nordisk Inc. at 1-844-363-4448 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Saxenda® delays gastric emptying. May impact absorption of concurrently administered oral medications. Use with caution (7).

USE IN SPECIFIC POPULATIONS

- Nursing Mothers: Discontinue drug or nursing (8.3).
- Pediatric Use: Safety and effectiveness not established and use not recommended (8.4).

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

REVISED: 9/2016

FULL PRESCRIBING INFORMATION: CONTENTS*
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**WARNING: RISK OF THYROID C-CELL TUMORS**

- Liraglutide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures in both genders of rats and mice. It is unknown whether Saxenda® causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as the human relevance of liraglutide-induced rodent thyroid C-cell tumors has not been determined [see Warnings and Precautions (5.1) and Nonclinical Toxicology (13.1)].

- Saxenda® is contraindicated in patients with a personal or family history of MTC and in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Counsel patients regarding the potential risk of MTC with use of Saxenda® 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 Saxenda® [see Contraindications (4), Warnings and Precautions (5.1)].

### 1 INDICATIONS AND USAGE

Saxenda® is 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 (obese), 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)

**Limitations of Use**

- Saxenda® is not indicated for the treatment of type 2 diabetes mellitus.

### 2 DOSAGE AND ADMINISTRATION

The recommended dosage of Saxenda® is 3 mg daily. The dose escalation schedule in Table 1 should be used to reduce the likelihood of gastrointestinal symptoms. If patients do not tolerate an increased dose during dose escalation, consider delaying dose escalation for approximately one additional week. Saxenda® should be discontinued, however, if a patient cannot tolerate the 3 mg dose, as efficacy has not been established at lower doses (0.6, 1.2, 1.8, and 2.4 mg).

**Table 1. Dose Escalation Schedule**

<table>
<thead>
<tr>
<th>Week</th>
<th>Daily Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.6 mg</td>
</tr>
<tr>
<td>2</td>
<td>1.2 mg</td>
</tr>
<tr>
<td>3</td>
<td>1.8 mg</td>
</tr>
<tr>
<td>4</td>
<td>2.4 mg</td>
</tr>
<tr>
<td>5 and onward</td>
<td>3 mg</td>
</tr>
</tbody>
</table>

Saxenda® should be taken once daily at any time of day, without regard to the timing of meals. Saxenda® can be injected subcutaneously in the abdomen, thigh, or upper arm. The injection site and timing can be changed without dose adjustment. Saxenda® must not be administered intravenously or intramuscularly.

When initiating Saxenda® in patients taking insulin secretagogues (such as sulfonylureas), consider reducing the dose of the insulin secretagogue (for example, by one-half) to reduce the risk for hypoglycemia, and monitor blood glucose. Saxenda® and insulin should not be used together [see Warnings and Precautions (5.4) and Adverse Reactions (6.1)]. Conversely, if discontinuing MTC and liraglutide use in patients with type 2 diabetes, monitor for an increase in blood glucose.

Evaluate the change in body weight 16 weeks after initiating Saxenda® and discontinue Saxenda® if the patient has not lost at least 4% of baseline body weight, since it is unlikely that the patient will achieve and sustain clinically meaningful weight loss with continued treatment.

If a dose is missed, the once-daily regimen should be resumed as prescribed with the next scheduled dose. An extra dose or increase in dose should not be taken to make up for the missed dose. If more than 3 days have elapsed since the last Saxenda® dose, patients should reinitiate Saxenda® at 0.6 mg daily and follow the dose escalation schedule in Table 1, which may reduce the occurrence of gastrointestinal symptoms associated with reinitiation of treatment.

Prior to initiation of Saxenda®, patients should be trained by their healthcare professional on proper injection technique. Training reduces the risk of administration errors such as needle sticks and incomplete dosing. Refer to the accompanying Instructions for Use for complete administration instructions with illustrations.

Saxenda® solution should be inspected prior to each injection, and the solution should be used only if it is clear, colorless, and contains no particles. SAXENDA® (liraglutide) injection contains no particles.

### 3 DOSAGE FORMS AND STRENGTHS

Solution for subcutaneous injection, pre-filled, multi-dose pen that delivers doses of 0.6 mg, 1.2 mg, 1.8 mg, 2.4 mg, or 3 mg (6 mg/mL, 3 mL).

### 4 CONTRAINDICATIONS

Saxenda® is contraindicated in:

- Patients with a personal or family history of medullary thyroid carcinoma (MTC) or patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2) [see Warnings and Precautions (5.1)].

- Patients with a prior serious hypersensitivity reaction to liraglutide or to any of the product components [see Warnings and Precautions (5.7)].

- Pregnancy [see Use in Specific Populations (8.1)]

### 5 WARNINGS AND PRECAUTIONS

#### 5.1 Risk of Thyroid C-Cell Tumors

Liraglutide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors (adenomas and/or carcinomas) at clinically relevant exposures in both genders of rats and mice [see Nonclinical Toxicology (13.1)]. Malignant thyroid C-cell carcinomas were detected in rats and mice. It is unknown whether Saxenda® will cause thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as the human relevance of liraglutide-induced rodent thyroid C-cell tumors has not been determined.

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

Saxenda® is contraindicated in patients with a personal or family history of MTC or in patients with MEN 2. Counsel patients regarding the potential risk for MTC with the use of Saxenda® 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 Saxenda®. Such monitoring may increase the risk of unnecessary procedures, due to low test specificity for serum.
calcitonin and a high background incidence of thyroid disease. Significantly elevated serum calcitonin may indicate MTC, and patients with MTC usually have calcitonin values greater than 50 ng/mL. If serum calcitonin is measured and found to be elevated, the patient should be further evaluated. Patients with thyroid nodules noted on physical examination or neck imaging should also be further evaluated.

5.2 Acute Pancreatitis

Based on spontaneous post approval reports, acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis, has been observed in patients treated with liraglutide. After initiation of Saxenda®, observe patients carefully for signs and symptoms of pancreatitis including persistent severe abdominal pain, sometimes radiating to the back and which may or may not be accompanied by vomiting. If pancreatitis is suspected, Saxenda® should promptly be discontinued and appropriate management should be initiated. If pancreatitis is confirmed, Saxenda® should not be restarted.

In Saxenda® clinical trials, acute pancreatitis was confirmed by adjudication in 9 (0.3%) of 2921 Saxenda®-treated patients and 1 (0.1%) of 1843 placebo-treated patients. In addition, there were 2 cases of acute pancreatitis in Saxenda®-treated patients who spontaneously reported this condition among 124 days after the last dose, and 1 additional case in a Saxenda®-treated patient during an off-treatment follow-up period within 2 weeks of discontinuing Saxenda®.

It is unknown whether patients with a history of pancreatitis are at increased risk of pancreatitis while taking Saxenda®, since these patients were excluded from clinical trials.

5.3 Acute Gallbladder Disease

In Saxenda® clinical trials, 1.5% of Saxenda®-treated patients reported adverse events of cholelithiasis versus 0.5% of placebo-treated patients. The incidence of cholecystitis was 0.6% in Saxenda®-treated patients versus 0.2% in placebo-treated patients. The majority of Saxenda®-treated patients with adverse events of cholelithiasis and cholecystitis required cholecystectomy. Substantial or rapid weight loss can increase the risk of cholelithiasis; therefore, if acute cholecystitis disease was greater in Saxenda®-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 recommended.

