**Warning: Risk of Thyroid C-cell Tumors**

Saxenda® (liraglutide) 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)
- 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).

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**Recent Major Changes**

Indications and Usage, Limitations of Use (1)..................10/2018

**Indications and Usage**

Saxenda® is a 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)
- 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).

**Contraindications**

- Hypersensitivity to liraglutide or any product components
- Personal or family history of medullary thyroid carcinoma 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).

**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%: anemia, nausea, hypoglycemia, diarrhea, constipation, vomiting, headache, decreased appetite, dyspepsia, fatigue, diziness, abdominal pain, and increased lipase (6.1).

**Use in Speciﬁc Populations**

- Pediatric Use: Safety and effectiveness not established and use not recommended (8.4).

See 17 for Patient Counseling Information and Medication Guide.

Revised: 10/2018

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**Prescribing Information: Contents**

1 Indications and Usage
2 Dosage and Administration
3 Dosage Forms and Strengths
4 Contraindications
5 Warnings and Precautions
6 Adverse Reactions
7 Drug Interactions
8 Use in Speciﬁc Populations
9 Overdosage
10 Description
11 Clinical Pharmacology
12 Nonclinical Toxicology
13 Clinical Studies
14 How Supplied/Storage and Handling
15 Patient Counseling Information

*Sections or subsections omitted from the full prescribing information are not listed.*
**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 ultrasonography is of uncertain value for early detection of MTC in patients treated with Saxenda® [see Contraindications (4), Warnings and Precautions (5.1)].

**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).

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>

**Limitations of Use**

- Saxenda® is not indicated for the treatment of type 2 diabetes mellitus.
- Saxenda® and Victoza® both contain the same active ingredient, liraglutide, and therefore should not be used together. Saxenda® should not be used in combination with any other GLP-1 receptor agonist.
- Saxenda® has not been studied in patients taking insulin. Saxenda® and insulin should not be used together [see Warnings and Precautions (5.4)].
- The safety and effectiveness of Saxenda® in combination with other products intended for weight loss, including prescription drugs, over-the-counter drugs, and herbal preparations, have not been established.

**DOSAGE AND ADMINISTRATION**

The solution should be used only if it is clear, colorless, and contains no particles. BMI is calculated by dividing weight in (kilograms) by height (in meters) squared. A chart for determining BMI based on height and weight is provided in Table 2.

### Table 2. BMI Conversion Chart

<table>
<thead>
<tr>
<th>Height (in)</th>
<th>Weight (lb)</th>
<th>BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>58</td>
<td>147.3</td>
<td>30.1</td>
</tr>
<tr>
<td>59</td>
<td>149.9</td>
<td>31.2</td>
</tr>
<tr>
<td>60</td>
<td>152.4</td>
<td>32.3</td>
</tr>
<tr>
<td>61</td>
<td>154.9</td>
<td>33.4</td>
</tr>
<tr>
<td>62</td>
<td>157.5</td>
<td>34.5</td>
</tr>
<tr>
<td>63</td>
<td>160.0</td>
<td>35.6</td>
</tr>
<tr>
<td>64</td>
<td>162.6</td>
<td>36.7</td>
</tr>
<tr>
<td>65</td>
<td>165.1</td>
<td>37.8</td>
</tr>
<tr>
<td>66</td>
<td>167.6</td>
<td>38.9</td>
</tr>
<tr>
<td>67</td>
<td>170.2</td>
<td>39.0</td>
</tr>
<tr>
<td>68</td>
<td>172.7</td>
<td>40.1</td>
</tr>
<tr>
<td>69</td>
<td>175.3</td>
<td>41.2</td>
</tr>
<tr>
<td>70</td>
<td>177.8</td>
<td>42.3</td>
</tr>
<tr>
<td>71</td>
<td>180.3</td>
<td>43.4</td>
</tr>
<tr>
<td>72</td>
<td>182.9</td>
<td>44.5</td>
</tr>
<tr>
<td>73</td>
<td>185.4</td>
<td>45.6</td>
</tr>
<tr>
<td>74</td>
<td>188.0</td>
<td>46.7</td>
</tr>
<tr>
<td>75</td>
<td>190.5</td>
<td>47.8</td>
</tr>
<tr>
<td>76</td>
<td>193.0</td>
<td>48.9</td>
</tr>
</tbody>
</table>

### 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-Cells 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 ultrasonography 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/L. If serum calcitonin is measured and found to be elevated, the patient should be further evaluated. Patients with thyroid nodules noted on physical examination or neck imaging should also be further evaluated.

