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, 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 (4.1, 5.1, 13.1).

— — — — RECENT MAJOR CHANGES — — — —
Indications and Usage, Limitations of Use (1)……………… 2020
Dosage and Administration (2.1, 2.2, 2.3)……………… 2020
Warnings and Precautions (5.2, 5.4, 5.5, 5.8)……………… 2020

— — — — 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), or
• 27 kg/m² or greater (overweight) in the presence of at least one weight-related comorbid condition (e.g., hypertension, type 2 diabetes mellitus, or dyslipidemia) (1). Pediatric patients aged 12 years and older with:
• body weight above 60 kg and
• an initial BMI corresponding to 30 kg/m² for adults (obese) by international cut-offs (1).

Limitations of Use:
• SAXENDA® contains liraglutide and should not be coadministered with other liraglutide-containing products or with any other GLP-1 receptor agonist (1).
• The safety and effectiveness of SAXENDA® in pediatric patients with type 2 diabetes have not been established (1).
• The safety and efficacy of SAXENDA® in combination with other products intended for weight loss have not been established (1).

— — — — DOSAGE AND ADMINISTRATION — — — —
Inject SAXENDA® subcutaneously in the abdomen, thigh, or upper arm once daily at any time of day, without regard to the timing of meals (2.2). The recommended dose of SAXENDA® is 3 mg daily (2.3).
• Initiate at 0.6 mg per day for one week. In weekly intervals, increase the dose until a dose of 3 mg is reached (2.3).
• If pediatric patients do not tolerate an increased dose during dose escalation, the dose may also be lowered to the previous level. Dose escalation for pediatric patients may take up to 6 weeks (2.3).
• Pediatric patients who do not tolerate 3 mg daily may have their dose reduced to 2.4 mg daily (2.3).
• Adult patients with type 2 diabetes should monitor blood glucose prior to starting SAXENDA® and during SAXENDA® treatment (2.3).

— — — — DOSAGE FORMS AND STRENGTHS — — — —
Injection: 6 mg/mL solution in a 3 mL pre-filled, single-patient-use pen that delivers doses of 0.6 mg, 1.2 mg, 1.8 mg, 2.4 mg or 3 mg (3).

— — — — CONTRAINDICATIONS — — — —
• Personal or family history of medullary thyroid carcinoma or Multiple Endocrine Neoplasia syndrome type 2 (4.5, 13.1).
• Hypersensitivity to liraglutide or any excipients in SAXENDA® (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).

• Hypoglycemia: Can occur in adults when SAXENDA® is used with an insulin secretagogue (e.g., a sulfonylurea) or insulin. The risk may be lowered by a reduction in the dose of concomitantly administered insulin secretagogues or insulin. In the pediatric clinical trial, patients did not have type 2 diabetes. Hypoglycemia occurred in SAXENDA®-treated pediatric patients. Inform all patients of the risk of hypoglycemia and educate them on the signs and symptoms 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, diarrhea, constipation, vomiting, injection site reactions, headache, hypoglycemia, dyspepsia, fatigue, dizziness, abdominal pain, increased lipase, upper abdominal pain, pyrexia, and gastroenteritis (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 concomitantly administered oral medications. Use with caution (7).

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.
Revised: 12/2020

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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 (13.2)).

- 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® (liraglutide) injection 3mg 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.
- Patients with a BMI of ≥27 kg/m² in the presence of at least one weight-related comorbid condition (e.g., hypertension, type 2 diabetes mellitus, dyslipidemia).

- Pediatric patients aged 12 years and older with:
  - Body weight above 60 kg and
  - An initial BMI corresponding to ≥30 kg/m² or greater (obese) by international cut-offs (see Table 1).

### 2 DOSAGE AND ADMINISTRATION

#### 2.1 Patient Selection

Select patients for SAXENDA® treatment as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management based on the BMI values provided in Tables 1 and 2.

- **Adults and Pediatric Patients**
  - 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 1.

#### 2.2 Important Administration Instructions

- **Prior to initiation of SAXENDA®**
  - Inspect SAXENDA® visually prior to each injection. Only use if solution is clear, colorless, and contains no particles.

- **Inject SAXENDA®** subcutaneously at any time of day, without regard to the timing of meals.

- **Inject SAXENDA®** subcutaneously in the abdomen, thigh, or upper arm. No dose adjustment is needed if changing the injection site and/or timing.

- **If a dose is missed**, resume the once-daily regimen as prescribed. If more than 3 days have elapsed since the last dose, increase the dose to make up for the missed dose.

- **If a dose is missed**, resume the once-daily regimen as prescribed. If more than 3 days have elapsed since the last dose, increase the dose to make up for the missed dose.

