HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use Victoza® safely and effectively. See full prescribing information for Victoza®.

Victoza® (liraglutide [rDNA origin] injection), solution for subcutaneous use

Initial U.S. Approval: 2010

BOXED WARNING
• Liraglutide causes thyroid C-cell tumors at clinically relevant exposures in both genders of rats and mice. It is unknown whether Victoza® 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, 13.1).

• Victoza® is contraindicated in patients with a personal or family history of MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Counsel patients regarding the potential risk of MTC and the symptoms of thyroid tumors (4.5.1).

ADVERSE REACTIONS
• Hypoglycemia
• Pancreatitis
• Hypersensitivity: Postmarketing reports of serious hypersensitivity reactions (e.g., anaphylactic shock) occur uncommonly. Use caution when initiating or escalating doses of Victoza® in patients with renal impairment (5.5).

• Maculopapular rash
• Pruritus
• Asthenia
• Headache
• Nausea
• Diarrhea

• Use with Medications Known to Cause Hypoglycemia
• Use with Oral Medications

WARNING: RISK OF THYROID C−CELL TUMORS
See full prescribing information for complete boxed warning.

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Recent Major Changes
03/2015 Boxed Warning
03/2015 Indications and Usage: Important Limitations of Use (1.1)
03/2015 Warnings and Precautions: Risk of Thyroid C−cell Tumors (5.1)
02/2015 Warnings and Precautions: Never Share a Victoza® Pen Between Patients (5.3)

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Victoza® (liraglutide [rDNA origin]) injection, solution for subcutaneous use

FULL PRESCRIBING INFORMATION

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 Victoza® 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)].

• Victoza® 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 for MTC with the use of Victoza® 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 Victoza® [see Contraindications (4) and Warnings and Precautions (5.1)].

1 INDICATIONS AND USAGE

Victoza® is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

1.1 Important Limitations of Use

• Victoza® is not recommended as first-line therapy for patients who have inadequate glycemic control on diet and exercise because of the uncertain relevance of the rodent C−cell tumor findings to humans. Prescribe Victoza® only to patients for whom the potential benefits are considered to outweigh the potential risk [see Warnings and Precautions (5.1)].

• Based on spontaneous postmarketing reports, acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis has been observed in patients treated with Victoza®.

• Victoza® has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for pancreatitis while using Victoza®. Other antidiabetic therapies should be considered in patients with a history of pancreatitis.

• Victoza® is not a substitute for insulin. Victoza® should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings.

• The concurrent use of Victoza® and prandial insulin has not been studied.

2 DOSAGE AND ADMINISTRATION

Victoza® can be administered once daily at any time of day, independently of meals, and can be injected subcutaneously in the abdomen, thigh or upper arm. The injection site and timing can be changed without dose adjustment.

For all patients, Victoza® should be initiated with a dose of 0.6 mg per day for one week. The 0.6 mg dose is a starting dose intended to reduce gastrointestinal symptoms during initial titration, and is not effective for glycemic control. After one week at 0.6 mg per day, the dose should be increased to 1.2 mg. If the 1.2 mg dose does not result in acceptable glycemic control, the dose can be increased to 1.8 mg.

When initiating Victoza®, consider reducing the dose of concomitantly administered insulin secretagogues (such as sulfonylureas) to reduce the risk of hypoglycemia [see Warnings and Precautions (5.4) and Adverse Reactions (6)].

When using Victoza® with insulin, administer as separate injections. Never mix. It is acceptable to inject Victoza® and insulin in the same body region but the injections should not be adjacent to each other. Victoza® solution should be inspected prior to each injection, and the solution should be used only if it is clear, colorless, and contains no particles.

If a dose is missed, the once-daily regimen should be resumed as prescribed with the next scheduled dose. An extra dose or increase in dose should not be taken to make up for the missed dose.

Based on the elimination half-life, patients should be advised to reinitiate Victoza® at 0.6 mg if more than 3 days have elapsed since the last Victoza® dose. This approach will mitigate any gastrointestinal symptoms associated with reinitiation of treatment. Upon reinitiation, Victoza® should be titrated at the discretion of the prescribing healthcare provider.

3 DOSAGE FORMS AND STRENGTHS

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

4 CONTRAINDICATIONS

Victoza® is contraindicated in patients with a personal or family history of medullary thyroid carcinoma (MTC) or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2).

Victoza® is contraindicated in patients with a prior serious hypersensitivity reaction to Victoza® or to any of the product components.

5 WARNINGS AND PRECAUTIONS

5.1 Risk of Thyroid C−Cell Tumors

Liraglutide causes dose-dependent and treatment-duration-dependent thyroid C−cell tumors (adenomas and/or carcinomas) at clinically relevant exposures in both genders of rats and mice [see Nonclinical Toxicology (13.1)]. Malignant thyroid C−cell carcinomas were detected in rats and mice. It is unknown whether Victoza® 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 Victoza® have been reported in the postmarketing period; the data in these reports are insufficient to establish or exclude a causal relationship between MTC and Victoza® use in humans.

Victoza® 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 Victoza® 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 Victoza®. 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 pancreatic tumors (including persistent severe abdominal pain, sometimes radiating to the back and which may or may not be accompanied by vomiting). If pancreatitis is suspected, Victoza® should promptly be discontinued and appropriate management should be initiated. If pancreatitis is confirmed, Victoza® should not be restarted. Consider antidiabetic therapies other than Victoza® in patients with a history of pancreatitis.

In clinical trials of Victoza®, there have been 13 cases of pancreatitis among Victoza®−treated patients and 1 case in a comparator (glimepiride) treated patient (2.7 vs. 0.5 cases per 1000 patient−years). Nine of the 13 cases with Victoza® were reported as acute pancreatitis and four were reported as chronic pancreatitis. In one case in a Victoza®−treated patient, pancreatitis, with necrosis, was observed and led to death, however clinical causality could not be established. Some patients had other risk factors for pancreatitis, such as a history of cholelithiasis or alcohol abuse.

5.3 Never Share a Victoza® Pen Between Patients

Victoza® pens must never be shared between patients, even if the needle is changed. Pen-sharing poses a risk for transmission of blood−borne pathogens.

5.4 Use with Medications Known to Cause Hypoglycemia

Patients receiving Victoza® in combination with an insulin secretagogue (e.g., sulfonylurea) or insulin may have an increased risk of hypoglycemia. The risk of hypoglycemia may be lowered by a reduction in the dose of sulfonylurea (or other concomitantly administered insulin secretagogues) or insulin [see Adverse Reactions (6.1)].

5.5 Renal Impairment

Victoza® has not been found to be directly nephrotoxic in animal studies or clinical trials. There have been postmarketing reports of acute renal failure and worsening of chronic renal failure, which may sometimes require hemodialysis in Victoza®−treated patients [see Adverse Reactions (6.2)]. Some of these events were reported in patients without known underlying renal disease. A majority of the reported events occurred in patients who had experienced nausea, vomiting, diarrhea, or dehydration [see Adverse Reactions (6.1)]. Some of the reported events occurred in patients receiving one or more medications known to affect renal function or hydration status. Altered renal function has been reversed in many of the reported cases with supportive treatment and discontinuation of potentially causative agents, including Victoza®. Use caution when initiating or escalating doses of Victoza® in patients with renal impairment [see Use in Specific Populations (8.6)].

6 Hypersensitivity Reactions

There have been postmarketing reports of serious hypersensitivity reactions (e.g., anaphylactic reactions and angioedema) in patients treated with Victoza®. If a hypersensitivity reaction occurs, the patient should discontinue Victoza® and other suspect medications and promptly seek medical advice.

Angioedema has also been reported with other GLP−1 receptor agonists. Use caution in a patient with a history of angioedema with another GLP−1 receptor agonist because it is unknown whether such patients will be predisposed to angioedema with Victoza®.

5.7 Macrovacular Outcomes

There have been no clinical studies establishing conclusive evidence of macrovacular risk reduction with Victoza® or any other antidiabetic drug.