#### 5.2 Acute Pancreatitis

Based on postmarketing 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 3291 Saxenda®-treated patients and 2 (0.1%) of 1843 placebo-treated patients. In addition, there were 2 cases of acute pancreatitis in Saxenda®-treated patients who prematurely withdrew from these clinical trials, occurring 74 and 124 days after the last dose. There were 2 additional cases in Saxenda®-treated patients, 1 during an off-treatment follow-up period within 2 weeks of discontinuing Saxenda®, and 1 that occurred in a patient who completed treatment and was subsequently evaluated for pancreatitis. Liraglutide has been studied in a limited number of 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 Saxenda®.

5.3 Acute Gallbladder Disease
In Saxenda® clinical trials, 2.2% of Saxenda®-treated patients reported adverse events of cholelithiasis versus 0.8% of placebo-treated patients. The majority of Saxenda®-treated patients with adverse events of cholelithiasis consulted a healthcare provider for this condition (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 12% of patients treated with Saxenda® had an increase in resting heart rate exceeding 100 bpm while at resting during treatment. Substantial or rapid weight loss can increase the risk of cholelithiasis; however, the incidence of acute gallbladder 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 indicated.

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 anti-diabetic drugs) 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.

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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 (2.3% versus 0.2% for Saxenda® and placebo, respectively), vomiting (1.7% versus 0.7% for Saxenda® and placebo, respectively), and abdominal distension. Other common adverse reactions that occurred at a higher incidence among 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>Condition</th>
<th>Saxenda® N=3384</th>
<th>Placebo N=1841</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gastrointestinal Disorders</strong></td>
<td></td>
<td></td>
</tr>
<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>

### Metabolism and Nutrition Disorders

- **Hypoglycemia in T2DM**
  - 12.7
  - 23.0
- **Decreased Appetite**
  - 2.3
  - 10.0

### Nervous System Disorders

- **Headache**
  - 12.8
  - 13.6
- **Dizziness**
  - 5.0
  - 6.9

### General Disorders and Administration Site Conditions

- **Fatigue**
  - 4.8
  - 7.5
- **Inject Site Erythema**
  - 0.2
  - 2.5
- **Inject Site Reaction**
  - 0.6
  - 2.5
- **Asthma**
  - 0.8
  - 2.1

### Infections and Infestations

- **Gastroenteritis**
  - 3.2
  - 4.7
- **Urinary Tract Infection**
  - 3.1
  - 4.3
- **Viral Gastroenteritis**
  - 1.6
  - 2.8

### Investigations

- **Increased Lipase**
  - 2.2
  - 5.3

### Psychiatric Disorders

- **Insomnia**
  - 1.7
  - 2.4
- **Anxiety**
  - 1.6
  - 2.0

### Adverse Reactions

- Documented hypoglycemia (defined as documented symptoms consistent with hypoglycemia in combination with a plasma glucose level less than or equal to 70 mg/dL) occurred in 48 (43.6%) of 110 Saxenda®-treated patients and 15 (27.3%) of 55 placebo-treated patients. The doses of sulfonylureas were reduced by 50% at the beginning of the trial per protocol. The frequency of hypoglycemia may be higher if the dose of sulfonylurea is not reduced. Among patients not 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 15 (27.3%) of 55 placebo-treated patients. 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 or hypoglycemia diaries. Spontaneously reported symptomatic episodes of unconfirmed hypoglycemia were reported by 46 (1.6%) of 2962 Saxenda®-treated patients and 19 (1.1%) of 1729 placebo-treated patients. Fasting plasma glucose values obtained at routine clinical visits less than or equal to 70 mg/dL, irrespective of hypoglycemic symptoms, were reported as “hypoglycemia” in 92 (3.1%) Saxenda®-treated patients and 13 (0.8%) placebo-treated patients.