- **Limitations of Use**
  - Pediatric patients aged 12 years and older with:
    - Body weight above 60 kg and
    - An initial BMI corresponding to ≥30 kg/m² or greater (obese) by international cut-offs.
  - The safety and effectiveness of SAXENDA® in pediatric patients with type 2 diabetes have not been established.
  - 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.

- **Pediatric Patients**
  - Pediatric patients who do not tolerate an increased dose during dose escalation, the dose may also be lowered to the previous dose.
  - Discontinue SAXENDA® if the patient cannot tolerate the 3 mg dose.
  - If patients do not tolerate an increased dose during dose escalation, consider delaying dose escalation for approximately one additional week.
  - 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.
  - In adult patients with type 2 diabetes, monitor blood glucose prior to starting SAXENDA® and during SAXENDA® treatment.

- **For pediatric patients**
  - The recommended maintenance dosage of SAXENDA® is 3 mg daily. Pediatric patients who do not tolerate 3 mg daily may have their maintenance dose reduced to 2.4 mg daily. Discontinue SAXENDA® if the patient cannot tolerate the 2.4 mg dose.

- **If pediatric patients do not tolerate an increased dose during dose escalation**, the dose may also be lowered to the previous level. Dose escalation for pediatric patients may take up to 8 weeks.

- **Evaluate the change in BMI after 12 weeks on the maintenance dose and discontinue SAXENDA®** if the patient has not had a reduction in BMI of at least 1% from baseline, since it is unlikely that the patient will achieve and sustain clinically meaningful weight loss with continued treatment.

### 3 DOSAGE FORMS AND STRENGTHS

- **Injection**: 6 mg/mL clear, colorless solution in a 3 mL pre-filled, single-patient-use pen that delivers doses of 0.6 mg, 1.2 mg, 1.8 mg, 2.4 mg, or 3 mg.
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 excipients in SAXENDA® [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 doses 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 lira-
glutide-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, difficulty swallowing, and/or hoarseness) [See Warnings and Precautions (5.1)].

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 calcitonin values in the absence of MTC, and with patients 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 spontaneous 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 nausea or 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 in adults, acute pancreatitis was confirmed by adjudication in 9 (0.3%) of 3291 SAXENDA®-treated patients compared to 1 (0.03%) of 3138 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 patients treated with SAXENDA® who had pancreatitis reported as an adverse reaction in 0.6% of SAXENDA®-treated patients and in 0.1% of placebo-treated patients.
Table 5. Adverse Reactions Occurring in ≥3% of SAXENDA®-treated Pediatric Patients and More Frequently than Placebo in a 56 Week Clinical Trial

<table>
<thead>
<tr>
<th>Reaction</th>
<th>SAXENDA® N=423</th>
<th>Placebo N=422</th>
<th>Placebo N=421</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>14.3%</td>
<td>14.3%</td>
<td>14.3%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>4.0%</td>
<td>4.0%</td>
<td>4.0%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>14.3%</td>
<td>14.3%</td>
<td>14.3%</td>
</tr>
<tr>
<td>Hypoglycemia*</td>
<td>4.8%</td>
<td>4.8%</td>
<td>4.8%</td>
</tr>
<tr>
<td>Gastroenteritis</td>
<td>3.2%</td>
<td>3.2%</td>
<td>3.2%</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>7.1%</td>
<td>7.1%</td>
<td>7.1%</td>
</tr>
<tr>
<td>Abdominal discomfort</td>
<td>0.8%</td>
<td>0.8%</td>
<td>0.8%</td>
</tr>
<tr>
<td>Constipation</td>
<td>2.4%</td>
<td>2.4%</td>
<td>2.4%</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>3.2%</td>
<td>3.2%</td>
<td>3.2%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>3.2%</td>
<td>3.2%</td>
<td>3.2%</td>
</tr>
<tr>
<td>Cough</td>
<td>3.2%</td>
<td>3.2%</td>
<td>3.2%</td>
</tr>
<tr>
<td>Depression</td>
<td>2.4%</td>
<td>2.4%</td>
<td>2.4%</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>2.4%</td>
<td>2.4%</td>
<td>2.4%</td>
</tr>
<tr>
<td>Pain in extremity</td>
<td>2.4%</td>
<td>2.4%</td>
<td>2.4%</td>
</tr>
<tr>
<td>Injection site pain</td>
<td>3.2%</td>
<td>3.2%</td>
<td>3.2%</td>
</tr>
<tr>
<td>Flatulence</td>
<td>0.0%</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Increased Blood Creatine Kinase</td>
<td>2.4%</td>
<td>2.4%</td>
<td>2.4%</td>
</tr>
<tr>
<td>Increased Lipase</td>
<td>0.8%</td>
<td>0.8%</td>
<td>0.8%</td>
</tr>
<tr>
<td>Rash</td>
<td>0.0%</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