5.4 Risk for Hypoglycemia with Concomitant Use of Anti-Diabetic Therapy

The risk for serious hypoglycemia is increased when Saxenda® is used in combination with insulin secretagogues (for example, sulfonylureas) in patients with type 2 diabetes mellitus. Therefore, patients may require a lower dose of sulfonylurea (or other concomitantly administered insulin secretagogues) in this setting [see Dosage and Administration (2) and Adverse Reactions (6.1)]. Saxenda® should not be used in patients taking insulin. Saxenda® can lower blood glucose [see Clinical Pharmacology (12.2)]. Monitor blood glucose parameters prior to starting Saxenda® and during Saxenda® treatment in patients with type 2 diabetes. If needed, adjust co-administered anti-diabetic drugs based on glucose monitoring results and risk of hypoglycemia.

5.5 Heart Rate Increase

Mean increases in resting heart rate of 2 to 3 beats per minute (bpm) were observed with routine clinical monitoring in Saxenda®-treated patients compared to placebo in clinical trials. More patients treated with Saxenda®, compared with placebo, had changes from baseline at two consecutive visits of more than 10 bpm (34% versus 19%, respectively) and 20 bpm (5% versus 2%, respectively). At least one resting heart rate exceeding 100 bpm was recorded for 6% of Saxenda®-treated patients compared with 4% of placebo-treated patients. In a post hoc analysis of two clinical studies for Saxenda® in patients with type 2 diabetes for a mean treatment duration of 45.9 weeks (median, 55.9 weeks). Of these, 1087 Saxenda®-treated patients and 497 placebo-treated patients have been exposed in their original randomized groups beyond the primary endpoint for an additional mean duration of 53.0 weeks (median, 56.9 weeks). Baseline characteristics included a mean age of 47 years, 71% women, 85% white, 39% with hypertension, BMI greater than or equal to 70 mg/dL) occurred in 48 (43.6%) of 110 Saxenda®-treated patients and 12 (27.3%) of 52 placebo-treated patients. The doses of sulfonylureas were reduced by 50% at the beginning of the trial period.

In a clinical trial, heart rate was monitored continuously for 24 hours. Saxenda® treatment was associated with a heart rate that was 4 to 9 bpm higher than that observed with placebo. The clinical significance of the heart rate elevation with Saxenda® treatment is unclear, especially for patients with cardiac and cerebrovascular disease as a result of limited exposure in these patients in clinical trials.

Heart rate should be monitored at regular intervals consistent with usual clinical practice. Patients should inform health care providers of palpitations or feelings of a racing heartbeat while at rest during Saxenda® treatment. For patients who experience a sustained increase in resting heart rate while taking Saxenda®, Saxenda® should be discontinued.

5.6 Renal Impairment

Patients treated with GLP-1 receptor agonists, including Saxenda®, have been reported of acute renal failure and worsening of chronic renal failure, sometimes requiring hemodialysis [see Adverse Reactions (6.2)]. Some of these events were reported in patients without known underlying renal disease. A majority of the reported events occurred in patients who had severe renal impairment and/or diabetes leading to volume depletion. Some of the reported events occurred in patients receiving one or more medications known to affect renal function or volume status. Altered renal function has been reversed in many of the reported cases with supportive treatment and discontinuation of potentially causative agents, including liraglutide. Use caution when initiating or escalating doses of Saxenda® in patients with renal impairment [see Use in Specific Populations (8.6)].

5.7 Hypersensitivity Reactions

There have been reports of serious hypersensitivity reactions (e.g., anaphylactic reactions and angioedema) in patients treated with liraglutide [see Adverse Reactions (6.1, 6.2)]. If a hypersensitivity reaction occurs, the patient should discontinue Saxenda® and seek medical advice. Discontinuing Saxenda® in patients who experience urticaria or angioedema might prevent further episodes.

In a post hoc analysis of two clinical studies for Saxenda® in patients with type 2 diabetes for a mean treatment duration of 45.9 weeks (median, 55.9 weeks). Of these, 1087 Saxenda®-treated patients and 497 placebo-treated patients have been exposed in their original randomized groups beyond the primary endpoint for an additional mean duration of 53.0 weeks (median, 56.9 weeks). Baseline characteristics included a mean age of 47 years, 71% women, 85% white, 39% with hypertension, 15% with type 2 diabetes, 34% with dyslipidemia, 29% with a BMI greater than 40 kg/m², and 9% with cardiovascular disease. Dosing was initiated and increased weekly to reach the 3 mg dose.

In clinical trials, 9.8% of patients treated with Saxenda® and 4.3% of patients treated with placebo prematurely discontinued treatment as a result of adverse reactions. The most common adverse reactions leading to discontinuation were nausea (2% versus 0.2% for Saxenda® and placebo, respectively), vomiting (1.7% versus less than 0.1%), and diarrhea (1.4% versus 0%). Adverse reactions reported in greater than or equal to 2% of Saxenda®-treated patients and more frequently than in placebo-treated patients are shown in Table 3.

### Table 3. Adverse Reactions Reported in Greater Than or Equal to 2% of Saxenda®-treated Patients and More Frequently than with Placebo

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Placebo (%)</th>
<th>Saxenda® (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>13.8</td>
<td>39.3</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>9.9</td>
<td>20.9</td>
</tr>
<tr>
<td>Constipation</td>
<td>8.5</td>
<td>19.4</td>
</tr>
<tr>
<td>Vomiting</td>
<td>3.9</td>
<td>15.7</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>2.7</td>
<td>9.6</td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>3.1</td>
<td>5.4</td>
</tr>
<tr>
<td>Upper Abdominal Pain</td>
<td>2.7</td>
<td>5.1</td>
</tr>
<tr>
<td>Gastroesophageal Reflux Disease</td>
<td>1.7</td>
<td>4.7</td>
</tr>
<tr>
<td>Abdominal Distension</td>
<td>3.0</td>
<td>4.5</td>
</tr>
<tr>
<td>Eruption</td>
<td>0.2</td>
<td>4.5</td>
</tr>
<tr>
<td>Flatulence</td>
<td>2.5</td>
<td>4.0</td>
</tr>
<tr>
<td>Dry Mouth</td>
<td>1.0</td>
<td>2.3</td>
</tr>
</tbody>
</table>

### Gastrointestinal Disorders

- Nausea: 12.6%
- Diarrhea: 13.6%
- Constipation: 6.9%  

### Nervous System Disorders

- Headache: 4.6%  
- Depression: 4.7%
- Urinary Tract Infection: 4.3%
- Gastroenteritis: 1.6%  

### Metabolism and Nutrition Disorders

- Hypoglycemia in T2DM: 12.7%
- Decreased Appetite: 2.3%
- Fatigue: 7.5%
- Nausea: 5.4%
- Injection Site Erythema: 2.5%
- Injection Site Reaction: 0.6%  