6 ADVERSE REACTIONS

The following serious adverse reactions are described below or elsewhere in the prescribing information:

• Risk of Thyroid C−Cell Tumors [see Warnings and Precautions (5.1)]

• Pancreatitis [see Warnings and Precautions (5.2)]

• Use with Medications Known to Cause Hypoglycemia [see Warnings and Precautions (5.4)]

• Renal Impairment [see Warnings and Precautions (5.5)]

• Hypersensitivity Reactions [see Warnings and Precautions (5.6)]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of Victoza® has been evaluated in 8 clinical trials [see Clinical Studies (14)].

• A double−blind 52−week monotherapy trial compared Victoza® 1.2 mg daily, Victoza® 1.8 mg daily, and glimepiride 8 mg daily.

• A double−blind 26 week add−on to metformin trial compared Victoza® 0.6 mg once−daily, Victoza® 1.2 mg once−daily, Victoza® 1.8 mg once−daily, placebo, and glimepiride 4 mg once−daily.

• A double−blind 26 week add−on to glimepiride trial compared Victoza® 0.6 mg daily, Victoza® 1.2 mg once−daily, Victoza® 1.8 mg once−daily, placebo, and rosiglitazone 4 mg once−daily.

• A 26 week add−on to metformin + glimepiride trial, compared double−blind Victoza® 1.8 mg once−daily, double−blind placebo, and open−label insulin glargine once−daily.

• A double−blind 26 week add−on to metformin + rosiglitazone trial compared Victoza® 1.2 mg once−daily, Victoza® 1.8 mg once−daily, and sitagliptin 100 mg once−daily.
Victoza® (liraglutide [rDNA origin] injection), solution for subcutaneous use

- An open-label 26-week trial compared insulin detemir as add-on to Victoza® 1.8 mg + metformin to continued treatment with Victoza® + metformin alone.

Withdrawals

The incidence of withdrawal due to adverse events was 7.8% for Victoza®-treated patients and 3.4% for comparator-treated patients in the five double-blind controlled trials of 26 weeks duration or longer. This difference was driven by withdrawals due to gastrointestinal adverse reactions, which occurred in 5.0% of Victoza®-treated patients and 0.5% of comparator-treated patients. In these five trials, the most common adverse reactions leading to withdrawal for Victoza®-treated patients were nausea (2.8% versus 0% for comparator) and vomiting (1.5% versus 0.1% for comparator). Withdrawal due to gastrointestinal adverse events mainly occurred during the first 2-3 months of the trials.

Common adverse reactions

Tables 1, 2, 3, and 4 summarize common adverse reactions (hypoglycemia is discussed separately) reported in seven of the eight controlled trials of 26 weeks duration or longer. Most of these adverse reactions were gastrointestinal in nature.

In the five double-blind clinical trials of 26 weeks duration or longer, gastrointestinal adverse reactions were reported in 41% of Victoza®-treated patients and were dose-related. Gastrointestinal adverse reactions occurred in 17% of comparator-treated patients. Common adverse reactions that occurred at a higher incidence among Victoza®-treated patients included nausea, vomiting, diarrhea, dyspepsia and constipation.

In the five double-blind and three open-label clinical trials of 26 weeks duration or longer, the percentage of patients who reported nausea declined over time. In the five double-blind trials approximately 13% of Victoza®-treated patients and 2% of comparator-treated patients reported nausea during the first 2 weeks of treatment.

In the 26-week open-label trial comparing Victoza® to exenatide, both in combination with metformin and/or sulfonylurea, gastrointestinal adverse reactions were reported at a similar incidence in the Victoza® and exenatide treatment groups (Table 3).

In the 26-week open-label trial comparing Victoza®, 1.2 mg, Victoza® 1.8 mg and sitagliptin 100 mg, all in combination with metformin, gastrointestinal adverse reactions were reported at a higher incidence with Victoza® than sitagliptin (Table 4).

In the remaining 26-week trial, all patients received Victoza® 1.8 mg + metformin during a 12-week run-in period. During the run-in period, 167 patients (17% of enrolled) withdrew from the trial: 76 (46% of withdrawals) of these patients doing so because of gastrointestinal adverse reactions and 15 (9% of withdrawals) doing so due to other adverse events. Only those patients who completed the run-in period with inadequate glycemic control were randomized to 26 weeks of add-on therapy with Victoza® 1.8 mg + metformin. During this randomized 26-week period, diarrhea was the only adverse reaction reported in 25% of patients treated with Victoza® 1.8 mg + metformin + insulin detemir (11.7%) and greater than in patients treated with Victoza® 1.8 mg and metformin alone (6.9%).

Table 1: Adverse reactions reported in ≥5% of Victoza®-treated patients in a 52-week monotherapy trial

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>All Victoza® N = 487</th>
<th>Glimepiride N = 248</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>28.4</td>
<td>8.5</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>17.1</td>
<td>8.9</td>
</tr>
<tr>
<td>Vomiting</td>
<td>10.9</td>
<td>3.6</td>
</tr>
<tr>
<td>Constipation</td>
<td>9.9</td>
<td>4.8</td>
</tr>
<tr>
<td>Headache</td>
<td>9.1</td>
<td>9.3</td>
</tr>
</tbody>
</table>

Table 2: Adverse reactions reported in ≥5% of Victoza®-treated patients and occurring more frequently with Victoza® compared to placebo: 26-week combination therapy trials

Add-on to Metformin Trial

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>All Victoza® + Metformin N = 724</th>
<th>Placebo + Metformin N = 121</th>
<th>Glimepiride + Metformin N = 242</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>15.2</td>
<td>4.1</td>
<td>3.7</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>10.4</td>
<td>4.1</td>
<td>3.7</td>
</tr>
<tr>
<td>Headache</td>
<td>9.0</td>
<td>6.6</td>
<td>9.5</td>
</tr>
<tr>
<td>Vomiting</td>
<td>6.5</td>
<td>0.8</td>
<td>0.4</td>
</tr>
</tbody>
</table>

Add-on to Glimepiride Trial

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>All Victoza® + Glimepiride N = 866</th>
<th>Placebo + Glimepiride N = 114</th>
<th>Rosiglitazone + Glimepiride N = 231</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>7.5</td>
<td>1.8</td>
<td>2.6</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>7.2</td>
<td>1.8</td>
<td>2.2</td>
</tr>
<tr>
<td>Constipation</td>
<td>5.3</td>
<td>8.9</td>
<td>1.7</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>5.2</td>
<td>8.9</td>
<td>2.6</td>
</tr>
</tbody>
</table>

Add-on to Metformin + Glimepiride

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Victoza® 1.8 + Metformin + Glimepiride N = 230</th>
<th>Placebo + Metformin + Glimepiride N = 114</th>
<th>Glargine + Metformin + Glimepiride N = 232</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>13.3</td>
<td>3.5</td>
<td>1.3</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>10.8</td>
<td>5.3</td>
<td>1.3</td>
</tr>
<tr>
<td>Headache</td>
<td>9.8</td>
<td>7.9</td>
<td>5.6</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>6.5</td>
<td>8.9</td>
<td>1.7</td>
</tr>
<tr>
<td>Vomiting</td>
<td>6.5</td>
<td>3.5</td>
<td>0.4</td>
</tr>
</tbody>
</table>

Add-on to Metformin + Rosiglitazone

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>All Victoza® + Metformin + Rosiglitazone N = 355</th>
<th>Placebo + Metformin + Rosiglitazone N = 175</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>34.6</td>
<td>8.6</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>14.1</td>
<td>6.3</td>
</tr>
<tr>
<td>Vomiting</td>
<td>12.4</td>
<td>2.9</td>
</tr>
<tr>
<td>Headache</td>
<td>8.2</td>
<td>4.6</td>
</tr>
<tr>
<td>Constipation</td>
<td>5.1</td>
<td>1.1</td>
</tr>
</tbody>
</table>