*Defined as blood glucose <70 mg/dL with or without symptoms of hypoglycemia in patients with type 2 diabetes not on concomitant insulin (Study 2, SAXENDA® N=423, Placebo N=421). See text below for further information regarding hypoglycemia in patients with and without type 2 diabetes. 1200mg = type 2 diabetes mellitus.
7 DRUG INTERACTIONS
7.1 Oral Medications SAXENDA® causes a delay of gastric emptying, and thereby has the potential to impact the absorption of concurrently administered oral medications. In clinical pharmacology trials, liraglutide did not affect the absorption of the tested orally administered medications to any clinically relevant degree. Nonetheless, monitor for potential consequences of delayed absorption of oral medications concomitantly administered with SAXENDA®. 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 associated risk for major birth defects and miscarriage. SAXENDA® 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 identified increased adverse embryo-fetal developmental outcomes from exposure during pregnancy. Liraglutide exposure was associated with early embryonic deaths and an imbalance in some fetal abnormalities in pregnant rats administered liraglutide during organogenesis at doses that approximate clinical exposure in rats at the maximum recommended human dose (MRHD) of 3 mg/day. In pregnant rabbits administered liraglutide during organogenesis, decreased fetal weight and an increased incidence of major fetal abnormalities were seen at exposures below the recommended oral exposure in animals (see Preclinical Safety Data). 8.2 Lactation Risk Summary There are no data on the presence of liraglutide in human milk, the effects on the breastfed infant, or effects on milk production. Liraglutide was present in the milk of lactating rats (see Data).

In lactating rats, liraglutide was present unchanged in milk at concentrations approximately 50% of maternal plasma concentrations.

8.4 Pediatric Use The safety and effectiveness of SAXENDA® as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management have been established in pediatric patients aged 12 years and older with body weight above 60 kg and an initial BMI ranging from 30 kg/m² or greater for adults (obese) by clinical cut-offs (see Table 2). Use of SAXENDA® for this indication is supported by a 56-week double-blind, placebo-controlled clinical trial in which children aged 12 to 17 years, a pharmacokinetic study in pediatric patients, and studies in adults with obesity (see Clinical Pharmacology (12.3) and Clinical Studies (14.1,14.2)).

In the pediatric clinical trial, there was one death due to suicide in a patient treated with saxenda. There were 4 serious adverse events in saxenda-treated patients, compared to placebo in children aged 12 to 17 years, and mean increases in resting heart rate of 3 to 7 bpm from baseline were observed with SAXENDA®-treated patients (see Warnings and Precautions (5.5)).

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

8.5 Geriatric Use In the SAXENDA® clinical trials, 232 (6.9%) of the SAXENDA®-treated patients were 65 years of age and older, 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 geriatric 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, and therefore, there have been postmarketing reports of acute renal failure and worsening of chronic renal failure with liraglutide, which may sometimes require hemodialysis. In the liraglutide QTc study in healthy volunteers, there was a significant increase in the QTc observed 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 (10.3)).

8.8 Gastroparesis SAXENDA® slows gastric emptying. SAXENDA® has not been studied in patients with pre-existing gastroparesis.

10 OVERDOSAGE Overdoses have been reported in clinical trials and post-marketing use of liraglutide. Effects have included severe nausea, severe vomiting and agitation. In the event of overdose, 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 methyl esterified carboxyl side on the remaining 31 amino acids of the native 29 amino acid GLP-1. The molecular formula of liraglutide is C 375H 574O 52N 72S 23 and the molecular weight is 3751.2 Daltons. The structural formula (Figure 1) is: 12 CLINICAL PHARMACOLOGY 12.1 Mechanism of Action Liraglutide is an acylated human glucagon-like peptide-1 (GLP-1) receptor agonist with 97% amino acid sequence homology to endogenous human GLP-1 (37-37). Like endogenous GLP-1, liraglutide binds to and activates the GLP-1 receptor, a cell-surface receptor coupled to adenylylcyclase 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 enzyme dipeptidyl peptidase IV (DPP-4), which cleaves short-lived neuropeptides (NEP). Unlike native GLP-1, liraglutide is stable against metabolic degradation by both peptidases and has a plasma half-life of 13 hours after subcutaneous administration. The pharmacoki netic 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 physiological regulator of appetite and calorie intake, and GLP-1 receptor agonism reduces food intake in rodents and plasma glucose in human volunteers. Liraglutide, which has a half-life of approximately 14 hours, is therefore suitable for once-daily administration.

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 inhibits glucagon secretion in the fed state and delays gastric emptying preprandially and postprandially. The magnitude of the effect is food-dependent. 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) in overweight and obese subjects treated with liraglutide 3 mg is similar to the Cmax observed in the liraglutide QTc study in healthy volunteers.