### Investigations

- Increased Lipase: 2.2%
- Insulin: 1.7%  

### Psychiatric Disorders

- Anxiety: 1.6%
- Depression: 2.4%  

*Documented symptomatic (defined as documented symptoms of hypoglycemia in combination with a plasma glucose level less than or equal to 70 mg/dL) in patients with type 2 diabetes (Study 2B)*

### General Disorders and Administration Site Conditions

- Insomnia: 7.1%
- Fatigue: 7.4%
- Headache: 5.6%
- Nausea: 5.5%
- Diarrhea: 4.7%
- Urinary Tract Infection: 4.3%
- Gastroenteritis: 1.6%

### Hypoglycemia

Saxenda® can lower blood glucose. In a clinical trial involving patients with type 2 diabetes mellitus and overweight or obesity, severe hypoglycemia (defined as requiring the assistance of another person) occurred in 3 (0.7%) of 422 Saxenda®-treated patients and in none of the 212 placebo-treated patients. Each of these 3 Saxenda®-treated patients was also taking a sulfonylurea. In the same trial, among patients taking a sulfonylurea, documented symptomatic hypoglycemia (defined as documented symptoms of hypoglycemia in combination with a plasma glucose less than or equal to 70 mg/dL) occurred in 48 (43.6%) of 110 Saxenda®-treated patients and 12 (27.3%) of 52 placebo-treated patients. The doses of sulfonylureas were reduced by 50% at the beginning of the trial period. The frequency of hypoglycemia may be higher if the dose of sulfonylurea is not reduced. Among patients not taking a sulfonylurea, documented symptomatic hypoglycemia occurred in 49 (15.7%) of 312 Saxenda®-treated patients and 12 (7.6%) of 157 placebo-treated patients. In Saxenda® clinical trials involving patients without type 2 diabetes mellitus, there was no systematic capturing or reporting of hypoglycemia, as patients were not provided with blood glucose meters at enrollment or during the trial.

### References

- No references provided in the document.

### Acknowledgements

- No acknowledgements provided in the document.
Gastrointestinal Adverse Reactions

In the clinical trials, approximately 68% of Saxenda®-treated patients and 39% of placebo-treated patients reported gastrointestinal disorders, the most frequently reported was nausea (39% and 14% of patients treated with Saxenda® and placebo, respectively). The percentage of patients reporting nausea declined as treatment continued. Other common adverse reactions that occurred at a higher incidence among Saxenda®-treated patients included diarrhea, constipation, dyspepsia, flatulence, mouth, gastritis, gastroparesis, reflux disease, flatulence, eructation and abdominal distension. Most episodes of gastrointestinal events were mild or moderate and did not lead to discontinuation of therapy (0.2% with Saxenda® versus 0.8% with placebo discontinued treatment). Saxenda® had a result as a gastrointestinal adverse reaction.

There have been reports of gastrointestinal adverse reactions, such as nausea, vomiting, and diarrhea, associated with volume depletion and renal impairment (See Warnings and Precautions (5.6)).

Anemia
Fatigue, Malaise, Dysepsia and Dizziness

Events of anemia, fatigue, malaise, dysepsia and dizziness were mainly reported within the first 12 weeks of treatment with Saxenda® and were often co-reported with gastrointestinal events such as nausea, vomiting, and diarrhea.

Immunogenicity

Patients treated with Saxenda® may develop anti-liraglutide antibodies. Anti-liraglutide antibodies were detected in 42 (2.8%) of 1505 Saxenda®-treated patients with a baseline measurement. Antibodies that had a neutralizing effect on liraglutide in an in vitro assay occurred in 18 (1.2%) of 1505 Saxenda®-treated patients. Presence of antibodies may be associated with a higher incidence of injection site reactions and reports of low blood glucose. In clinical trials, there were four patients with antihuman insulin antibodies as defined as mild and resolved while patients continued on treatment.

The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, the incidence of antibodies to Saxenda® cannot be directly compared with the incidence of antibodies of other products.

Allergic Reactions

Urticaria was reported in 0.7% of Saxenda®-treated patients and 0.5% of placebo-treated patients. Anaphylactic reactions, asthma, bronchial hyperreactivity, bronchospasm, oropharyngeal swelling, facial swelling, angioedema, pharyngeal edema, type IV hypersensitivity reactions have been reported in patients treated with liraglutide in clinical trials. Cases of anaphylactic reactions with additional symptoms such as hypotension, palpitations, dyspnea, and edema have been reported with marketed use of liraglutide. Anaphylactic reactions may potentially be life-threatening.

Injection Site Reactions

Injection site reactions were reported in approximately 13.9% of Saxenda®-treated patients and 10.5% of placebo-treated patients. The most common reactions, each reported by 1% to 2.5% of Saxenda®-treated patients and more commonly than by placebo-treated patients, included erythema, pruritus, and rash at the injection site. 0.6% of Saxenda®-treated patients and 0.5% of placebo-treated patients discontinued treatment due to injection site reactions.

Breast Cancer

In Saxenda® clinical trials, breast cancer confirmed by adjudication was reported in 14 (0.6%) of 2379 Saxenda®-treated women compared with 3 (0.2%) of 1300 placebo-treated women, including invasive cancer (11 Saxenda® and 2 placebo-treated women) and ductal carcinoma in situ (3 Saxenda® and 1 placebo-treated woman). The majority of cancers were estrogen- and progesterone-receptor positive. There were too few cases to determine whether these cases were related to Saxenda®. In addition, there are insufficient data to determine whether Saxenda® has an effect on pre-existing breast neoplasia.

Papillary Thyroid Cancer

In Saxenda® clinical trials, papillary thyroid carcinoma confirmed by adjudication was reported in 7 (0.2%) of 3291 Saxenda®-treated patients compared with no cases among 1843 placebo-treated patients. Four of these papillary thyroid carcinomas were less than 1 cm in size and were detected in a surgical pathology specimens after thyroidecmy prompted by findings identified prior to treatment.

Colorectal Neoplasms

In Saxenda® clinical trials, benign colorectal neoplasms (mostly colon adenomas) confirmed by adjudication were reported in 17 (0.5%) of 3291 Saxenda®-treated patients compared with 4 (0.2%) of 1843 placebo-treated patients. Two positively adjudicated cases of malignant colorectal carcinoma were reported in Saxenda®-treated patients (0.1%) and none in placebo-treated patients.

Cardiac Conduction Disorders

In Saxenda® clinical trials, 11 (0.3%) of 3384 Saxenda®-treated patients compared with none of the 1941 placebo-treated patients had a cardiac conduction disorder, reported as first degree atrio-ventricular block, right bundle branch block, or left bundle branch block.

Hypotension

Adverse reactions related to hypotension (that is, reports of hypotension, orthostatic hypotension, circulatory collapse, and decrease of blood pressure) were reported more frequently in Saxenda® (11%) compared with placebo (0.5%) in Saxenda® clinical trials. Systolic blood pressure decreases to less than 80 mmHg were observed in 4 (0.1%) Saxenda®-treated patients compared with no placebo-treated patients. One of the Saxenda®-treated patients had hypotension associated with gastrointestinal adverse reactions and renal failure (See Warnings and Precautions (5.6)).