Table 3: Adverse Reactions reported in ≥5% of Victoza®-treated patients in a 26-Week Open-Label Trial versus Exenatide

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Victoza® 1.8 mg once daily + metformin and/or sulfonylureas N = 235</th>
<th>Exenatide 10 mg twice daily + metformin and/or sulfonylureas N = 232</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>25.5</td>
<td>20.0</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>12.3</td>
<td>12.1</td>
</tr>
<tr>
<td>Vomiting</td>
<td>6.8</td>
<td>10.3</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>8.9</td>
<td>4.7</td>
</tr>
<tr>
<td>Headache</td>
<td>6.0</td>
<td>9.9</td>
</tr>
<tr>
<td>Constipation</td>
<td>5.1</td>
<td>2.6</td>
</tr>
</tbody>
</table>

Table 4: Adverse Reactions reported in ≥5% of Victoza®-treated patients in a 26-Week Open-Label Trial versus Sitagliptin

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>All Victoza® + metformin N = 439</th>
<th>Sitagliptin 100 mg/day + metformin N = 219</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>23.9</td>
<td>4.6</td>
</tr>
<tr>
<td>Headache</td>
<td>10.3</td>
<td>10.0</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>9.3</td>
<td>4.6</td>
</tr>
<tr>
<td>Vomiting</td>
<td>8.7</td>
<td>4.1</td>
</tr>
</tbody>
</table>

Immunogenicity

Consistent with the potentially immunogenic properties of protein and peptide pharmaceuticals, patients treated with Victoza® may develop anti-liraglutide antibodies. Approximately 50-70% of Victoza®-treated patients in the five double-blind clinical trials of 26 weeks duration or longer were tested for the presence of anti-liraglutide antibodies at the end of treatment. Low titers (concentrations not requiring dilution of serum) of anti-liraglutide antibodies were detected in 8.6% of these Victoza®-treated patients. Sampling was not performed uniformly across all patients in the clinical trials, and this may have resulted in an underestimate of the actual percentage of patients who developed antibodies. Cross-reacting anti-liraglutide antibodies to native glucagon-like peptide-1 (GLP-1) occurred in 6.9% of the Victoza®-treated patients in the double-blind 52-week monotherapy trial and in 4.8% of the Victoza®-treated patients in the double-blind 26-week add-on combination therapy trials. These cross-reacting antibodies were not tested for neutralizing effect against native GLP-1, and thus the potential for clinically significant neutralization of native GLP-1 was not assessed. Antibodies that had a neutralizing effect on liraglutide in an in vitro assay occurred in 2.3% of the Victoza®-treated patients in the double-blind 52-week monotherapy trial and in 1.0% of the Victoza®-treated patients in the double-blind 26-week add-on combination therapy trials.

Among Victoza®-treated patients who developed anti-liraglutide antibodies, the most common category of adverse events was that of infections, which occurred among 40% of these patients compared to 36%, 34% and 35% of antibody-negative Victoza®-treated, placebo-treated and active-control-treated patients, respectively. The specific infections which occurred with greater frequency among Victoza®-treated antibody-positive patients were primarily nonserious upper respiratory tract infections, which occurred among 11% of Victoza®-treated antibody-positive patients, and among 7%, 7% and 5% of antibody-negative Victoza®-treated, placebo-treated and active-control-treated patients, respectively. Antibody formation was not associated with reduced efficacy on liraglutide in an immunogenicity event composite analysis. In the eight clinical trials of at least 26 weeks duration, hypoglycemia requiring the assistance of another person for treatment occurred in 11 Victoza®-treated patients (2.3 cases per 1000 patient-years) and in 1 case in a comparator-treated patient (0.5 cases per 1000 patient-years). Most of these hypoglycemia thyroid cancers were <1 cm in greatest diameter and were diagnosed in surgical pathology specimens after thyroidectomy prompted by findings on protocol-specified screening with serum calcitonin or thyroid ultrasound.

Hypoglycemia

In the eight clinical trials of at least 26 weeks duration, hypoglycemia requiring the assistance of another person for treatment occurred in 11 Victoza®-treated patients (2.3 cases per 1000 patient-years) and in
two exenatide-treated patients. Of these 11 Victoza®-treated patients, six patients were concomitantly using metformin and a sulfonylurea, one was concomitantly using metformin and a dipeptidyl peptidase-4 (DPP-4) inhibitor, one was concomitantly using metformin and a glucagon-like peptide-1 (GLP-1) receptor agonist, one was concomitantly using metformin and a thiazolidinedione, and two were receiving exenatide alone. The long-term clinical effects of the increase in pulse rate have not been established (see Warnings and Precautions (5.7)).

6.2 Post-Marketing Experience

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

- Medullary thyroid carcinoma (see Warnings and Precautions (5.1))
- Dehydration resulting from nausea, vomiting and diarrhea. (see Warnings and Precautions (5.5) and Patient Counseling Information (17.3))
- Increased serum creatinine, acute renal failure or worsening of chronic renal failure, sometimes requiring hemodialysis. (see Warnings and Precautions (5.5) and Patient Counseling Information (17.3))
- Angioedema and anaphylactic reactions. (see Contraindications (4), Warnings and Precautions (5.6), Patient counseling Information (17.6))
- Allergic reactions: rash and pruritus
- Acute pancreatitis, hemorrhagic and necrotizing pancreatitis sometimes resulting in death (see Warnings and Precautions (5.2))

7 DRUG INTERACTIONS

7.1 Oral Medications

Victoza® causes a delay of gastric emptying, and thereby has the potential to impact the absorption of concomitantly administered oral medications. In clinical pharmacology trials, Victoza® did not affect the absorption of the tested orally administered medications to any clinically relevant degree. Nonetheless, caution should be exercised when oral medications are concomitantly administered with Victoza®.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C

There are no adequate and well-controlled studies of Victoza® in pregnant women. Victoza® should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Liraglutide has been shown to be teratogenic in rats at or above 0.8 times the human systemic exposures resulting from the maximum recommended human dose (MRHD) of 1.8 mg/kg based on plasma area under the time-concentration curve (AUC). Liraglutide has been shown to cause reduced growth and increased total major abnormalities in rabbits at systemic exposures below human exposure at the MRHD based on plasma AUC.

Female rats given subcutaneous doses of 0.1, 0.25 and 1.0 mg/kg/day liraglutide beginning 2 weeks before mating through gestation day 17 had estimated systemic exposures 0.8-, 3-, and 11-times the human exposure at the MRHD based on plasma AUC in comparison. The number of early embryonic deaths in the 1 mg/kg/day group increased slightly. Fetal abnormalities and variations in kidneys and blood vessels, irregular ossification of the skull, and a more complete state of ossification occurred at all doses. Mottled liver and minimally kinked ribs occurred at the highest dose. The incidence of fetal malformations in liraglutide-treated groups exceeding concurrent and historical controls were micromegapharynx and/or narrowed opening into larynx at 0.1 mg/kg/day and umbilical hernia at 0.1 and 0.25 mg/kg/day. Pregnant rabbits given subcutaneous doses of 0.01, 0.025 and 0.05 mg/kg/day liraglutide from gestation day 6 through day 18 inclusive, had estimated systemic exposures less than the human exposure at the MRHD of 1.8 mg/kg/day at all doses, based on plasma AUC. Liraglutide decreased fetal weight and dose-dependently increased the incidence of total major fetal abnormalities at all doses. The incidence of malformations exceeded concurrent and historical controls at 0.01 mg/kg/day (kidneys, scapula, >0.01 mg/kg/day (eyes, forelimb), 0.025 mg/kg/day (brain, tail, and sacral vertebrae, major blood vessels and heart, umbilicus), ≥0.025 mg/kg/day (sternum) and at 0.05 mg/kg/day (parietal bones, major blood vessels). Irregular ossification and/or skeletal abnormalities occurred in the skull and jaw, vertebrae and ribs, sternum, pelvis, tail, and scapula; and dose-dependent minor skeletal variations were observed. Visceral abnormalities occurred in blood vessels, lungs, liver, and esophagus. Bilobed or birefractured gallbladder was seen in all treatment groups, but not in the control group.