12.3 Pharmacokinetics Liraglutide is rapidly subcutaneous administration, maximum concentrations of liraglutide are achieved at 11 hours post dosing. The average liraglutide steady state concentration (AUC(0-24)) reached approximately 116 ng/mL in obese (BMI 30-40 kg/m²) subjects following administration of SAXENDA®. Liraglutide exposures increased 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 (anterolateral, ventrogluteal, 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 26-35 L (for a person weighing 80 kg) and 100 L (for a person weighing 180 kg). The ratio 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
achieved 5% and 10% weight loss for 56 weeks. The mean age was 46 years (range 18-73), 81% were women, 84% were Caucasian, and 10% were Hispanic/Latino. Mean baseline body weight was 105.3 kg and mean BMI was 37.1 kg/m².

14 CLINICAL STUDIES
14.1 Weight Management Trials in Adults with Overweight or Obesity
The safety and efficacy of SAXENDA® for chronic weight management for weight loss with reduced caloric intake and increased physical activity were studied in 3-56-week, randomized, double-blind, placebo-controlled trials. In all studies, SAXENDA® was titrated to 3 mg daily during a 4-week period. All studies were conducted in patients with at least one weight-related comorbid condition such as treated or untreated dyslipidemia or hypertension; patients with type 2 diabetes were randomized in a 2:1 ratio to either SAXENDA® or placebo. Patients were randomized in a 2:1 ratio to either SAXENDA® or placebo. The study drug was titrated 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 (225 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, 85% were Caucasian, 10% were African American, and 11% were Hispanic/Latino. Mean baseline body weight was 108.9 kg and mean BMI was 37.1 kg/m².

Study 1 was a 56-week trial that enrolled 635 patients with type 2 diabetes and with either overweight or obesity (as defined above). Patients were to have an HbA1c of 7% and be treated with metformin, a sulfonilurea, or a glitazone as single agent or combination therapy for at least 1 year (caloric intake 1200-3000 kcal/day) in a run-in period lasting up to 12 weeks. Patients who lost at least 5% of their body weight after 4 to 12 weeks during the run-in were then randomized, with equal allocation, to receive either SAXENDA® or placebo. 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.

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 were randomized in a 2:1 ratio to either SAXENDA® or placebo. The 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 in all treatment groups were discontinued due to an adverse reaction and 13% of patients in the 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 5 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®-treated 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 with a weight loss of at least 5% or 10% and those who achieved 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% weight, and the percentage of patients gaining more than 0.5% weight. The study drug was titrated in the randomized treatment period, the results may not reflect those expected in the general population.

Table 6 presents the results for the changes in body 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 gained more than 0.5% of body weight from randomization to week 56.
### Table 6. Changes in Weight at Week 56 for Studies 1, 2, and 3

<table>
<thead>
<tr>
<th>Study 1 (Obesity or overweight with comorbidity)</th>
<th>Study 2 (Type 2 diabetes with obesity or overweight)</th>
<th>Study 3 (Obesity or overweight with comorbidity following at least 5% weight loss with diet)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SAXENDA® N=2487 Placebo N=1244</strong></td>
<td><strong>SAXENDA® N=423 Placebo N=212</strong></td>
<td><strong>SAXENDA® N=212 Placebo N=210</strong></td>
</tr>
<tr>
<td><strong>Weight</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline mean (SD) (kg)</td>
<td>106.2 (21.2)</td>
<td>106.5 (21.3)</td>
</tr>
<tr>
<td>Percent change from baseline (LSMean)</td>
<td>-4.5* (-5.2; -3.8)</td>
<td>-4.9* (-6.8; -3.5)</td>
</tr>
<tr>
<td>Difference from placebo (LSMean) (95% CI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% of Patients losing greater than or equal to 5% body weight</td>
<td>62.3% 34.4%</td>
<td>49.0% 16.4%</td>
</tr>
<tr>
<td>Difference from placebo (LSMean) (95% CI)</td>
<td>27.9* (23.9; 31.9)</td>
<td>22.6* (13.9; 31.3)</td>
</tr>
<tr>
<td>% of Patients losing greater than 10% body weight</td>
<td>33.9% 15.4%</td>
<td>22.4% 5.5%</td>
</tr>
<tr>
<td>Difference from placebo (LSMean) (95% CI)</td>
<td>18.5* (15.2; 21.7)</td>
<td>18.5* (11.7; 25.3)</td>
</tr>
</tbody>
</table>

SD = Standard Deviation; CI = Confidence Interval

* p < 0.0001 compared to placebo. Type 1 error was controlled across the three endpoints.