Laboratory Abnormalities

Liver Enzymes

Increases in alanine aminotransferase (ALT) greater than or equal to 10 times the upper limit of normal were observed in 5 (0.15%) Saxenda®-treated patients (two of whom had ALT greater than or equal to 20 times the upper limit of normal) from the group of 3291 Saxenda®-treated placebo-treated patient during the Saxenda® clinical trials. Because clinical evaluation to exclude alternative causes of ALT and aspartate aminotransferase (AST) increases was not done in most cases, relationship to Saxenda® is uncertain. Some increases in ALT and AST were associated with other confounding factors (such as gallstones).

Serum Calcitonin

Calcitonin, a biological marker of MTC, was measured throughout the clinical development program (See Warnings and Precautions (5.1)). More patients treated with Saxenda® in the clinical trials had anti-liraglutide antibodies (0.1%) compared with placebo (0.0%). Among patients with pre-treatment serum calcitonin less than 20 ng/L, none had calcitonin elevations to greater than 50 ng/L at the end of the trial.

Serum Lipase and Amylase

Serum lipase and amylase were routinely measured in the serum of the trial was 1.2% in Saxenda®-treated patients and 0.6% in placebo-treated patients. Calculin values greater than 20 ng/L at the end of the trial occurred in 0.5% of Saxenda®-treated patients and 0.2% of placebo-treated patients; among patients with pre-treatment serum calcitonin less than 20 ng/L, none had calcitonin elevations to greater than 50 ng/L at the end of the trial.

6.2 Postmarketing Experience

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

Neoplasms

Medullary thyroid carcinoma (See Warnings and Precautions (5.1)).

Gastrointestinal Disorders

Acute pancreatitis, hemorrhagic and necrotizing pancreatitis, sometimes resulting in death (See Warnings and Precautions (5.2)).

Metabolism and Nutrition Disorders

Dehydration resulting from nausea, vomiting and diarrhea (See Adverse Reactions (6.1)).

Renal and Urinary Disorders

Infections and infestations, acute renal failure or worsening of chronic renal failure, sometimes requiring hemodialysis (See Warnings and Precautions (5.6)).

General Disorders and Administration Site Conditions

Allergic reactions: rash and pruritus (See Adverse Reactions (6.1)).
compared to F₂ generation rats descended from controls, but differences did not reach statistical significance for any group.

8.3 Nursing Mothers
It is not known whether Saxenda® is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for tumorigenicity shown for liraglutide in animal studies, a decision should be made whether to discontinue nursing or to discontinue Saxenda®, taking into account the importance of the drug to the mother. In lactating rats, liraglutide was excreted unchanged in milk at concentrations approximately 50% of maternal plasma concentrations.

8.4 Pediatric Use
Safety and effectiveness of Saxenda® have not been established in pediatric patients. Saxenda® is not recommended for use in pediatric patients.

8.5 Geriatric Use
In the Saxenda® clinical trials, 232 (6.9%) of the Saxenda®-treated patients were 65 years of age and over, and 17 (0.5%) of the Saxenda®-treated patients were 75 years of age and over. No overall differences in safety or effectiveness were observed between these patients and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

8.6 Renal Impairment
There is limited experience with Saxenda® in patients with mild, moderate, and severe renal impairment, including end-stage renal disease. However, there have been postmarketing reports of acute renal failure and worsening of chronic renal failure with liraglutide, which may sometimes require hemodialysis (see Warnings and Precautions (5.6) and Adverse Reactions (6.2)). Saxenda® should be used with caution in this patient population (see Clinical Pharmacology (12.3)).

8.7 Hepatic Impairment
There is limited experience in patients with mild, moderate, or severe hepatic impairment. Therefore, Saxenda® should be used with caution in this patient population (see Clinical Pharmacology (12.3)).

8.8 Gastroprosopas Saxenda® shows gastric emptying. Saxenda® has not been studied in patients with pre-existing gastroparesis.

10 OVERDOSAGE
Overdoses have been reported in clinical trials and postmarketing use of liraglutide. Effects have included severe nausea and severe vomiting. In the event of overdosage, appropriate supportive treatment should be initiated according to the patient’s clinical signs and symptoms.

11 DESCRIPTION
Saxenda® contains liraglutide, an analog of human GLP-1 and acts as a GLP-1 receptor agonist. The peptide precursor of liraglutide, produced by a process that includes expression of recombinant DNA in Saccharomyces cerevisiae, has been engineered to be 97% homologous to native human GLP-1 by substituting arginine for lysine at position 34. Liraglutide is made by attaching a C-16 fatty acid (palmitic acid) with a glutamic acid spacer on the remaining lysine residue at position 26 of the precursor peptide. The molecular formula of liraglutide is C₁₉₇H₂₁₅N₄₀O₅₁ and the molecular weight is 3751.2 Daltons. The structural formula (Figure 1) is:

Figure 1. Structural Formula of Liraglutide
Saxenda® is a clear, colorless solution. Each 1 mL of Saxenda® solution contains 6 mg of liraglutide and the following inactive ingredients: disodium phosphate dihydrate, 142 mg; propylene glycol, 14 mg; phenol, 5.5 mg; and water for injection. Each pre-filled pen contains a 3 mL solution of Saxenda® equivalent to 18 mg liraglutide (free-base, anhydrous).

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action
Liraglutide is an acylated human glucagon-like peptide-1 (GLP-1) receptor agonist with 52 amino acid sequence homology to endogenous human GLP-1 (7-37). Like endogenous GLP-1, liraglutide binds to and activates the GLP-1 receptor, a cell-surface receptor coupled to adenylyl cyclase activation through the stimulatory G protein, GS. Endogenous GLP-1 has a half-life of 1.5-2 minutes due to degradation by the ubiquitous endogenous enzymes, dipeptidyl peptidase 4 (DPP-4) and neutral endopeptidases (NEP). Unlike native GLP-1, liraglutide is stable against metabolic degradation by both peptidases and has a plasma half-life of 12-13 hours following subcutaneous administration. The pharmacokinetic profile of liraglutide, which makes it suitable for once-daily administration, is a result of self-association that delays absorption, plasma protein binding, and stability against metabolic degradation by DPP-4 and NEP.

GLP-1 is a physiologically relevant regulator of appetite and calorie intake and the GLP-1 receptor is present in several areas of the brain involved in appetite regulation. In animal studies, peripheral administration of liraglutide resulted in the presence of liraglutide in specific brain regions regulating appetite, including the hypothalamus. Although liraglutide activated neurons in brain regions known to regulate appetite, specific brain regions mediating the effects of liraglutide on appetite were not identified in rats.

12.2 Pharmacodynamics
Liraglutide lowers body weight through decreased calorie intake. Liraglutide does not increase 24-hour energy expenditure.

As with other GLP-1 receptor agonists, liraglutide 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) in healthy volunteers
The effect of liraglutide on cardiac repolarization was tested in a QTc study. Liraglutide at steady-state concentrations after daily doses up to 1.8 mg did not produce QTc prolongation. The maximum liraglutide plasma concentration (Cmax) was observed in overweight and obese subjects treated with liraglutide 5 mg is similar to the Cmax observed in the liraglutide QTc study in healthy volunteers.