### Gastrointestinal Adverse Reactions

In the clinical trials, approximately 68% of Saxenda®-treated patients and 41% of placebo-treated patients reported gastrointestinal side effects (see Adverse Reactions (6.3)). The most commonly reported gastrointestinal side effects were nausea and diarrhea, associated with weight loss and increased adipose tissue (see Warnings and Precautions (5.6)).
Clinical trials, benign colorectal neoplasms (mostly treated patients compared with 7 clinical trials. Because is contraindicated during pregnancy because weight increased mortality. There are no cases of malignancy, which may develop anti-liraglutide therapy with Saxenda® (0.3%) compared with placebo (0.5%) in Saxenda®-treated patients. 0.6% in placebo-treated patients (two of whom had ALT greater than 20 U/L). In placebo-treated patients, 2.1% had a lipase elevation greater than or equal to 2 times the upper limit of normal at the end of the treatment. The clinical significance of these lipase elevations is unknown in the absence of other signs and symptoms of pancreatitis. see Warnings and Precautions 5.2).

6.2 Post-Marketing Experience
The following adverse reactions have been reported during post-approval 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
Increased serum creatinine, acute renal failure or worsening of chronic renal failure [see Warnings and Precautions 5.6]
General Disorders and Administration Site Conditions
Allergic reactions: rash and pruritus [see Adverse Reactions 6.1]
Immune System Disorders
Angioedema and anaphylactic reactions [see Warnings and Precautions 5.7]
Hepatobiliary Disorders
Elevated transaminases, hypertriglyceridemia, cholestasis and hepatitis [see Adverse Reactions 6.1]

7 DRUG INTERACTIONS
7.1 Oral Medications
Saxenda® causes a delay of gastric emptying, and thereby has the potential to impact the absorption of concomitantly administered oral medications. In clinical pharmacology trials, liraglutide did not affect pharmacokinetics and pharmacodynamics of oral medications, including insulin, oral hypoglycemic agents, and oral contraceptives. However, withdrawal of patients with the active ingredient of Saxenda® was not evaluated. In patients with type 2 diabetes who received Saxenda®-treated patients compared with 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-related reactions.

In an intramuscular toxicology study in beagle dogs, predicted maximum achieved plasma concentrations of liraglutide were within the range of those expected in humans. The safety and efficacy of liraglutide were demonstrated in clinical trials in patients with type 2 diabetes, including patients with clinical trial evidence of angioedema and anaphylaxis in clinical trials. saxenda®-treated patients had hypoglycemia associated with gastrointestinal adverse reactions and renal failure [see Warnings and Precautions 5.6].

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
Risk Summary
Saxenda® is contraindicated during pregnancy because weight loss offers no potential benefit to a pregnant woman and may result in fetal harm [see Clinical Considerations]. There are no available data with liraglutide in pregnant women to inform a drug substance exposure in utero. The woman should not be used during pregnancy. If a patient wishes to become pregnant, or pregnancy occurs, treatment with Saxenda® should be discontinued.

Animal reproduction studies using increased adverse embryo-fetal developmental outcomes from exposure during pregnancy.

Saxenda® (liraglutide) injection

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 post-baseline assessment. Antibodies that had a neutralizing effect on liraglutide were in an in vitro assay 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, these events were usually classified 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, comparison of incidence rates among product candidates or across indications is complicated and may not be possible.

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, oral/nasal swelling, facial swelling, angioedema, pharyngeal edema, type IV hypersensitivity reactions have been reported in patients treated with liraglutide in clinical trials. Cases of anaphylaxis 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-related reactions.
Safety and effectiveness of Saxenda® have not been established in pediatric patients. Saxenda® is not recommended for use in pediatric patients.

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.

There is limited exposure with Saxenda® in patients with mild, moderate, and severe renal impairment, including end-stage renal disease. However, there have been no pharmacokinetic studies conducted in patients with 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)].