Includes all randomized subjects who had a baseline body weight measurement. All available body weight data during the 56 week treatment period are included in the analysis. In Studies 1 and 2 missing values for week 56 were handled using multiple imputations analysis. In Study 3 missing values for week 56 were handled using weighted regression analysis.

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 interpret this figure is to select a change in body weight of interest on the horizontal axis and note the corresponding proportions of patients (vertical axis) in each treatment group who achieved at least that degree of weight loss. For example, note that the vertical line arising from -10% in Study 1 intersects the SAXENDA® and placebo curves at approximately 34% and 15%, respectively, which correspond to the values shown in Table 6.

---

**Figure 2. Change in body weight (%) from baseline to week 56 (Study 1 on left and Study 2 on right)**

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

---

**Figure 3. Change from baseline (%) in body weight (Study 1 on left and Study 2 on right)**

Observed values for patients on study drug completing each scheduled visit, and ITT with multiple imputations (ITT-MI)

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**Figure 4. Change from baseline (%) in body weight during Study 3**

Observed values for patients on study drug completing each scheduled visit, and ITT with weighted average (ITT-WA)
**Effect of SAXENDA® on Body Weight in a 160-week Trial (Study 1, Subset of Patients with Abnormal Blood Glucose at Randomization)**

The numbers and percentages of patients known to have lost greater than or equal to 5% body weight at week 56 and/or week 160 in Study 1 (patients with abnormal glucose at randomization only) are summarized in Table 7 for descriptive purposes.

**Table 7. Changes in Weight at Week 56 and Week 160 for Study 1 (Subset of Patients with Abnormal Blood Glucose at Randomization)**

<table>
<thead>
<tr>
<th></th>
<th>N = 1505</th>
<th>Placebo N = 749</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline mean body weight (SD, kg)</td>
<td>107.5 (23.6)</td>
<td>107.9 (23.8)</td>
</tr>
<tr>
<td>Number (%) of patients known to lose greater than or equal to 5% body weight at 56 weeks</td>
<td>817 (56%)</td>
<td>182 (25%)</td>
</tr>
<tr>
<td>Number (%) of patients known to lose greater than or equal to 5% body weight at 160 weeks</td>
<td>429 (28%)</td>
<td>102 (14%)</td>
</tr>
<tr>
<td>Number (%) of patients known to lose greater than or equal to 5% body weight at both 56 weeks and 160 weeks</td>
<td>391 (26%)</td>
<td>74 (10%)</td>
</tr>
<tr>
<td>Number (%) of patients with weight assessment at 160 weeks</td>
<td>747 (50%)</td>
<td>322 (43%)</td>
</tr>
</tbody>
</table>

SD = Standard Deviation

Includes all randomized subjects who had a baseline body weight measurement. All available body weight data at 56 and 160 weeks are included in the analysis.

**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 8 for Study 1 (patients without diabetes mellitus) and Table 9 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 8. Mean Changes in Anthropometry and Cardiometabolic Parameters in Study 1 (Patients without Diabetes)**

<table>
<thead>
<tr>
<th></th>
<th>SAXENDA®</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>Change from Baseline (LSMean)</td>
<td>Change from Baseline (LSMean)</td>
</tr>
<tr>
<td>Waist Circumference (cm)</td>
<td>115.0</td>
<td>-8.2</td>
</tr>
<tr>
<td>Systolic Blood Pressure (mmHg)</td>
<td>123.0</td>
<td>-6.3</td>
</tr>
<tr>
<td>Diastolic Blood Pressure (mmHg)</td>
<td>78.7</td>
<td>-2.7</td>
</tr>
<tr>
<td>Heart Rate (bpm)²</td>
<td>71.4</td>
<td>2.6</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>5.5</td>
<td>-0.3</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dL)</td>
<td>193.8</td>
<td>-3.2</td>
</tr>
<tr>
<td>LDL Cholesterol (mg/dL)</td>
<td>111.8</td>
<td>-3.1</td>
</tr>
<tr>
<td>HDL Cholesterol (mg/dL)</td>
<td>51.4</td>
<td>2.3</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)²</td>
<td>125.7</td>
<td>-13.0</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 and BMI stratum as fixed factors, and the baseline value as covariate.