12.3 Pharmacokinetics
Absorption - Following subcutaneous administration, maximum concentrations of liraglutide are achieved at 11 hours post dosing. The average liraglutide steady state concentration (AUCτ) reached approximately 116 ng/mL in obese (BMI 30-40 kg/m²) subjects following administration of Saxenda®. Liraglutide exposure was dose proportionally in the dose range of 0.6 mg to 3 mg. The intra-subject coefficient of variation for liraglutide AUC was 11% following single dose administration. Liraglutide exposures were considered similar among three subcutaneous injection sites (upper arm, abdomen, and thigh). Absolute bioavailability of liraglutide following subcutaneous administration is approximately 55%.

Distribution - The mean apparent volume of distribution after subcutaneous administration of liraglutide 3 mg is 20-25 L (for a peak weight approx. 100 kg). The mean volume of distribution after intravenous administration of liraglutide is 0.07 L/kg. Liraglutide is extensively bound to plasma protein (greater than 98%).

Metabolism - During the initial 24 hours following administration of a single [3H]-liraglutide dose to healthy subjects, the major component in plasma was unchanged liraglutide. Liraglutide was extensively metabolized in a similar manner to large proteins without a specific organ as a major route of elimination.

Elimination - Following a [3H]-liraglutide dose, intact liraglutide was not detected in urine or feces. Only a minor part of the administered dose was excreted as liraglutide-related metabolites in urine or feces (6% and 5%, respectively). The majority of urine and feces radioactivity was excreted during the first 6-8 days. The mean apparent clearance following subcutaneous administration of a single dose of liraglutide is approximately 0.9-1.4 L/h with an elimination half-life of approximately 13 hours, making liraglutide suitable for once-daily administration.

Specific Populations
Elderly - No dosage adjustment is required based on age. Age had no effect on the pharmacokinetics of liraglutide based on a population pharmacokinetic study in elderly subjects (age 65-85 years) and population pharmacokinetic analyses of data from overweight and obese patients 18 to 82 years of age (see Use in Specific Populations (8.5)).

Gender - Based on the results of population pharmacokinetic analyses conducted in patients with body weight range of 60-234 kg. The exposure of liraglutide decreases as baseline body weight increases.

Pediatric - Saxenda® has not been studied in pediatric patients (see Use in Specific Populations (8.4)).

Renal Impairment - The single-dose pharmacokinetics of liraglutide were evaluated in subjects with varying degrees of renal impairment. Subjects with mild and moderate renal impairment and in end-stage renal disease was on average 35%, 19%, and 30% lower, respectively (see Use in Specific Populations (8.6)).

Hepatic Impairment - The single-dose pharmacokinetics of liraglutide were evaluated in subjects with varying degrees of hepatic impairment. Subjects with mild (Child Pugh score 5-6) to severe (Child Pugh score greater than 9) hepatic impairment were included in the trial. Compared to healthy subjects, liraglutide AUC in subjects with mild, moderate and severe hepatic impairment was on average 11%, 14% and 42% lower, respectively (see Use in Specific Populations (8.7)).

Drug Interactions
In vivo assessment of drug-drug interactions
Liraglutide has low potential for pharmacokinetic drug-drug interactions related to cytochrome P450 (CYP) and plasma protein binding.

In vivo assessment of drug-drug interactions
The drug-drug interaction studies were performed at steady state, with liraglutide administered 1-2 hours prior to concomitant medication. Each of the in vitro drug-drug interaction studies were performed at steady state.

Figure 2. Structural Formula of Liraglutide
Saxenda® (liraglutide) injection
A 104-week caringicinogenicity study was conducted in male and female CD-1 mice at doses of 0.03, 0.2, 1, and 3 mg/kg/day liraglutide administered by bolus subcutaneous injection yielding systemic exposures 0.2-, 2-, 10-, and 43-times the exposure in obese humans, respectively. The minimum recommended clinical dose (MRHD) of 3 mg/day based on plasma AUC comparison. A dose-related increase in benign thyroid C-cell adenomas was seen in the 1 and the 3 mg/kg/day groups with incidences of 13% and 19% in males and 6% and 25% in females, respectively. C-cell adenomas did not occur in similar study groups of 0.2 mg/kg/day or below. Treatment-related malignant C-cell carcinomas occurred in 3% of females in the 3 mg/kg/day group. Thyroid C-cell carcinomas are rare findings during carcinogenic testing in mice. A treatment-related increase in fibromas was seen on the dorsal skin and subcutis, the body surface used for drug injection, in males in the 3 mg/kg/day group. These fibrosarcomas were attributed to the local concentration of drug near the injection site. The liraglutide concentration in the clinical formulation (6 mg/mL) is 10-times higher than the concentration in the formulation used to administer 3 mg/kg/day liraglutide to mice in the carcinogenicity study (0.6 mg/mL).

A 104-week carcinogenicity study was conducted in male and female Sprague Dawley rats at doses of 0.075, 0.25, and 0.75 mg/kg/day liraglutide administered by bolus subcutaneous injection with exposures 0.5-, 2-, and 7-times the exposure in obese humans, respectively, resulting from the MRHD based on plasma AUC comparison. A treatment-related increase in benign thyroid C-cell adenomas was seen in males in the 0.25 and 0.75 mg/kg/day liraglutide groups with incidences of 12%, 16%, 20%, and 46% and in all female liraglutide-treated groups with incidences of 10%, 27%, 33%, and 56% in 0 (control), 0.075, 0.25, and 0.75 mg/kg/day groups, respectively. A treatment-related increase in malignant thyroid C-cell carcinomas was observed in all male liraglutide-treated groups with incidences of 2%, 8%, 6%, and 14% and in females at 0.25 and 0.75 mg/kg/day with incidences of 0%, 0%, 4%, and 6% in 0 (control), 0.075, 0.25, and 0.75 mg/kg/day groups, respectively. Thyroid C-cell carcinomas are rare findings during carcinogenic testing in rats.

Studies in mice demonstrated that liraglutide-induced C-cell proliferation was dependent on the GLP-1 receptor and that liraglutide did not cause activation of the RARα receptor during transcription (RET) proto- oncogene in thyroid C-cells. Human relevance of thyroid C-cell tumors in mice and rats is unknown and has not been determined by clinical studies or nonclinical studies (see Boxed Warning and Warnings and Precautions (5.1)). Liraglutide was negative with and without metabolic activation in the Ames test for mutagenicity and in a human peripheral blood lymphocyte chromosome aberration test for clastogenicity. Liraglutide was negative in repeat-dose in vivo micronucleus tests in rats.