Saxenda® is a clear, colorless solution. Each 1 mL of Saxenda® is not recommended for use in patients with severe renal impairment by 12% and 13%, respectively. There was no difference in AUC between severe and end-stage renal disease was on average 35%, 19%, 29% and 30% lower, respectively. Similar differences in safety or effectiveness were observed between these 65 to 83 years) and population pharmacokinetic analyses of data from overweight and obese patients of a single dose of liraglutide is approximately 0.9-1.4 L/h with an mean apparent clearance following subcutaneous administration of liraglutide related to cytochrome P450 and plasma protein binding and stability against metabolic degradation by DPP-4 and NEP.

Liraglutide is an acylated human glucagon-like peptide-1 (GLP-1) receptor agonist with a molecular weight of 3752.1 Daltons. The structural formula (Figure 1) is:

**12.2 Pharmacodynamics**

Liraglutide lowers body weight through decreased calorie intake. 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 of 1.8 mg/kg/day liraglutide did not produce QTC prolongation. The maximum plasma liraglutide concentration (Cmax) in overweight and obese subjects treated with liraglutide 3 mg is similar to the Cmax observed in the liraglutide QTC study in healthy volunteers.

Liraglutide is a physiological regulator of appetite and calorie intake, and endogenous GLP-1 has a half-life of approximately 1-2 minutes. It is rapidly inactivated by DPP-4 and NEP.

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

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

Distribution - The mean apparent volume of distribution after subcutaneous administration of liraglutide 3 mg is 20-25 L (for a person weighing approximately 100 kg). The mean volume of distribution of liraglutide was approximately 1.3 L/kg in overweight and obese patients.

Absorption - Liraglutide is rapidly absorbed following subcutaneous injection yielding peak plasma concentrations within 0.5-1.5 hours.

Drugs that inhibit DPP-4 may interfere with the metabolism of liraglutide and increase its exposure. The drug-drug interaction studies were performed at steady state. Atorvastatin Cmax of liraglutide at steady state. Liraglutide lowered ethinylestradiol and levonorgestrel Cmax by 12% and 13%, respectively. There was no effect of liraglutide on the overall exposure (AUC) of ethinylestradiol. Liraglutide increased the levonorgestrel Cmax by 18%.

Liraglutide delayed Tmax, for both ethinylestradiol and levonorgestrel by 1.5 h.

Digoxin A single dose of digoxin 1 mg was administered 7 hours after the dose of liraglutide at steady state. The concomitant administration of liraglutide resulted in a reduction of liraglutide AUC by 16%; Cmax decreased by 31%. Digoxin median time to maximal concentration (Tmax) was delayed from 1 h to 1.5 h.

Levonorgestrel A single dose of levonorgestrel 20 mg was administered 5 minutes after the dose of liraglutide at steady state. Levonorgestrel Cmax was decreased by 38% and median Tmax was delayed from 1 h to 3 h with liraglutide.

Acetaminophen Liraglutide did not change the overall exposure (AUC) of acetaminophen following a single dose of acetaminophen 1000 mg, administered 8 hours after the dose of liraglutide at steady state. Acetaminophen Cmax was decreased by 31% and median Tmax was delayed up to 15 minutes.

Glucagon Liraglutide did not change the overall exposure (AUC) of glucagon following co-administration of a single dose of glucagon 500 mg with liraglutide at steady state. Glucagon Cmax increased by 37% while median Tmax did not change.

Insulin Liraglutide No pharmacokinetic interaction was observed between liraglutide and insulin determin when separate subcutaneous injections of insulin detemir 0.5 Unit/kg (single-dose) and liraglutide 1.8 mg (steady state) were administered to patients with type 2 diabetes mellitus.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