In pregnant female rats given subcutaneous doses of 0.1, 0.25 and 1.0 mg/kg/day liraglutide from gestation day 6 through weaning or termination of nursing on lactation day 24, estimated systemic exposures were 0.8-, 3-, and 11-times human exposure at the MRHD of 1.8 mg/kg/day, based on plasma AUC. A slight delay in parturition was observed in the majority of treated rats. Group mean body weight of neonatal rats from liraglutide-treated dams was lower than neonatal rats from control group dams. Bloody scabs and agitated behavior occurred in male rats descended from dams treated with 1 mg/kg/day liraglutide. Group mean body weight from birth to postpartum day 14 tended lower in F2 generation rats descended from liraglutide-treated rats compared to F1 generation rats descended from controls, but differences did not reach statistical significance for any group.

8.3 Nursing Mothers

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

8.4 Pediatric Use

Safety and effectiveness of Victoza® have not been established in pediatric patients. Victoza® is not recommended in pediatric patients.

8.5 Geriatric Use

In the Victoza® clinical trials, a total of 797 (20%) of the patients were 65 years of age and over and in 113 (2.8%) were 75 years of age and over. No overall differences in safety or effectiveness were observed between these patients and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

8.6 Renal Impairment

There is limited experience with Victoza® in patients with mild, moderate, and severe renal impairment, including end-stage renal disease. However, there have been postmarketing reports of acute renal failure and worsening of chronic renal failure, which may sometimes require hemodialysis (see Warnings and Precautions (5.5) and Adverse Reactions (6.2)). Victoza® should be used with caution in this patient population. No dose adjustment of Victoza® is recommended for patients with renal impairment (see Clinical Pharmacology (12.3)).

8.7 Hepatic Impairment

There is limited experience in patients with mild, moderate or severe hepatic impairment. Therefore, Victoza® should be used with caution in this patient population. No dose adjustment of Victoza® is recommended for patients with hepatic impairment (see Clinical Pharmacology (12.3)).
8.8 Gastropareis

Victoza® slows gastric emptying. Victoza® has not been studied in patients with pre-existing gastropareis.

10 OVERDOSE

Overdoses have been reported in clinical trials and post-marketing use of Victoza®. Effects have included severe nausea and severe vomiting. In the event of overdose, appropriate supportive treatment should be initiated according to the patient’s clinical signs and symptoms.

11 DESCRIPTION

Victoza® contains liraglutide, an analog of human GLP-1 and acts as a GLP-1 receptor agonist. The peptide precursor of liraglutide, produced by a process that includes expression of recombinant DNA in Saccharomyces cerevisiae, has been engineered to be 97% homologous to native human GLP-1 by substituting arginine for lysine at position 34. Liraglutide is made by attaching a C-16 fatty acid (palmitic acid) with a glutamic acid spacer on the remaining lysine residue at position 26 of the peptide precursor. The molecular formula of liraglutide is C₁₇₂H₂₆₅N₄₃O₅₁ and the molecular weight is 3751.2 Daltons. The structural formula (Figure 1) is:

\[
\text{C-16 fatty acid (palmitic acid)}
\]

Figure 1: Structural Formula of liraglutide

Victoza® is a clear, colorless solution. Each 1 mL of Victoza® solution contains 6 mg of liraglutide. Each pre-filled pen contains a 3 mL solution of Victoza® equivalent to 18 mg liraglutide (free-base, anhydrous) and the following inactive ingredients: disodium phosphate dihydrate, 1.42 mg; propylene glycol, anhydrous) and the following inactive ingredients: disodium phosphate dihydrate, 1.42 mg; propylene glycol, 14 mg; phenol, 5.5 mg; and water for injection.

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(7-37). GLP-1(7-37) represents <20% of total circulating endogenous GLP-1. Like GLP-1(7-37), liraglutide activates the GLP-1 receptor, a membrane-bound cell-surface receptor coupled to adenyl cyclase by the stimulatory G-protein, Gs, in pancreatic beta cells. Liraglutide increases intracellular cAMP (cAMP) leading to insulin release in the presence of elevated glucose concentrations. This insulin secretion subsides as blood glucose concentrations decrease and approach euglycemia. Liraglutide also decreases glucagon secretion in a glucose-dependent manner. The mechanism of blood glucose lowering also involves a delay in gastric emptying.

GLP-1(7-37) has a half-life of 1.5-2 minutes due to degradation by the ubiquitous endogenous enzymes, dipeptidyl peptidase IV (DPP-IV) and neutral endopeptidases (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 pharmacokinetic profile of liraglutide, which makes it suitable for once daily administration, is a result of self-association that delays absorption, plasma protein binding and stability against metabolic degradation by DPP-IV and NEP.

12.2 Pharmacodynamics

Victoza®’s pharmacodynamic profile is consistent with its pharmacokinetic profile observed after single subcutaneous administration as Victoza® lowered fasting, premeal and postprandial glucose throughout the day [see Clinical Pharmacology (12.3)].

Fasting and postprandial glucose was measured before and up to 5 hours after a standardized meal after treatment to steady state with 0.6, 1.2 and 1.8 mg Victoza® or placebo. Compared to placebo, the postprandial plasma glucose AUC₀-300min was 35% lower after Victoza® 1.2 mg and 38% lower after Victoza® 1.8 mg.

Glucose-dependent insulin secretion

The effect of a single dose of 7.5 mcg/kg (~ 0.7 mg) Victoza® on insulin secretion rates (ISR) was investigated in 10 patients with type 2 diabetes during graded glucose infusion. In these patients, on average, the ISR response was increased in a glucose-dependent manner (Figure 2).

Figure 2: Mean Insulin Secretion Rate (ISR) versus Glucose Concentration Following Single-Dose Victoza® 7.5 mcg/kg (~ 0.7 mg) or Placebo in Patients with Type 2 Diabetes (N=10) During Graded Glucose Infusion

12.3 Pharmacokinetics

Absorption - Following subcutaneous administration, maximum concentrations of liraglutide are achieved at 8-12 hours post dosing. The mean peak (Cₚₚₚₚ) and total (AUC) exposures of liraglutide were 35 ng/mL and 960 ng·h/mL, respectively, for a subcutaneous single dose of 0.6 mg. After subcutaneous single dose administrations, Cₚₚₚₚ and AUC of liraglutide increased proportionally over the therapeutic dose range of 0.6 mg to 1.8 mg. At 1.8 mg Victoza®, the average steady state concentration of liraglutide over 24 hours was approximately 128 ng/mL. AUC₀-∞ was equivalent between upper arm and abdomen, and between upper arm and thigh. AUC₀-∞ from thigh was 22% lower than that from abdomen. However, liraglutide exposures were considered comparable among these three subcutaneous injection sites. Absolute bioavailability of liraglutide following subcutaneous administration is approximately 55%.

Distribution - The mean apparent volume of distribution after subcutaneous administration of Victoza® 0.6 mg is approximately 13 L. The mean volume of distribution after intravenous administration of Victoza® is 0.07 L/kg. Liraglutide is extensively bound to plasma protein (~98%).

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

Elimination - Following a [H]liraglutide dose, intact liraglutide was not detected in urine or feces. Only a minor part of the administered radioactivity was excreted as liraglutide-related metabolites in urine or feces (6% and 5%, respectively). The majority of urine and feces radioactivity was excreted during the first 6-8 days. The mean apparent clearance following subcutaneous administration of a single dose of liraglutide is approximately 1.2 L/h with an elimination half-life of approximately 13 hours, making Victoza® suitable for once daily administration.

Specific Populations

12.3.1 Elderly - Age had no effect on the pharmacokinetics of Victoza® based on a pharmacokinetic study in healthy elderly subjects (65 to 83 years) and population pharmacokinetic analyses of patients 18 to 80 years of age [see Use in Specific Populations (8.5)].