In rat fertility studies using subcutaneous doses of 0.1, 0.25 and 1 mg/kg/day liraglutide, males were treated for 4 weeks prior to and throughout mating and females were treated 2 weeks prior to and throughout gestation until day 17. No direct adverse effects on male fertility was observed at doses up to 1 mg/kg/day, a high dose yielding an estimated systemic exposure 11-times the exposure in obese humans at the MRHD, based on plasma AUC comparison. In female rats, an increase in early embryonic deaths occurred at 1 mg/kg/day. Reduced body weight gain and food consumption were observed in females at the 1 mg/kg/day dose. In female Sprague Dawley rats at doses of 0.075, 0.25, and 0.75 mg/kg/day liraglutide administered by bolus subcutaneous injection with exposures 0.5-, 2- and 7-times the exposure in obese humans, respectively, resulting from the MRHD based on plasma AUC comparison. A dose-related increase in benign thyroid C-cell adenomas was seen in males in the 0.25 and 0.75 mg/kg/day liraglutide groups with incidences of 12%, 16%, 20%, and 46% and in all female liraglutide-treated groups with incidences of 10%, 27%, 33%, and 56% in 0 (control), 0.075, 0.25, and 0.75 mg/kg/day groups, respectively. A treatment-related increase in malignant thyroid C-cell carcinomas was observed in all male liraglutide-treated groups with incidences of 2%, 8%, 6%, and 14% and in females at 0.25 and 0.75 mg/kg/day with incidences of 0%, 0%, 4%, and 6% in 0 (control), 0.075, 0.25, and 0.75 mg/kg/day groups, respectively. Thyroid C-cell carcinomas are rare findings during carcinogenic testing in rats.

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The time courses of weight loss with Saxenda® and placebo from baseline through week 56 are depicted in Figures 3 and 4.

**Effect of Saxenda® on Anthropometry and Cardiometabolic Parameters**

Changes in waist circumference and cardiometabolic parameters with Saxenda® are shown in Table 5 for Study 1 (patients without diabetes mellitus) and Table 6 for Study 2 (patients with type 2 diabetes). Results from Study 3, which also enrolled patients without diabetes mellitus, were similar to Study 1.

### Table 5. Mean Changes in Anthropometry and Cardiometabolic Parameters in Study 1 (Patients without Diabetes)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Saxenda® Placebo</th>
<th>Saxenda® minus Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waist Circumference (cm)</td>
<td>Baseline</td>
<td>Change from Baseline</td>
</tr>
<tr>
<td></td>
<td>N = 2487</td>
<td>(LSMean)</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dL)*</td>
<td>193.8 +/- 3.2</td>
<td>Baseline</td>
</tr>
<tr>
<td>LDL Cholesterol (mg/dL)*</td>
<td>118.8 +/- 3.1</td>
<td>Baseline</td>
</tr>
<tr>
<td>HDL Cholesterol (mg/dL)*</td>
<td>51.4 +/- 2.3</td>
<td>Baseline</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)*</td>
<td>125.7 +/- 13.0</td>
<td>Baseline</td>
</tr>
</tbody>
</table>

### Table 6. Mean Changes in Anthropometry and Cardiometabolic Parameters in Study 2 (Patients with Diabetes Mellitus)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Saxenda® Placebo</th>
<th>Saxenda® minus Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waist Circumference (cm)</td>
<td>Baseline</td>
<td>Change from Baseline</td>
</tr>
<tr>
<td></td>
<td>N = 423</td>
<td>(LSMean)</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dL)*</td>
<td>171.0 +/- 1.4</td>
<td>Baseline</td>
</tr>
<tr>
<td>LDL Cholesterol (mg/dL)*</td>
<td>86.4 +/- 0.9</td>
<td>Baseline</td>
</tr>
<tr>
<td>HDL Cholesterol (mg/dL)*</td>
<td>45.2 +/- 4.8</td>
<td>Baseline</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)*</td>
<td>156.2 +/- 14.5</td>
<td>Baseline</td>
</tr>
</tbody>
</table>

### Risk of Thyroid C-cell Tumors

Long-term exposure to doses of Saxenda® that may cause hypoglycemia may increase the risk of cholelithiasis. Cholelithiasis may also occur in the absence of substantial or rapid weight loss. Patients should be instructed to contact their physician if cholelithiasis is suspected.

### Acute Pancreatitis

Patients should be informed of the potential risk for acute pancreatitis. Explain that persistent severe abdominal pain that may radiate to the back and which may or may not be accompanied by vomiting, is the hallmark symptom of acute pancreatitis. Instruct patients to discontinue Saxenda® promptly and contact their physician if persistent severe abdominal pain occurs.

### Acute Gallbladder Disease

Patients should be informed that substantial or rapid weight loss can increase the risk of cholelithiasis. Cholelithiasis may also occur in the absence of substantial or rapid weight loss. Patients should be instructed to contact their physician if cholelithiasis is suspected for appropriate clinical follow-up.

### Hypoglycemia in Patients with Type 2 Diabetes Mellitus on Anti-Diabetic Therapy

Patients with type 2 diabetes mellitus on anti-diabetic therapy should be advised to monitor their blood glucose levels and report symptoms of hypoglycemia to their physician.

### Heart Rate Increase

Patients should be informed to report symptoms of sustained periods of heart pounding or racing while at rest to their physician. For patients who experience a sustained increase in resting heart rate after taking Saxenda®, Saxenda® should be discontinued.

### Dehydration and Renal Impairment

Patients treated with Saxenda® should be advised of the potential risk of dehydration due to gastrointestinal adverse reactions and take precautions to avoid fluid depletion. Patients should be informed of the potential risk for worsening renal function, which in some cases may require dialysis.
Hypersensitivity Reactions
Patients should be informed that serious hypersensitivity reactions have been reported during use of liraglutide. If symptoms of hypersensitivity reactions occur, patients must stop taking Saxenda® and seek medical advice promptly.

Suicidal Behavior and Ideation
Patients treated with Saxenda® should be advised to report emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior. Patients should be informed that if they experience suicidal thoughts or behaviors, Saxenda® should be discontinued.

Jaundice and Hepatitis
Inform patients that jaundice and hepatitis have been reported during postmarketing use of liraglutide. Instruct patients to contact their physician if they develop jaundice.

Never Share a Saxenda® Pen Between Patients
Patients should be informed that they should never share a Saxenda® pen with another person, even if the needle is changed. Sharing of the pen between patients may pose a risk of transmission of infection.
What is the most important information I should know about Saxenda®?

Serious side effects may happen in people who take Saxenda®, 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 rats and mice, Saxenda® and medicines that work like Saxenda® caused thyroid tumors, including thyroid cancer. It is not known if Saxenda® will cause thyroid tumors or a type of thyroid cancer called medullary thyroid carcinoma (MTC) in people.

Do not use Saxenda® 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 Saxenda®?

Saxenda® is an injectable prescription medicine that may help some obese or overweight adults who also have weight related medical problems lose weight and keep the weight off.

- Saxenda® should be used with a reduced calorie diet and increased physical activity.
- Saxenda® is not for the treatment of type 2 diabetes mellitus.
- Saxenda® and Victoza® have the same active ingredient, liraglutide.
- Saxenda® and Victoza® should not be used together.
- Saxenda® should not be used with other GLP-1 receptor agonist medicines.
- Saxenda® and insulin should not be used together.
- It is not known if Saxenda® is safe and effective when taken with other prescription, over-the-counter, or herbal weight loss products.
- It is not known if Saxenda® changes your risk of heart problems or stroke or of death due to heart problems or stroke.
- It is not known if Saxenda® can be used safely in people who have had pancreatitis.
- It is not known if Saxenda® is safe and effective in children under 18 years of age. Saxenda® is not recommended for use in children.

Who should not use Saxenda®?