2. See Warnings and Precautions (5.5)

3. Values are baseline median, median % change, and the Hodges-Lehmann estimate of the median treatment difference.

**Table 9. Mean Changes in Anthropometry and Cardiometabolic Parameters in Study 2 (Patients with Diabetes Mellitus)**

<table>
<thead>
<tr>
<th></th>
<th>SAXENDA®</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>Change from Baseline (LSMean)</td>
<td>Change from Baseline (LSMean)</td>
</tr>
<tr>
<td>Waist Circumference (cm)</td>
<td>119.1</td>
<td>-6.1</td>
</tr>
<tr>
<td>Systolic Blood Pressure (mmHg)</td>
<td>129.8</td>
<td>-3.0</td>
</tr>
<tr>
<td>Diastolic Blood Pressure (mmHg)</td>
<td>79.0</td>
<td>-1.0</td>
</tr>
<tr>
<td>Heart Rate (bpm)²</td>
<td>74.0</td>
<td>2.0</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>7.9</td>
<td>-1.3</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dL)</td>
<td>171.9</td>
<td>-1.4</td>
</tr>
<tr>
<td>LDL Cholesterol (mg/dL)</td>
<td>86.4</td>
<td>0.9</td>
</tr>
<tr>
<td>HDL Cholesterol (mg/dL)</td>
<td>45.2</td>
<td>4.8</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)²</td>
<td>158.2</td>
<td>-14.5</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 background treatment and HbA1c stratum as fixed factors, and the baseline value as covariate.

2. See Warnings and Precautions (5.5)

3. Baseline value is the geometric mean

4. Values are baseline median, median % change, and the Hodges-Lehmann estimate of the median treatment difference.

**14.2 Weight Management Trial in Pediatric Patients Ages 12 and Older with Obesity**

SAXENDA® was evaluated in a 56-week, double-blind, randomized, parallel group, placebo controlled multi-center trial in 251 pubertal pediatric patients aged 12 to 17 years, with BMI corresponding to 30 kg/m² or greater for adults by international cut-off points [see Dosage and Administration (2.1)] and BMI of 95th percentile or greater for age and sex (NCT02918279). After a 12-week treatment run-in period, patients were randomized 1:1 to SAXENDA® once-daily or placebo once-daily. The SAXENDA® dose was titrated to 3 mg over a 4- to 8-week period based on tolerability as judged by the investigator. Escalation of the trial product was not allowed if the subject had a self-monitored plasma glucose (SMPG) < 56 mg/dL or < 70 mg/dL in the presence of symptoms of hypoglycemia during the week prior to or during the dose escalation visits. The proportion of patients who reached the 3 mg dose was 82.4%; for 8.8% of patients 2.4 mg was the maximum tolerated dose.

The mean age was 14.5 years: 40.6% of patients were male, 86.7% were White, 0.8% were Asian, 8% were Black or African American, 22.3% were of Hispanic or Latino ethnicity. The mean baseline body weight was 100.8 kg, and mean Body Mass Index (BMI) was 35.6 kg/m².

The proportions of patients who discontinued study drug were 19.2% for the SAXENDA®-treated group and 20.6% for the placebo-treated group. 10.4% of patients treated with SAXENDA® and no patients treated with placebo discontinued treatment due to an adverse reaction [see Adverse Reactions (6.1)].

The primary endpoint was change in BMI SDS. At baseline, mean BMI SDS was 3.14 in the SAXENDA® group and 3.20 in the placebo group. At week 56, treatment with SAXENDA® resulted in statistically significant reduction in BMI SDS from baseline compared to placebo. The observed mean change in BMI SDS from baseline to week 56 was -0.23 in the SAXENDA® group and -0.00 in the placebo group. The estimated treatment difference in BMI SDS reduction from baseline between SAXENDA® and placebo was -0.22 with a 95% confidence interval of -0.37 to -0.08; p=0.0022.

The time course of change in BMI SDS with SAXENDA® and placebo from baseline through week 56 are depicted in Figure 5.

**Figure 5. Change from Baseline in BMI SDS**

Changes in weight and BMI with SAXENDA® are shown in Table 10. Changes in waist circumference and cardiometabolic parameters with SAXENDA® are shown in Table 11.

**Table 10. Changes in Weight and BMI at Week 56 for Study 4 (Pediatric Patients Ages 12 to Less than 18)**

<table>
<thead>
<tr>
<th></th>
<th>SAXENDA®</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline mean Body Weight (kg)</td>
<td>39.3</td>
<td>102.2</td>
</tr>
<tr>
<td>Mean Change from Baseline (%)</td>
<td>-2.65</td>
<td>2.37</td>
</tr>
<tr>
<td>BMI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline mean BMI (kg/m²)</td>
<td>35.3</td>
<td>35.8</td>
</tr>
<tr>
<td>Mean Change from Baseline (%)</td>
<td>-4.29</td>
<td>0.35</td>
</tr>
<tr>
<td>Proportion of patients with greater than or equal to 5% reduction in baseline BMI at week 56 (%)</td>
<td>43.3%</td>
<td>18.7%</td>
</tr>
<tr>
<td>Proportion of patients with greater than or equal to 10% reduction in baseline BMI at week 56 (%)</td>
<td>26.1%</td>
<td>8.1%</td>
</tr>
</tbody>
</table>