Gender - Based on the results of population pharmacokinetic analyses, females have 34% lower weight-adjusted clearance of Victoza® compared to males. Based on the exposure response data, no dose adjustment is necessary based on gender.

Race and Ethnicity - Race and ethnicity had no effect on the pharmacokinetics of Victoza® based on the results of population pharmacokinetic analyses that included Caucasian, Black, Asian and Hispanic/Non-Hispanic subjects.

Body Weight - Body weight significantly affects the pharmacokinetics of Victoza® based on results of population pharmacokinetic analyses. The exposure of liraglutide decreases with an increase in baseline body weight. However, the 1.2 mg and 1.8 mg daily doses of Victoza® provided a marked systemic exposures over the body weight range of 40 – 160 kg evaluated in the clinical trials. Liraglutide was not studied in patients with body weight >160 kg.

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

Renal Impairment - The single-dose pharmacokinetics of Victoza® were evaluated in subjects with varying degrees of renal impairment. Subjects with mild (estimated creatinine clearance 50-80 mL/min) to severe (estimated creatinine clearance <30 mL/min) renal impairment and subjects with end-stage renal disease requiring dialysis were included in the trial. Compared to healthy subjects, liraglutide AUC in mild, moderate, and severe renal impairment and in end-stage renal disease was on average 35%, 19%, 29% and 30% lower, respectively [see Use in Specific Populations (8.6)].

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

Drug Interactions

In vitro assessment of drug-drug interactions

Victoza® has low potential for pharmacokinetic drug-drug interactions related to cytochrome P450 (CYP) and plasma protein binding.

In vivo assessment of drug-drug interactions

The drug-drug interaction studies were performed at steady state with Victoza® 1.8 mg/day. Before administration of concomitant treatment, subjects underwent a 0.6 mg weekly dose increase to reach the maximum dose of 1.8 mg/day. Administration of the interacting drugs was timed so that Cₚₚₚₚ of Victoza® (8-12 h) would coincide with the absorption peak of the co-administered drugs.

Digoxin

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

Lisinopril

A single dose of lisinopril 20 mg was administered 5 minutes after the dose of Victoza® at steady state. The co-administration with Victoza® resulted in a reduction of lisinopril AUC by 15%; Cₚₚₚₚ decreased by 27%. Lisinopril median Tₘₚₚₚₚ was delayed from 6 h to 8 h with Victoza®.
A 104-week carcinogenicity study was conducted in male and female Sprague Dawley rats at doses of 0.075, 0.25 and 0.75 mg/kg/day liraglutide administered by bolus subcutaneous injection with exposures 0.5-, 2- and 8-times the human exposure, respectively, at the MRHD based on plasma AUC comparison. A treatment-related increase in benign thyroid C-cell adenomas was observed in males in 0.25 and 0.75 mg/kg/day liraglutide groups with incidences of 12%, 16%, 42%, and 46% and in all female liraglutide-treated groups with incidences of 10%, 27%, 33%, and 56% in control; 0.075, 0.25, and 0.75 mg/kg/day groups. Treatment-related malignant C-cell carcinomas occurred in 3% of females in the 3.0 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 exposed for drug injection, in males in the 3 mg/kg/day group. These fibrosarcomas were attributed to the high local concentration of drug near the injection site. The liraglutide concentration in the clinical formulation (6 mg/mL) is 10 times higher than the concentration in the formulation used to administer 3 mg/kg/day liraglutide to mice in the carcinogenicity study (0.6 mg/mL).

A 104-week carcinogenicity study was conducted in male and female Sprague Dawley rats at doses of 0.075, 0.25 and 0.75 mg/kg/day liraglutide administered by bolus subcutaneous injection with exposures 0.5-, 2- and 8-times the human exposure, respectively, resulting from the MRHD based on plasma AUC comparison. A treatment-related increase in benign thyroid C-cell adenomas was seen in males in the 0.25 and 0.75 mg/kg/day liraglutide groups with incidences of 12%, 16%, 42%, and 46% and in all female liraglutide-treated groups with incidences of 10%, 27%, 33%, and 56% in control; 0.075, 0.25, and 0.75 mg/kg/day groups. Treatment-related malignant C-cell carcinomas was observed in all male liraglutide-treated groups with incidences of 2%, 8%, 6%, and 14% and in females at 0.25 and 0.75 mg/kg/day with incidences of 0%, 0%, 4%, and 6% in control; 0.075, 0.25, and 0.75 mg/kg/day groups, respectively. Thyroid C-cell carcinomas are rare findings during carcinogenicity testing in rats. Studies in mice demonstrated that liraglutide-induced C-cell proliferation was dependent on the GLP-1 receptor and that liraglutide did not cause activation of the ReArranged during Transfection (RET) proto-oncogene in thyroid C-cells. Human relevance of thyroid C-cell tumors in mice and rats is unknown and has not been determined by clinical studies or nonclinical studies (see Boxed Warning and Warnings and Precautions (5.1)). Liraglutide was negative with and without metabolic activation in the Ames test for mutagenicity and in a human peripheral blood lymphocyte chromosome aberration test for clastogenicity. Liraglutide was negative in repeat-dose in vivo micronucleus tests in rats.

In rat fertility studies using subcutaneous doses of 0.1, 0.25 and 1.0 mg/kg/day liraglutide, males were treated for 4 weeks prior to and through mating and females were treated 2 weeks prior to and throughout mating until gestation day 17. No direct adverse effects on male fertility was observed at doses up to 1.0 mg/kg/day, a repeated systemic exposure yielding an estimated maximum plasma exposure of 11-14 times the human exposure at the MRHD, based on plasma AUC. In fetal rats, an increase in early embryonic deaths occurred at 1.0 mg/kg/day. Reduced body weight gain and food consumption were observed in females at the 1.0 mg/kg/day dose.

13 CLINICAL STUDIES

A total of 6090 patients with type 2 diabetes participated in 8 phase 3 trials. There were 5 double-blind (one of these trials had an open-label active control insulin glargine arm), randomized, controlled clinical trials, one of 52 weeks duration and four of 26 weeks duration. There were also three 26 weeks open-label trials, one comparing Victoza® to twice-daily exenatide, one comparing Victoza® to sitagliptin and one comparing Victoza®-metformin-insulin detemir to Victoza®-metformin alone. These multinational trials were conducted to evaluate the glycemic efficacy and safety of Victoza® in type 2 diabetes as monotherapy and in combination with one or two oral anti-diabetic medications or insulin detemir. The 7 add-on combination therapy trials enrolled patients who were previously treated with anti-diabetic therapy, and approximately two-thirds of patients in the monotherapy trial also were previously treated. In total, 272 (4%) of the 6090 patients in these 8 trials were new to anti-diabetic therapy. In these 8 clinical trials, patients ranged in age from 18-80 years old and 54% were men. Approximately 82% of patients were Caucasian, and 6% were Black. In the 5 trials where ethnicity was captured, 10% of patients were Hispanic/Latino (n=630).

In each of the placebo controlled trials, treatment with Victoza® produced clinically and statistically significant improvements in hemoglobin A1c and fasting plasma glucose (FPG) compared to placebo. All Victoza®-treated patients started at 0.6 mg/day. The dose was increased in weekly intervals by 0.6 mg to reach 1.2 mg or 1.8 mg for patients randomized to these higher doses. Victoza® 0.6 mg is not effective for glycemic control and is intended only as a starting dose to reduce gastrointestinal intolerance (see Dosage and Administration (2)).

14.1 Monotherapy

In this 52-week trial, 746 patients were randomized to Victoza® 1.2 mg, Victoza® 1.8 mg, or glimepiride 8 mg. Patients who were randomized to glimepiride were initially treated with 2 mg daily for two weeks, increasing to 4 mg daily for another two weeks, and finally increasing to 8 mg daily. Treatment with Victoza® 1.8 mg and 1.2 mg resulted in a statistically significant reduction in HbA1c compared to glimepiride (Table 6). The percentage of patients who discontinued due to ineffective therapy was 3.6% in the Victoza® 1.8 mg treatment group, 6.0% in the Victoza® 1.2 mg treatment group, and 10.1% in the glimepiride-treatment group.