A 104-week carcinogenicity 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, at the maximum recommended human 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 3 mg/kg/day group and in females in the 3 mg/kg/day group. Thyroid C-cell tumors are rare findings during carcinogenicity testing in mice. A treatment-related increase in fibrosarcomas 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 carcinogenic properties of liraglutide. Injection site is 13% in males and 16% and 20% in females, respectively. C-cell adenomas did not occur in control groups or 0.03 and 0.2 mg/kg/day groups. Treatment-related malignant C-cell carcinomas were seen only in females in the 3 mg/kg/day group. Thyroid C-cell tumors are rare findings during carcinogenicity testing in mice. A treatment-related increase in fibrosarcomas 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 carcinogenic properties of liraglutide. Injection site is 13% in males and 16% and 20% in females, respectively. C-cell adenomas did not occur in control groups or 0.03 and 0.2 mg/kg/day groups. Treatment-related malignant C-cell carcinomas were seen only in females in the 3 mg/kg/day group. Thyroid C-cell tumors are rare findings during carcinogenicity testing in mice.
Patients were stratified based on the presence or absence of abnormal blood glucose measurements at randomization (2254 of the 3731 patients) were treated for a total of 160 weeks. At baseline, mean age was 45 years (range 18-78), 79% were women, 84% were Caucasian, 13% were African American, and 11% were Hispanic/Latino. Mean baseline body weight was 99.6 kg and mean BMI was 35.6 kg/m².

4.1 CLINICAL STUDIES

The safety and efficacy of Saxenda® for chronic weight management in conjunction with reduced caloric intake and increased physical activity were studied in three 56-week, randomized, double-blind, placebo-controlled trials. In all studies, Saxenda® was titrated to 3 mg daily during a 4-week period. All patients received instruction for a reduced caloric diet (approximately 500 kcal/day deficit) and exercise counseling (recommended increase in physical activity of at least 150 mins/week) that began with the first dose of study medication or placebo and continued throughout the trial.

Study 1 enrolled 3731 patients with obesity (BMI greater than or equal to 30 kg/m²) and those patients with abnormal glucose measurements at randomization (2254 of the 3731 patients) were treated for a total of 160 weeks. At baseline, mean age was 45 years (range 18-78), 79% were women, 84% were Caucasian, 12% were African American, and 11% were Hispanic/Latino. Mean baseline body weight was 105.9 kg and mean BMI was 37.1 kg/m².

Study 2 was a 56-week trial that enrolled 423 patients with type 2 diabetes and with either overweight or obesity (as defined above). Patients were to have an HbA1c of 7-10% and be treated with metformin, a sulfonylurea, or a glitazone as single agent or in any combination, or with diet and exercise alone. Patients were randomized in a 2:1 ratio to receive either Saxenda® or placebo. Patients were stratified based on the presence or absence of abnormal blood glucose measurements at randomization. All patients were treated for up to 56 weeks. Those patients with abnormal glucose measurements at randomization (2254 of the 3731 patients) were treated for a total of 160 weeks. At baseline, mean age was 45 years (range 18-78), 50% were women, 83% were Caucasian, 12% were African American, and 10% were Hispanic/Latino. Mean baseline body weight was 103.3 kg and mean BMI was 38.3 kg/m².

Study 3 was a 56-week trial that enrolled 422 patients with obesity (BMI greater than or equal to 30 kg/m²) or with overweight (BMI 27.2-29.9 kg/m²) and at least one weight-related comorbid condition such as treated or untreated dyslipidemia or hypertension; patients with type 2 diabetes mellitus were excluded. Patients were randomized in a 2:1 ratio to either Saxenda® or placebo. The mean age was 55 years (range 18-82), 50% were women, 83% were Caucasian, 12% were African American, and 10% were Hispanic/Latino. Mean baseline body weight was 105.9 kg and mean BMI was 37.1 kg/m².

The cumulative frequency distributions of change in body weight from baseline to week 56 are shown in Figure 2 for Studies 1 and 2. One way to compare the magnitude of change in body weight is the area under the curve (AUC) comparison. A treatment-related increase in mean body weight of 1% or greater was observed in all studies. The AUC comparison was performed for patients with least 5% of their screening body weight after 4 to 12 weeks during the run-in period and then randomized, with equal allocation, to receive either Saxenda® or placebo for 56 weeks. The mean age was 46 years (range 18-73), 81% were women, 84% were Caucasian, 13% were African American, and 7% were Hispanic/Latino. Mean baseline body weight was 99.6 kg and mean BMI was 35.6 kg/m².