Full Analysis Set. For body weight and BMI, baseline values are means, changes from baseline at week 56 are estimated means (least-squares) and treatment contrasts at week 56 are estimated treatment differences. Missing observations were imputed from the placebo arm based on a jump to reference multiple (x100) imputation approach.
Table 11. Mean Changes in Anthropometry and Cardiometabolic Parameters in Study 4 (Pediatric Patients Ages 12 to Less than 18)

<table>
<thead>
<tr>
<th></th>
<th><strong>SAXENDA®</strong></th>
<th><strong>Placebo</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 125</td>
<td>N = 126</td>
</tr>
<tr>
<td></td>
<td>Baseline</td>
<td>Change from Baseline</td>
</tr>
<tr>
<td>Waist Circumference (cm)</td>
<td>105</td>
<td>-4.35</td>
</tr>
<tr>
<td>Systolic Blood Pressure (mmHg)</td>
<td>116</td>
<td>-1.21</td>
</tr>
<tr>
<td>Diastolic Blood Pressure (mmHg)</td>
<td>72</td>
<td>0.77</td>
</tr>
<tr>
<td>Heart Rate (bpm)**</td>
<td>75</td>
<td>1.67</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>5.3</td>
<td>-0.10</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dL)**</td>
<td>154.2</td>
<td>0.84</td>
</tr>
<tr>
<td>LDL Cholesterol (mg/dL)**</td>
<td>85.5</td>
<td>1.74</td>
</tr>
<tr>
<td>HDL Cholesterol (mg/dL)**</td>
<td>42.7</td>
<td>5.14</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)**</td>
<td>109.1</td>
<td>-0.12</td>
</tr>
</tbody>
</table>

** Baseline values are means. Changes from baseline at week 56 are estimated means (least-squares) and treatment contrasts at week 56 are estimated treatment differences. Missing observations were imputed from the placebo arm based on a jump to reference multiple (100) imputation approach.

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

Liraglutide 1.8 mg (Victoza®) is used in the treatment of type 2 diabetes mellitus in adults. The efficacy of liraglutide at doses below 3 mg daily 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 5.3 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 of 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 the 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).

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

SAXENDA® injection: 6 mg/mL clear, colorless solution in a 3 mL single-patient-use pre-filled pen that delivers doses of 0.6 mg, 1.2 mg, 1.8 mg, 2.4 mg or 3 mg is available in the following package sizes:

3 x SAXENDA® pen NDC 0169-2800-13
5 x SAXENDA® pen NDC 0169-2800-15

16.2 Recommended Storage

Prior to first use, SAXENDA® should be stored in a refrigerator between 36°F to 46°F (2°C to 8°C). Do not store in the freezer or directly adjacent to the refrigerator cooling element. Do not freeze SAXENDA® and do not use SAXENDA® if it has been frozen.

After initial use of the SAXENDA® pen, the pen can be stored for 30 days at controlled room temperature (59°F to 86°F; 15°C to 30°C) or in a refrigerator (36°F to 46°F; 2°C to 8°C). Keep the pen cap on when not in use. Protect SAXENDA® from excessive heat and sunlight. Always remove and safely discard the needle after administration and store the SAXENDA® pen without an injection needle attached. This will reduce the potential for contamination, infection, and leakage while also ensuring dosing accuracy.

17 PATIENT COUNSELING INFORMATION

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

Instructions

Advise 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 adult patients to discontinue SAXENDA® if they have not achieved 4% weight loss by 16 weeks of treatment. Instruct pediatric patients 12 years of age and older to discontinue SAXENDA® if they have not achieved a BMI reduction of 1% from baseline after 12 weeks on the maintenance dose.

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 (5.5)].

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 may 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

Inform pediatric patients of the risk of hypoglycemia and educate all patients on the signs and symptoms of hypoglycemia. Inform adult patients with type 2 diabetes mellitus on an insulin secretagogue (e.g., sulfonylurea) or insulin that they may have an increased risk of hypoglycemia when using SAXENDA® and 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 used for adults with obesity or overweight (excess weight) who also have weight-related medical problems, and children aged 12 to 17 years with a body weight above 132 pounds (60 kg) and obesity to help them lose weight and keep the weight off.

SAXENDA® should be used with a reduced calorie diet and increased physical activity.

SAXENDA® and VICTOZA® have the same active ingredient, liraglutide, and should not be used together with or with other GLP-1 receptor agonist medicines.

It is not known if SAXENDA® is safe and effective when taken with other prescription, over-the-counter medicines, or herbal weight loss products.

It is not known if SAXENDA® is safe and effective in children under 12 years of age.