Table 6: Results of a 52-week monotherapy trial

<table>
<thead>
<tr>
<th></th>
<th>Victoza® 1.8 mg</th>
<th>Victoza® 1.2 mg</th>
<th>Glimepiride 8 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intent-to-Treat Population (N)</td>
<td>246</td>
<td>251</td>
<td>248</td>
</tr>
<tr>
<td>HbA1c (%) (Mean)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>8.2</td>
<td>8.2</td>
<td>8.2</td>
</tr>
<tr>
<td>Change from baseline</td>
<td>-1.1</td>
<td>-0.8</td>
<td>-0.5</td>
</tr>
<tr>
<td>(adjusted mean)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Difference from glimepiride arm (adjusted mean)</td>
<td>-0.6**</td>
<td>-0.3*</td>
<td></td>
</tr>
<tr>
<td>95% Confidence Interval</td>
<td>(-0.8, -0.4)</td>
<td>(-0.5, -0.1)</td>
<td></td>
</tr>
<tr>
<td>Percentage of patients achieving A1c &lt;7%</td>
<td>51</td>
<td>43</td>
<td>28</td>
</tr>
</tbody>
</table>

Fasting Plasma Glucose (mg/dL) (Mean)

|                          |                |                |                 |
| Baseline                 | 172            | 168            | 172             |
| Change from baseline     | -26            | -15            | -5              |
| (adjusted mean)          |                |                |                 |
| Difference from glimepiride arm (adjusted mean) | -20**          | -10            |                 |
| 95% Confidence Interval  | (-29, -12)     | (-19, -1)      |                 |

Body Weight (kg) (Mean)

|                          |                |                |                 |
| Baseline                 | 92.6           | 92.1           | 93.3            |
| Change from baseline     | -2.5           | -2.1           | +1.1            |
| (adjusted mean)          |                |                |                 |
| Difference from glimepiride arm (adjusted mean) | -3.6**         | -3.2**         |                 |
| 95% Confidence Interval  | (-4.3, -2.9)   | (-3.8, -2.5)   |                 |

*p-value < 0.05
**p-value < 0.001

Figure 3: Mean HbA1c for patients who completed the 52-week trial and for the Last Observation Carried Forward (LOCF, intent-to-treat) data at Week 52 (Monotherapy)

14.2 Combination Therapy

Add-on to Metformin

In this 26-week trial, 1091 patients were randomized to Victoza® 0.6 mg, Victoza® 1.2 mg, Victoza® 1.8 mg, placebo, or glimepiride 4 mg (one-half of the maximal approved dose in the United States), all as add-on to metformin. Randomization occurred after a 6-week run-in period consisting of a 3-week initial forced metformin titration period followed by a maintenance period of another 3 weeks. During the titration period, doses of metformin were increased up to 2000 mg/day. Treatment with Victoza® 1.2 mg and 1.8 mg as add-on to metformin resulted in a significant mean HbA1c reduction relative to placebo add-on to metformin and resulted in a similar mean HbA1c reduction relative to glimepiride 4 mg add-on to metformin (Table 7). The percentage of patients who discontinued due to ineffective therapy was 5.4% in the Victoza® 1.8 mg + metformin treatment group, 3.3% in the Victoza® 1.2 mg + metformin treatment group, 23.8% in the placebo + metformin treatment group, and 3.7% in the glimepiride + metformin treatment group.
Table 7: Results of a 26-week trial of Victoza® as add-on to metformin

<table>
<thead>
<tr>
<th>HbA1c (%) (Mean)</th>
<th>Victoza® 1.8 mg + Metformin</th>
<th>Victoza® 1.2 mg + Metformin</th>
<th>Placebo + Metformin</th>
<th>Glimepiride 4 mg† + Metformin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intent-to-Treat Population (N)</td>
<td>242</td>
<td>240</td>
<td>121</td>
<td>242</td>
</tr>
<tr>
<td>Baseline</td>
<td>8.4</td>
<td>8.3</td>
<td>8.4</td>
<td>8.4</td>
</tr>
<tr>
<td>Change from baseline (adjusted mean)†</td>
<td>-1.0</td>
<td>-1.0</td>
<td>-0.1</td>
<td>-1.0</td>
</tr>
<tr>
<td>Difference from placebo + metformin arm (adjusted mean)†</td>
<td>-1.1**</td>
<td>-1.1**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>95% Confidence Interval</td>
<td>(-1.3, -0.9)</td>
<td>(-1.3, -0.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Difference from glimepiride + metformin arm (adjusted mean)†</td>
<td>0.0</td>
<td>0.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>95% Confidence Interval</td>
<td>(-0.2, 0.2)</td>
<td>(-0.2, 0.2)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Percentage of patients achieving HbA1c <7%: 42 vs 35 vs 11 vs 36

Table 8: Results of a 26-week open-label trial of Victoza® Compared to Sitagliptin (both in combination with metformin)

<table>
<thead>
<tr>
<th>HbA1c (%) (Mean)</th>
<th>Victoza® 1.8 mg + Metformin</th>
<th>Victoza® 1.2 mg + Metformin</th>
<th>Placebo + Metformin</th>
<th>Glimepiride 4 mg† + Metformin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intent-to-Treat Population (N)</td>
<td>218</td>
<td>221</td>
<td>116</td>
<td>219</td>
</tr>
<tr>
<td>Baseline</td>
<td>8.4</td>
<td>8.4</td>
<td>8.4</td>
<td>8.5</td>
</tr>
<tr>
<td>Change from baseline (adjusted mean)†</td>
<td>-1.5</td>
<td>-1.2</td>
<td>-0.9</td>
<td>-0.6**</td>
</tr>
<tr>
<td>Difference from sitagliptin arm (adjusted mean)†</td>
<td>-0.6** (0.8, -0.4)</td>
<td>-0.7** (0.5, -0.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>95% Confidence Interval</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percentage of patients achieving HbA1c &lt;7%</td>
<td>56</td>
<td>44</td>
<td>25</td>
<td>57</td>
</tr>
</tbody>
</table>

Table 9: Results of a 26-week open-label trial of Insulin detemir as add-on to Victoza® + metformin compared to continued treatment with Victoza® + metformin alone in patients not achieving HbA1c <7% after 12 weeks of Metformin and Victoza®

<table>
<thead>
<tr>
<th>Intent-to-Treat Population (N)</th>
<th>162</th>
<th>157</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c (%) (Mean)</td>
<td>7.6</td>
<td>7.6</td>
</tr>
<tr>
<td>Baseline (week 0)</td>
<td>-1.5</td>
<td>0</td>
</tr>
<tr>
<td>Change from baseline (adjusted mean)</td>
<td>-0.5</td>
<td>0</td>
</tr>
<tr>
<td>Difference from Victoza® + metformin arm (LS mean)†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>95% Confidence Interval</td>
<td>(-1.7, -0.4)</td>
<td>(-0.7, -0.4)</td>
</tr>
<tr>
<td>Percentage of patients achieving HbA1c &lt;7%</td>
<td>43</td>
<td>17</td>
</tr>
</tbody>
</table>

Add-on to Sulfonylurea

In this 26-week trial, 1041 patients were randomized to Victoza® 0.6 mg, Victoza® 1.2 mg, Victoza® 1.8 mg, placebo, or rosiglitazone 4 mg (one-half of the maximal approved dose in the United States), all as add-on to glimepiride. Randomization occurred after a 4-week run-in period consisting of an initial, 2-week, forced-glimepiride titration period followed by a maintenance period of another 2 weeks. During the titration period, doses of glimepiride were increased to 4 mg/day. The doses of glimepiride could be reduced (at the discretion of the investigator) from 4 mg/day to 3 mg/day or 2 mg/day (minimum) after randomization, in the event of unacceptable hypoglycemia or other adverse events. Treatment with Victoza® 1.2 mg and 1.8 mg as add-on to glimepiride resulted in statistically significant reductions in mean HbA1c compared to placebo add-on to glimepiride (Table 10). The percentage of patients who discontinued due to ineffective therapy was 3.0% in the Victoza® 1.8 mg + glimepiride treatment group, 3.5% in the Victoza® 1.2 mg + glimepiride treatment group, 17.5% in the placebo + glimepiride treatment group, and 6.9% in the rosiglitazone + glimepiride treatment group.
Victoza® (liraglutide [rDNA origin] injection), solution for subcutaneous use

In this 26-week trial, 581 patients were randomized to Victoza® 1.8 mg, placebo, or insulin glargine, as add-on to metformin and sulfonylurea (Table 11). The percentage of patients who discontinued due to ineffective therapy was 0.4% in the Victoza® treatment group and 0% in the exenatide treatment group. Both treatment groups had a mean decrease from baseline in body weight of approximately 3 kg.