The proportions of patients who discontinued study drug in the 56-week trials were 27% for the Saxenda®-treated group and 35% for the placebo-treated group, and in the 160-week trial the proportions of patients who discontinued were 47% and 55%, respectively. In the 56-week trials, approximately 10% of patients treated with Saxenda® and 4% of patients treated with placebo discontinued treatment due to an adverse reaction [see Adverse Reactions (6.1)]. The majority of patients who discontinued Saxenda® due to adverse reactions did so during the first 12 months of treatment. In the 160-week trial, the proportions of patients who discontinued due to an adverse reaction was 13% and 6% for Saxenda® and placebo-treated patients, respectively.

Effect of Saxenda® on Body Weight in 56-week Trials

For Study 1 and Study 2, the primary efficacy parameters were mean percent change in body weight and the percentages of patients achieving greater than or equal to 5% and 10% weight loss from baseline to week 56. For Study 3, the primary efficacy parameters were mean percent change in body weight from randomization to week 56, the percentage of patients not gaining more than 0.5% body weight from randomization (i.e., after run-in) to week 56, and the percentage of patients achieving greater than or equal to 5% weight loss from randomization to week 56. Because losing at least 5% of fasting body weight through lifestyle intervention during the 4- to 12-week run-in was a condition for their continued participation in the randomized treatment period, the results may not reflect those expected in the general population.

Table 4 presents the results for the changes in weight observed in Studies 1, 2, and 3. After 56 weeks, treatment with Saxenda® resulted in a statistically significant reduction in weight compared with placebo. Statistically significantly greater proportions of patients treated with Saxenda® achieved 5% and 10% weight loss than those treated with placebo. In Study 3, statistically significantly more patients randomized to Saxenda® than placebo had not gained more than 0.5% of body weight from randomization to week 56.
Baseline mean body weight (SD) (kg) 107.5 (21.6) 107.9 (21.8)
Number (%) of patients known to lose greater than or equal to 5% body weight at 56 weeks 371 (56%) 182 (25%)
Number (%) of patients known to lose greater than or equal to 5% body weight at 160 weeks 424 (28%) 102 (14%)
Number (%) of patients known to lose greater than or equal to 5% body weight at both 56 and 160 weeks 391 (26%) 74 (10%)
Number (%) of patients with weight assessment at 160 weeks 747 (50%) 322 (43%)

**Effect of Saxenda® on Anthropometry and Cardiometabolic Parameters in 56-week Trials**

Changes in waist circumference and cardiometabolic parameters with Saxenda® are shown in Table 6 for Study 1 (patients without diabetes mellitus) and Table 7 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 6. Mean Changes in Anthropometry and Cardiometabolic Parameters in Study 1 (Patients without Diabetes Mellitus)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline</th>
<th>Change from Baseline (LSMean)</th>
<th>Saxenda® N=1505</th>
<th>Placebo N=749</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waist Circumference (cm)</td>
<td>115.0</td>
<td>-8.2</td>
<td>114.5</td>
<td>4.0</td>
</tr>
<tr>
<td>Systolic Blood Pressure (mmHg)</td>
<td>123.0</td>
<td>-4.3</td>
<td>123.3</td>
<td>-1.5</td>
</tr>
<tr>
<td>Diastolic Blood Pressure (mmHg)</td>
<td>78.7</td>
<td>-2.7</td>
<td>78.9</td>
<td>-1.8</td>
</tr>
<tr>
<td>Heart Rate (bpm)</td>
<td>71.4</td>
<td>2.6</td>
<td>71.3</td>
<td>0.1</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dL)*</td>
<td>193.8</td>
<td>-3.2</td>
<td>194.4</td>
<td>-0.9</td>
</tr>
<tr>
<td>LDL Cholesterol (mg/dL)*</td>
<td>111.8</td>
<td>-3.1</td>
<td>112.3</td>
<td>-0.7</td>
</tr>
<tr>
<td>HDL Cholesterol (mg/dL)*</td>
<td>51.4</td>
<td>2.3</td>
<td>50.9</td>
<td>0.5</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)*</td>
<td>125.7</td>
<td>-13.0</td>
<td>128.3</td>
<td>-4.1</td>
</tr>
</tbody>
</table>

Based on last observation carried forward method while on study drug

1. Least squares mean adjusted for treatment, country, sex, pre-diabetes status at screening, baseline BMI stratum and an interaction between pre-diabetes status at screening and BMI stratum as fixed factors, and the baseline value as covariate.