Do not use Saxenda® if:

- you or any of your family have a history of medullary thyroid carcinoma.
- you have Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). This is a disease where people have tumors in more than one gland in their body.
- you are allergic to liraglutide or any of the ingredients in Saxenda®. See the end of this Medication Guide for a list of ingredients in Saxenda®.
- Symptoms of a serious allergic reaction may include:
  - swelling of your face, lips, tongue, or throat
  - problems breathing or swallowing
  - fainting or feeling dizzy
  - very rapid heartbeat
  - severe rash or itching
  - symptoms such as a bottle, you must follow the "Check the Saxenda® flow with each new pen" (see the detailed Patient Instructions for Use that comes with this Medication Guide).

Talk with your healthcare provider if you are not sure if you have any of these conditions.
- are pregnant or planning to become pregnant. Saxenda® may harm your unborn baby.

Before taking Saxenda®, tell your healthcare provider about all of your medical conditions, including if you:

- have any of the conditions listed in the section “What is the most important information I should know about Saxenda®?”
- are taking certain medications called GLP-1 receptor agonists.
- are allergic to liraglutide or any of the other ingredients in Saxenda®. See the end of this Medication Guide for a list of ingredients in Saxenda®.
- have severe problems with your stomach, such as slowed emptying of your stomach (gastroparesis) or problems with digesting food.
- have or have had problems with your pancreas, kidneys or liver.
- have or have had depression or suicidal thoughts.
- are pregnant or plan to become pregnant. Saxenda® may harm your unborn baby. Talk to your healthcare provider if you become pregnant while taking Saxenda®. If you are pregnant you should stop using Saxenda®.
- are breastfeeding or plan to breastfeed. It is not known if Saxenda® passes into your breast milk. You and your healthcare provider should decide if you will take Saxenda® or breastfeed. You should not do both without talking with your healthcare provider first.

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

How should I use Saxenda®?

- Use Saxenda® exactly as prescribed by your healthcare provider. Your dose should be increased after using Saxenda® for 1 week until you reach the 3 mg dose. After that, do not change your dose unless your healthcare provider tells you to.
- Saxenda® is injected 1 time each day, at any time during the day.
- You can take Saxenda® with or without food.
- Your healthcare provider should start you on a diet and exercise program when you start taking Saxenda®. Stay on this program while you are taking Saxenda®.
- Saxenda® comes in a prefilled pen.
- Your healthcare provider must teach you how to inject Saxenda® before you use it for the first time. If you have questions or do not understand the instructions, talk to your healthcare provider or pharmacist. Read the Patient Instructions for Use that come with this Medication Guide for detailed information about the right way to use your Saxenda® pen.
- Pen needles are not included. Use the Saxenda® pen with Novo Nordisk disposable needles. You may need a prescription to get pen needles from your pharmacist. Ask your healthcare provider which needle size is best for you.
- When starting a new prefilled Saxenda® pen, you must follow the “Check the Saxenda® flow with each new pen” (see the detailed Patient Instructions for Use that comes with this Medication Guide). You only need to do this 1 time with each new pen. You should also do this if you drop your pen. If you do the “Check the Saxenda® flow with each new pen” before each injection, you will run out of medicine too soon.
- Inject your dose of Saxenda® under the skin (subcutaneous injection) in your stomach area (abdomen), upper leg (thigh), or upper arm, as instructed by your healthcare provider. Do not inject into a vein or muscle.
- If you take too much Saxenda®, call your healthcare provider right away. Too much Saxenda® may cause severe nausea and vomiting.
- If you miss your daily dose of Saxenda®, use Saxenda® as soon as you remember. Then take your next daily dose as usual on the following day. Do not take an extra dose of Saxenda® or increase your dose on the following day to make up for your missed dose. If you miss your dose of Saxenda® for 3 days or more, call your healthcare provider to talk about how to restart your treatment.
- Never share your Saxenda® pen or needles with another person. You may give an infection to them, or get an infection from them.
What are the possible side effects of Saxenda®?

- Saxenda® may cause serious side effects, including: possible thyroid tumors, including cancer. See "What is the most important information I should know about Saxenda®?"
- Inflammation of the pancreas (pancreatitis). Stop using Saxenda® 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. Saxenda® 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 your skin or eyes (jaundice)
  - fever
  - clay-colored stools
- Low blood sugar (hypoglycemia) in people with type 2 diabetes mellitus who also take medicines to treat type 2 diabetes mellitus. Saxenda® can cause low blood sugar in people with type 2 diabetes mellitus who also take medicines used to treat type 2 diabetes mellitus (such as sulfonylureas). In some people, the blood sugar may get so low that they need another person to help them. If you take a sulfonylurea medicine, the dose may need to be lowered while you use Saxenda®. Signs and symptoms of low blood sugar may include:
  - shakiness
  - sweating
  - headache
  - dizziness
  - confusion
  - irritability

Nausea is most common when first starting Saxenda®, but decreases over time in most people as their body gets used to the medicine. Nausea is most common when first starting Saxenda®, but decreases over time in most people as their body gets used to the medicine.

Tell your healthcare provider about how to recognize and treat low blood sugar. Make sure that your family and other people who are around you a lot know how to recognize and treat low blood sugar. You should check your blood sugar before you start taking Saxenda® and while you take Saxenda®.

- Increased heart rate. Saxenda® can increase your heart rate while you are at rest. Your healthcare provider should check your heart rate while you take Saxenda®. Tell your healthcare provider if you feel your heart racing or pounding in your chest and it lasts for several minutes when taking Saxenda®.
- Kidney problems (kidney failure). Saxenda® may cause nausea, vomiting or diarrhea leading to loss of fluids (dehydration). Dehydration may cause kidney failure which can lead to the need for dialysis. This can happen in people who have never had kidney problems before. Drinking plenty of fluids may reduce your chance of dehydration.

Call your healthcare provider right away if you have nausea, vomiting, or diarrhea that does not go away, or if you cannot drink liquids by mouth.

- Serious allergic reactions. Serious allergic reactions can happen with Saxenda®. Stop using Saxenda®, and get medical help right away if you have any symptoms of a serious allergic reaction. See "Who should not use Saxenda®?"

- 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 Saxenda® include:

- Nausea
- Headache
- Constipation
- Low blood sugar (hypoglycemia)
- Decreased appetite
- Upset stomach
- Stomach pain
- Change in enzyme (lipase) levels in your blood

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of Saxenda®. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

Keep your Saxenda® pen, pen needles, and all medicines out of the reach of children.

General information about the safe and effective use of Saxenda®.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use Saxenda® for a condition for which it was not prescribed. Do not give Saxenda® 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 Saxenda® that is written for health professionals.

What are the ingredients in Saxenda®?

Active ingredient: liraglutide

Inactive ingredients: disodium phosphate dihydrate, propylene glycol, phenol and water for injection

For more information, go to saxenda.com or call 1-844-363-4448.

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

For information about Saxenda®, contact: Novo Nordisk Inc. 800 Scudders Mill Road, Plainsboro, NJ 08536 1-844-363-4448

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

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Instructions for Use

- Read these instructions carefully before using your Saxenda® pen.
- Do not use your pen without proper training from your healthcare provider. Make sure that you know how to give yourself an injection with the pen before you start your treatment.
- If you are blind or have poor eyesight and cannot read the dose counter on the pen, do not use this pen without help. Get help from a person with good eyesight who is trained to use the Saxenda® pen.
- You can refresh your training at any time by watching the online training video at www.saxenda.com.
- Start by checking your pen to make sure that it contains Saxenda®, then look at the pictures below to get to know the different parts of your pen and needle.