Table 11: Results of a 26-week trial of Victoza® as add-on to metformin and sulfonylurea

<table>
<thead>
<tr>
<th></th>
<th>Victoza® 1.8 mg + Metformin</th>
<th>Placebo + Metformin</th>
<th>Rosiglitazone 4 mg + Metformin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HbA1c (%) (Mean)</strong></td>
<td>8.5</td>
<td>8.3</td>
<td>8.1</td>
</tr>
<tr>
<td>Intent-to-Treat</td>
<td>230</td>
<td>228</td>
<td>214</td>
</tr>
<tr>
<td><strong>Fasting Plasma Glucose (mg/dL) (Mean)</strong></td>
<td>8.4</td>
<td>8.4</td>
<td>8.4</td>
</tr>
<tr>
<td>Change from baseline (adjusted mean)</td>
<td>-1.3</td>
<td>-0.2</td>
<td>-1.1</td>
</tr>
<tr>
<td>Difference from placebo + metformin + glimepiride arm (adjusted mean)</td>
<td>-1.1**</td>
<td>-1.1**</td>
<td>-1.1**</td>
</tr>
<tr>
<td>Percentage of patients achieving A1c &lt;7%</td>
<td>42</td>
<td>35</td>
<td>7</td>
</tr>
</tbody>
</table>

Add-on to Metformin and Sulfonylurea

In this 26-week trial, 533 patients were randomized to Victoza® 1.2 mg, placebo, or insulin glargine, as add-on to metformin and thiazolidinedione. Treatment with Victoza® as add-on to metformin and thiazolidinedione resulted in a statistically significant mean reduction in HbA1c compared to placebo add-on to metformin and thiazolidinedione (Table 11). The percentage of patients who discontinued due to ineffective therapy was 1.7% in the Victoza® 1.8 mg + metformin + rosiglitazone treatment group, 0.4% in the insulin glargine + metformin + glimepiride treatment group, and 11.3% in the placebo + metformin + glimepiride treatment group.

Table 12: Results of a 26-week trial of Victoza® as add-on to metformin and thiazolidinedione

<table>
<thead>
<tr>
<th></th>
<th>Victoza® 1.8 mg + Metformin + Rosiglitazone</th>
<th>Placebo + Metformin + Rosiglitazone</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HbA1c (%) (Mean)</strong></td>
<td>8.6</td>
<td>8.5</td>
</tr>
<tr>
<td>Intent-to-Treat</td>
<td>178</td>
<td>177</td>
</tr>
<tr>
<td><strong>Fasting Plasma Glucose (mg/dL) (Mean)</strong></td>
<td>8.4</td>
<td>8.4</td>
</tr>
<tr>
<td>Change from baseline (adjusted mean)</td>
<td>-1.5</td>
<td>-1.5</td>
</tr>
<tr>
<td>Difference from placebo + metformin + rosiglitazone arm (adjusted mean)</td>
<td>-0.9**</td>
<td>-0.9**</td>
</tr>
<tr>
<td>Percentage of patients achieving A1c &lt;7%</td>
<td>54</td>
<td>57</td>
</tr>
</tbody>
</table>
**Victoza® (liraglutide [rDNA origin] injection), solution for subcutaneous use**

**16 HOW SUPPLIED/STORAGE AND HANDLING**

**16.1 How Supplied**
Victoza® is available in the following package sizes containing disposable, pre-filled, multi-dose pens. Each individual pen delivers doses of 0.6 mg, 1.2 mg, or 1.8 mg (6 mg/mL, 3 mL).

- 2 x Victoza® pen NDC 0169-4060-12
- 3 x Victoza® pen NDC 0169-4060-13

Each Victoza® pen is for use by a single patient. A Victoza® pen must never be shared between patients, even if the needle is changed.

**16.2 Recommended Storage**
Prior to first use, Victoza® should be stored in a refrigerator between 36°F to 46°F (2°C to 8°C) (Table 14). Do not store in the freezer or directly adjacent to the refrigerator cooling element. Do not freeze Victoza® and do not use Victoza® if it has been frozen.

After initial use of the Victoza® 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. Victoza® should be protected from excessive heat and sunlight. Always remove and safely discard the needle after each injection and store the Victoza® pen without an injection needle attached. This will reduce the potential for contamination, infection, and leakage while also ensuring dosing accuracy. Always use a new needle for each injection to prevent contamination.

**14 Table 14: Recommended Storage Conditions for the Victoza® Pen**

<table>
<thead>
<tr>
<th>Prior to first use</th>
<th>After first use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Refrigerated</td>
<td>Room Temperature</td>
</tr>
<tr>
<td>36°F to 46°F (2°C to 8°C)</td>
<td>59°F to 86°F (15°C to 30°C)</td>
</tr>
<tr>
<td>Until expiration date</td>
<td>30 days</td>
</tr>
<tr>
<td>Refrigerated</td>
<td>Refrigerated</td>
</tr>
<tr>
<td>36°F to 46°F (2°C to 8°C)</td>
<td>36°F to 46°F (2°C to 8°C)</td>
</tr>
</tbody>
</table>

**17 PATIENT COUNSELING INFORMATION**

**17.1 FDA-Approved Medication Guide**
See separate leaflet.

**17.2 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 physician (see Boxed Warning and Warnings and Precautions (5.1)).

**17.3 Dehydration and Renal Failure**
Patients treated with Victoza® should be advised of the potential risk of dehydration due to gastrointestinal adverse reactions and take precautions to avoid fluid depletion. Patients should be informed of the potential risk for worsening renal function, which in some cases may require dialysis.

**17.4 Pancreatitis**
Patients should be informed of the potential risk for pancreatitis. Explain that persistent severe abdominal pain that may radiate to the back and which may or may not be accompanied by vomiting, is the hallmark symptom of acute pancreatitis. Instruct patients to discontinue Victoza® promptly and contact their physician if persistent severe abdominal pain occurs (see Warnings and Precautions (5.2)).

**17.5 Never Share a Victoza® Pen Between Patients**
Advise patients that they must never share a Victoza® pen with another person, even if the needle is changed, because doing so carries a risk for transmission of blood-borne pathogens.

**17.6 Hypersensitivity Reactions**
Patients should be informed that serious hypersensitivity reactions have been reported during post-marketing use of Victoza®. If symptoms of hypersensitivity reactions occur, patients must stop taking Victoza® and seek medical advice promptly (see Warnings and Precautions (5.6)).

**17.7 Instructions**
Patients should be informed of the potential risks and benefits of Victoza® and of alternative modes of therapy. Patients should also be informed about the importance of adherence to dietary instructions, regular physical activity, periodic blood glucose monitoring and A1C testing, recognition and management of hypoglycemia and hyperglycemia, and assessment for diabetes complications. During periods of stress such as fever, trauma, infection, or surgery, medication requirements may change and patients should be advised to seek medical advice promptly.

Patients should be advised that the most common side effects of Victoza® are headache, nausea and diarrhea. Nausea is most common when first starting Victoza®, but decreases over time in the majority of patients and does not typically require discontinuation of Victoza®.