**Cardiovascular Outcomes Trial of Liraglutide 1.8 mg in Patients with Type 2 Diabetes and Cardiovascular Disease**

Liraglutide 1.8 mg (Victozia®) is used in the treatment of type 2 diabetes mellitus in adults. The efficacy of liraglutide at doses below 3 mg/day has not been established for chronic weight management. The LEADER trial (NCT01179048) randomized 9340 patients with inadequately controlled type 2 diabetes and cardiovascular disease to liraglutide 1.8 mg or placebo in addition to standard of care treatments for type 2 diabetes for a median duration of 3.5 years. Patients either were 50 years of age or older with established, stable cardiovascular, cerebrovascular, peripheral vascular disease, chronic renal failure or chronic heart failure (80% of patients), or were 60 years of age or older and had other specified risk factors for vascular disease (20% of patients). The population was 64% male, 78% Caucasian, 10% Asian and 8% Black, 12% of the population was Hispanic or Latino.

In total, 96.8% of the patients completed the trial; vital status was known at the end of the trial for 99.7%. The primary endpoint was the time from randomization to first occurrence of a major adverse cardiovascular event (MACE) defined as: cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke. No increased risk for MACE was observed with liraglutide 1.8 mg. The total number of primary component MACE endpoints was 1302 (608 (13.0%) with liraglutide 1.8 mg and 694 (14.9%) with placebo).

### Table 7. Mean Changes in Anthropometry and Cardiometabolic Parameters in Study 2 (Patients with Diabetes Mellitus)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline</th>
<th>Change from Baseline (LSMean)</th>
<th>Saxenda® N=423</th>
<th>Placebo N=244</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waist Circumference (cm)</td>
<td>118.1</td>
<td>-6.0</td>
<td>117.3</td>
<td>-2.8</td>
</tr>
<tr>
<td>Systolic Blood Pressure (mmHg)</td>
<td>128.9</td>
<td>-3.0</td>
<td>129.2</td>
<td>-0.4</td>
</tr>
<tr>
<td>Diastolic Blood Pressure (mmHg)</td>
<td>79.0</td>
<td>-1.0</td>
<td>79.3</td>
<td>-0.6</td>
</tr>
<tr>
<td>Heart Rate (bpm)</td>
<td>74.0</td>
<td>2.0</td>
<td>74.0</td>
<td>1.5</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dL)*</td>
<td>171.0</td>
<td>-1.4</td>
<td>169.4</td>
<td>2.4</td>
</tr>
<tr>
<td>LDL Cholesterol (mg/dL)*</td>
<td>86.4</td>
<td>0.9</td>
<td>85.2</td>
<td>3.3</td>
</tr>
<tr>
<td>HDL Cholesterol (mg/dL)*</td>
<td>45.2</td>
<td>4.8</td>
<td>45.4</td>
<td>1.9</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)*</td>
<td>152.6</td>
<td>-14.5</td>
<td>155.8</td>
<td>-0.7</td>
</tr>
</tbody>
</table>

Based on last observation carried forward method while on study drug

1. Least squares mean adjusted for treatment, country, sex, background treatment, baseline HbA1c stratum and an interaction between background treatment and HbA1c stratum as fixed factors, and the baseline value as covariate.

17. **PATIENT COUNSELING INFORMATION**

### FDA-Approved Medication Guide

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

### Instructions

Adviser patients to take Saxenda® exactly as prescribed. Instruct patients to follow the dose escalation schedule and to not take more than the recommended dose.

Instruct patients to discontinue Saxenda® if they have not achieved 4% weight loss by 16 weeks of treatment.

### Risk of Thyroid C-cell Tumors

Inform patients that liraglutide causes benign and malignant thyroid C-cell tumors in mice and rats 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 health care provider (see Boxed Warning and Warnings and Precautions (5.1)).

### Acute Pancreatitis

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

### 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.

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

Educate patients on the signs and symptoms of hypoglycemia. Advise patients with type 2 diabetes mellitus on glycemic lowering therapy to report signs and/or symptoms of hypoglycemia to their healthcare provider.