It is not known if SAXENDA® is safe and effective in children aged 12 to 17 years with type 2 diabetes.

Who should not use SAXENDA®?

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).

- 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®.

- you are pregnant or plan 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:

- are taking certain medicines called GLP-1 receptor agonists.

- 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, or mental health issues.

- are breastfeeding or plan to breastfeed. It is not known if SAXENDA® passes into your breast milk.

- Your and your healthcare provider should decide if you will use SAXENDA® or breastfeed.

Tell your healthcare provider about all the medicines you take including prescription, over-the-counter medicines, vitamins, and herbal supplements. SAXENDA® slow stomach emptying 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 insulin and sulfonylurea medicines. Talk with your healthcare provider if you are not sure if you take any of these medicines.

How should I use SAXENDA®?

- The instructions for Use that comes with SAXENDA®.

- Use SAXENDA® exactly as prescribed by your healthcare provider.

- Your healthcare provider should show you how to use SAXENDA® before you use it for the first time.

- 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.

- Start SAXENDA® with 0.6 mg per day in your first week. In your second week, increase your daily dose to 1.2 mg. In the third week, increase your daily dose to 1.8 mg. In the fourth week, increase your daily dose to 2.4 mg and in the fifth week onwards, increase your daily dose to the full dose of 3 mg. After that, do not change your dose unless your healthcare provider tells you to. Children may reduce their dose to 2.4 mg daily if the maximum dose is not tolerated.

- SAXENDA® is applied 1 time each day, at any time during the day.

- Inject your dose of SAXENDA® under the skin (subcutaneously) 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. Taking too much SAXENDA® may cause severe nausea, severe vomiting, and low blood sugar (hypoglycemia).

- If you miss your daily dose of SAXENDA®, just 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.

- You can take SAXENDA® with or without food.

- Throw away the used SAXENDA® pen after 30 days.

Your healthcare provider should start you on a reduced calorie diet and increased physical activity when you start taking SAXENDA®.

Stay on this program while you are taking SAXENDA®.

What are the possible side effects of SAXENDA®?

SAXENDA® may cause serious side effects, including:

- 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 stomach area (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

- Increased risk of low blood sugar (hypoglycemia) in adults with type 2 diabetes mellitus who also take medicines to treat type 2 diabetes mellitus such as sulfonylureas or insulin.

- Risk of low blood sugar (hypoglycemia) in children who are 12 years of age and older without type 2 diabetes mellitus

- Signs and symptoms of low blood sugar may include:
  - Shakiness
  - Weakness
  - Dizziness
  - Confusion
  - Nausea
  - Headache
  - Drowsiness
  - Irritability
  - Hunger
  - Fast heartbeat
  - Feeling jittery

Take to your healthcare provider about how to recognize and treat low blood sugar. You should know how to treat low 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 rate pounding or racing in your chest and it lasts for several minutes.

- 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. Stop using SAXENDA® and get medical help right away if you have any symptoms of a serious allergic reaction including:
  - Swelling of your face, lips, tongue, or throat
  - Breathing or swallowing problems
  - Fainting or feeling dizzy
  - Very rapid heartbeat
  - 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 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 ingredients: liraglutide

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

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

For information about SAXENDA® go to www.SAXENDA.com or 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. Revised: 12/2020

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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 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, single-patient-use 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. Pen needles are not included with your Saxenda® pen.

**Saxenda® pen and needle (example)**

<table>
<thead>
<tr>
<th>Pen scale</th>
<th>Pen window</th>
<th>Dose counter</th>
<th>Dose selector</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pen cap</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**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.

**Step 2. Check the Saxenda® flow with each new pen.**

- Hold the pen with the needle pointing up. Press and hold in the dose button until the dose counter shows 0. The G must line up with the dose pointer. A drop of Saxenda® will appear at the needle tip.
- If no drop appears, repeat Step 2 above 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® still does not appear.

**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.
- 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 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 4. Inject your dose**

- Insert the needle into your skin as you have been instructed by your healthcare provider.
- 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.

**Step 5. Dispose of used pen.**

- 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.

- Do not attach a new needle to your pen until you are ready to take your injection.
- Do not split your dose using 2 pens. Use a calculator to plan the doses as instructed by your healthcare provider.
- Only if trained or told by your healthcare provider, you may split your dose between your current pen and a new pen. Use a calculator to plan the doses as instructed by your healthcare provider.

**SAXENDA® (liraglutide) injection 3mg Instructions for Use**

- Be very careful to calculate correctly.
- If you are not sure how to split your dose using 2 pens, then select and inject the dose you need with a 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.

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.

• 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.

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.

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).

This Medication Guide and Instructions for Use have been approved by the U.S. Food and Drug Administration.