Your pen is a prefilled dial-a-dose pen. It contains 18 mg of liraglutide, and you can select doses of 0.6 mg, 1.2 mg, 1.8 mg, 2.4 mg and 3 mg. Your pen is made to be used with NovoFine® or NovoTwist® disposable needles up to a length of 8 mm.

### Saxenda® pen and needle (example)

1. **Step 1. Prepare your pen with a new needle**
   - Wash your hands with soap and water.
   - Check the name and colored label of your pen, to make sure that it contains Saxenda®. This is especially important if you take more than 1 type of medicine.
   - Pull off the pen cap.
   - Check that Saxenda® in your pen is clear and colorless. Look through the pen window. If Saxenda® looks cloudy, do not use the pen.
   - Take a new needle, and tear off the paper tab.

2. **Step 2. Check the Saxenda® flow with each new pen.**
   - Check the Saxenda® flow before your first injection with each new pen. If your Saxenda® pen is already in use, go to Step 3 “Select your dose”.
   - Turn the dose selector until the dose counter shows the flow check symbol (----).
   - Hold the pen with the needle pointing up. Press and hold in the dose button until the dose counter shows 0. The 0 must line up with the dose pointer. A drop of Saxenda® will appear at the needle tip.
   - If no drop appears, repeat Step 2 as shown in Figures G and H up to 6 times. If there is still no drop, change the needle and repeat Step 2 as shown in Figures G and H 1 more time.
   - Do not use the pen if a drop of Saxenda® does not appear.

3. **Step 3. Select your dose**
   - Turn the dose selector until the dose counter shows your dose (0.6 mg, 1.2 mg, 1.8 mg, 2.4 mg or 3 mg). Make sure you know the dose of Saxenda® you should use. If you select the wrong dose, you can turn the dose selector forward or backwards to the correct dose.
   - Always use the dose counter and the dose pointer to see how many mg you select.
   - Do not set the dose by counting the number of clicks you hear.
   - Do not use the pen scale to set the dose. It does not show exactly how much Saxenda® is left in your pen.
   - Only doses of 0.6 mg, 1.2 mg, 1.8 mg, 2.4 mg or 3 mg can be selected with the dose selector. The selected dose must line up exactly with the dose pointer to make sure that you get a correct dose.
   - The dose selector changes the dose. Only the dose counter and dose pointer will show how many mg you select for each dose. You can select up to 3 mg each dose. When your pen contains less than 3 mg the dose counter stops before 3 mg is shown.
   - The dose selector clicks differently when turned forward, backwards or past the number of mg left. Do not count the pen clicks.

4. **Step 4. Inject your dose**
   - Insert the needle into your skin as your healthcare provider has shown you.
   - Make sure you can see the dose counter. Do not cover it with your fingers. This could stop the injection.

Always make sure that a drop appears at the needle tip before you use a new pen for the first time. This makes sure that Saxenda® flows. If no drop appears, you will not inject any Saxenda®, even though the dose counter may move. This may mean that there is a blocked or damaged needle.

A small drop may remain at the needle tip, but it will not be injected. Only check the Saxenda® flow before your first injection with each new pen.

### Check the name and colored label of your pen

- **Pen scale**
- **Pen window**
- **Dose counter**
- **Dose selector**

- **NovoFine®**
  - **Outer needle cap**
  - **Inner needle cap**
  - **Needle**
  - **Paper tab**

- **NovoTwist®**
  - **Outer needle cap**
  - **Inner needle cap**
  - **Needle**
  - **Paper tab**

**Flow check symbol**

Example: 0.6 mg selected

Example: Approx. 3 mg left

Example: Dose counter stopped: 2.4 mg left

Example: Dose counter stopped: 0 mg left
• Press and hold down the dose button until the dose counter shows 0. The 0 must line up with the dose pointer. You may then hear or feel a click.

• Keep the needle in your skin after the dose counter has returned to 0 and count slowly to 6.

• If the needle is removed earlier, you may see a stream of Saxenda® coming from the needle tip. If this happens, the full dose will not be delivered.

• Remove the needle from your skin. If blood appears at the injection site, press lightly. Do not rub the area.

• Put the pen cap on your pen after each use to protect Saxenda® from light.

• Keep the needle in a sharps container as soon as possible.

• Never try to put the inner needle cap back on the needle. You may stick yourself with the needle.

Always remove the needle from your pen. This prevents contamination, infection, leakage of Saxenda®, and blocked needles leading to the wrong dose. If the needle is blocked, you will not inject any Saxenda®.

Always dispose of the needle after each injection.

• Do not throw away in the household trash. Put the needle and any empty Saxenda® pen or any pen used for 30 days still containing Saxenda® in a FDA-cleared sharps disposal container right away after use.

• If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:
  - made of a heavy-duty plastic
  - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out upright and stable during use
  - leak-resistant
  - 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 the safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA’s website at: http://www.fda.gov/safesharpsdisposal

Do not dispose of your used sharps disposal container in your household trash unless your community guidelines permit this. Do not recycle your used sharps disposal container.

Safely dispose of Saxenda® that is out of date or no longer needed.

How to handle a blocked needle?

Change the needle as described in Step 5, and repeat all steps starting with Step 1. “Prepare your pen with a new needle”. Make sure you select the full dose you need.

Never touch the dose counter when you inject. This can stop the injection.

If you do not have a sharps container, follow a 1-handed needle recapping method. Carefully slip the needle into the outer needle cap. Dispose of the needle in a sharps container as soon as possible.

Important

• Caregivers must be very careful when handling used needles to prevent needle sticks and cross infection.

• Never use a syringe to withdraw Saxenda® from your pen.

• Always carry an extra pen and new needles with you, in case of loss or damage.

• Always keep your pen and needles out of reach of others, especially children.

• Do not share your Saxenda® pen or needles with anyone else. You may give an infection to them or get an infection from them.

• Always keep your pen with you. Do not leave it in a car or other place where it can get too hot or too cold.

Caring for your pen

• Do not drop your pen or knock it against hard surfaces. If you drop it or suspect a problem, attach a new needle and check the Saxenda® flow before you inject.

• Do not try to repair your pen or pull it apart.

• Do not expose your pen to dust, dirt or liquid.

• Do not wash, soak, or lubricate your pen. If necessary, clean it with mild detergent on a moistened cloth.

How should I store my Saxenda® pen?

• Store your new, unused Saxenda® pens in the refrigerator at 36°F to 46°F (2°C to 8°C).

• Store your pen in use for 30 days at 59°F to 86°F (15°C to 30°C) or in a refrigerator at 36°F to 46°F (2°C to 8°C).

• The Saxenda® pen you are using should be thrown away after 30 days, even if it still has Saxenda® left in it.

• Do not freeze Saxenda®. Do not use Saxenda® if it has been frozen.

• Unused Saxenda® pens may be used until the expiration date printed on the label, if kept in the refrigerator.

• Keep Saxenda® away from heat and out of the light.