**Heart Rate Increase**

Inform patients to report symptoms of sustained periods of heart pounding or racing while at rest to their healthcare provider. Discontinue Saxenda® in patients who experience a sustained increase in resting heart rate.

**Dehydration and Renal Impairment**

Advise patients of the risk of dehydration due to gastrointestinal adverse reactions and to take precautions to avoid fluid depletion. Inform patients of the potential risk for worsening renal function, which in some cases may require dialysis.

**Hypersensitivity Reactions**

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

**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 Saxenda®.

**Jaundice and Hepatitis**

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

**Never Share a Saxenda® Pen Between Patients**

Inform patients 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 complete list of ingredients in Saxenda®.
- Symptoms of a serious allergic reaction may include:
  - swelling of your face, lips, tongue, or throat
  - fainting or feeling dizzy
  - very rapid heartbeat
  - problems breathing or swallowing
  - severe rash or itching
- You are pregnant or planning to become pregnant. Saxenda® may harm your unborn baby.
- You 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 use Saxenda® or breastfeed.
- You have or have had depression or suicidal thoughts.
- You have any of the conditions listed in the section “What is the most important information I should know about Saxenda®?”
- 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®.
- You have severe problems with your stomach, such as slowed emptying of your stomach (gastroparesis) or problems with digesting food.
- You have or have had problems with your pancreas, kidneys or liver.
- You have or have had depression or suicidal thoughts.
- You are pregnant or plan to become pregnant. Saxenda® may harm your unborn baby. Tell your healthcare provider if you become pregnant while taking Saxenda®. If you are pregnant you should stop using Saxenda®.
- You 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 use 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 sulfamoylurea medicines or insulin.

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. Tell 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 use 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 sulfamoylurea 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.
- Before each injection, check to see that the pen needle is not clogged. 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)
  - 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
  - drowsiness
  - nausea
  - headache
  - decreased appetite
  - irritability
  - hunger
  - fast heartbeat
  - feeling jittery
  - diarrhea
  - vomiting
  - upset stomach
  - stomach pain
  - thirst
  - irritability

Talk to 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 “What is the most important information I should know about 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
- vomiting
- constipation
- diarrhea
- decreased appetite
- upset stomach
- tiredness
- dizziness
- stomach pain
- change in enzyme (lipase) levels in your blood

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 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

Saxenda®, Victoza®, NovoFine®, and NovoTwist® are registered trademarks of Novo Nordisk A/S.


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

Revised: SEPTEMBER 2016, VERSION 2
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 6 mm.

Saxenda® pen and needle (example)

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® is 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.
- 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.
- If no drop appears, repeat Step 2 above as shown in Figures G and H up to 8 times. If there is still no drop, change the needle and repeat Step 2 as shown in Figures G and H more than 8 times.
- Do not use the pen if a drop of Saxenda® still does not appear. Contact Novo Nordisk at 1-844-363-4448.
- 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.
- 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. You will hear a "click" every time you turn the dose selector. 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.

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 ( ).
- Pull off the outer needle cap and throw it away. A drop of Saxenda® may appear at the needle tip. This is normal, but you must still check the Saxenda® flow, if you use a new pen for the first time.
- Always use a new needle for each injection. This will prevent contamination, infection, leakage of Saxenda® or blocked needles leading to the wrong dose.
- Do not use a bent or damaged needle.
- Do not attach a new needle to your pen until you are ready to take your injection.

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.

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.

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.
• 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.

How to identify a blocked or damaged needle?

• If 0 does not appear in the dose counter after continuously pressing the dose button, you may have used a blocked or damaged needle.

• If this happens you have not received any Saxenda®, even though the dose counter has moved from the original dose that you have set.

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.

You may see a drop of Saxenda® at the needle tip after injecting. This is normal and does not affect your dose.

Step 5. After your injection

• Carefully remove the needle from the pen. Do not put the needle caps back on the needle, to avoid needle sticks.

• Place the needle in a sharps container right away to reduce the risk of needle sticks.

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

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.

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.

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.

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