Physicians should instruct their patients to read the Patient Medication Guide before starting Victoza® therapy and to read each time the prescription is renewed. Patients should be instructed to inform their doctor or pharmacist if they develop any unusual symptom, or if any known symptom persists or worsens.

Inform patients not to take an extra dose of Victoza® to make up for a missed dose. If a dose is missed, the once-daily regimen should be resumed as prescribed with the next scheduled dose.

If more than 3 days have elapsed since the last dose, the patient should be advised to reinstitute Victoza® at 0.6 mg to mitigate any gastrointestinal symptoms associated with reinitiation of treatment. Victoza® should be titrated at the discretion of the prescribing physician (see Dosage and Administration (2)).

**17.8 Laboratory Tests**
Patients should be informed that response to all diabetic therapies should be monitored by periodic measurements of blood glucose and A1C levels, with a goal of decreasing these levels towards the normal range. A1C is especially useful for evaluating long-term glycemic control.
Read this Medication Guide before you start using Victoza® and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

What is the most important information I should know about Victoza®?

Victoza® may cause serious side effects, including:
- Possible thyroid tumors, including cancer. Tell your healthcare provider if you get a lump or swelling in your neck, hoarseness, trouble swallowing, or shortness of breath. These may be symptoms of thyroid cancer. In studies with rats and mice, Victoza® and medicines that work like Victoza® caused thyroid tumors, including thyroid cancer. It is not known if Victoza® will cause thyroid tumors or a type of thyroid cancer called medullary thyroid carcinoma (MTC) in people.
- Do not use Victoza® 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 Victoza®?

Victoza® is an injectable prescription medicine that may improve blood sugar (glucose) in adults with type 2 diabetes mellitus, and should be used along with diet and exercise.
- Victoza® is not recommended as the first choice of medicine for treating diabetes.
- It is not known if Victoza® can be used in people who have had pancreatitis.
- Victoza® is not a substitute for insulin and is not for use in people with type 1 diabetes or people with diabetic ketoacidosis.
- It is not known if Victoza® can be used with mealtime insulin.
- It is not known if Victoza® is safe and effective for use in children.

Who should not use Victoza®?

Do not use Victoza® 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 Victoza®. See the end of this Medication Guide for a complete list of ingredients in Victoza®.

What should I tell my healthcare provider before using Victoza®?

Before using Victoza®, tell your healthcare provider if you:
- have or have had problems with your pancreas, kidneys, or liver
- have severe problems with your stomach, such as slowing emptying of your stomach (gastroparesis) or problems with digesting food
- have any other medical conditions
- are pregnant or plan to become pregnant. It is not known if Victoza® will harm your unborn baby. Tell your healthcare provider if you become pregnant while using Victoza®.
- are breastfeeding or plan to breastfeed. It is not known if Victoza® passes into your breast milk. You should not use Victoza® while breastfeeding without first talking with your healthcare provider.
- tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Victoza® may affect the way some medicines work and some medicines may affect the way Victoza® works.
- Before using Victoza®, talk to your healthcare provider about low blood sugar and how to manage it. Tell your healthcare provider if you are taking other medicines to treat diabetes, including insulin or sulfonylureas.

How should I use Victoza®?

- Read the Instructions for Use that comes with Victoza®.
- Use Victoza® exactly as your healthcare provider tells you to.
- Your healthcare provider should show you how to use Victoza® before you use it for the first time.
- Victoza® is injected under the skin (subcutaneously) of your stomach (abdomen), thigh, or upper arm. Do not inject Victoza® into a muscle (intramuscularly) or vein (intravenously).
- Use Victoza® 1 time each day, at any time of the day.
- If you miss a dose of Victoza®, take the missed dose at the next scheduled dose. Do not take 2 doses of Victoza® at the same time.
- Victoza® may be taken with or without food.
- Do not mix insulin and Victoza® together in the same injection.
- You may give an injection of Victoza® and insulin in the same body area (such as your stomach area), but not right next to each other.
- Change (rotate) your injection site with each injection. Do not use the same site for each injection.
- Do not share your Victoza® pen with other people, even if the needle has been changed. You may give other people a serious infection, or get a serious infection from them.

Your dose of Victoza® and other diabetes medicines may need to change because of:
- change in level of physical activity or exercise, weight gain or loss, increased stress, illness, change in diet, or because of other medicines you take.

What are the possible side effects of Victoza®?

Victoza® may cause serious side effects, including:
- See “What is the most important information I should know about Victoza®?”
- Inflammation of your pancreas (pancreatitis). Stop using Victoza® 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.
- Low blood sugar (hypoglycemia). Your risk for getting low blood sugar may be higher if you use Victoza® with another medicine that can cause low blood sugar, such as a sulfonylurea or insulin.

Signs and symptoms of low blood sugar may include:
- Dizziness or light-headedness
- Sweating
- Confusion or drowsiness
- Headache
- Blurred vision
- Slurred speech
- Shakiness
- Fast heartbeat
- Anxiety, irritability, or mood changes
- Hunger
- Weakness
- Feeling jittery

Kidney problems (kidney failure). In people who have kidney problems, diarrhea, nausea, and vomiting may cause a loss of fluids (dehydration) which may cause kidney problems to get worse.

Serious allergic reactions. Stop using Victoza® and get medical help right away, if you have any symptoms of a serious allergic reaction including itching, rash, or difficulty breathing.
The most common side effects of Victoza® may include headache, nausea, diarrhea, vomiting, anti-liraglutide antibodies in your blood. Talk to your healthcare provider about any side effect that bothers you or does not go away. These are not all the possible side effects of Victoza®. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of Victoza®. Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use Victoza® for a condition for which it was not prescribed. Do not give Victoza® to other people, even if they have the same symptoms that you have. It may harm them.

This Medication Guide summarizes the most important information about Victoza®. If you would like more information, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about Victoza® that is written for health professionals.

For more information, go to victoza.com or call 1-877-484-2869.

What are the ingredients in Victoza®?
Active Ingredient: Liraglutide
Inactive Ingredients: disodium phosphate dihydrate, propylene glycol, phenol and water for injection

This Medication Guide has been approved by the U.S. Food and Drug Administration.
Instructions for Use
Victoza® (liraglutide [rDNA origin] injection)

First read the Medication Guide that comes with your Victoza® pen and then read these Patient Instructions for Use for information about how to use your Victoza® pen the right way. These instructions do not take the place of talking with your healthcare provider about your medical condition or your treatment.

Do not share your Victoza® Pen with other people, even if the needle has been changed. You may give other people a serious infection, or get a serious infection from them.

Your Victoza® pen contains 3 mL of Victoza® and will deliver doses of 0.6 mg, 1.2 mg or 1.8 mg. The number of doses that you can take with a Victoza® pen depends on the dose of medicine that is prescribed for you. Your healthcare provider will tell you how much Victoza® to take.

Victoza® pen should be used with Novo Nordisk disposable needles. Talk to your healthcare provider or pharmacist for more information about needles for your Victoza® pen.

Important Information
¬ Do not share your Victoza® pen with other people, even if the needle has been changed. You may give other people a serious infection, or get a serious infection from them.
¬ Always use a new needle for each injection. Do not reuse or share your needles with other people. You may give other people a serious infection, or get a serious infection from them.
¬ Keep your Victoza® pen and all medicines out of the reach of children.
¬ If you drop your Victoza® pen, repeat “First Time Use For Each New Pen” (steps A through D).
¬ Be careful not to bend or damage the needle.
¬ Do not use the cartridge scale to measure how much Victoza® to inject.
¬ Be careful when handling used needles to avoid needle stick injuries.
¬ You can use your Victoza® pen for up to 30 days after you use it the first time.

First Time Use for Each New Pen

Step A. Check the Pen
- Take your new Victoza® pen out of the refrigerator.
- Wash hands with soap and water before use.
- Check pen label before each use to make sure it is your Victoza® pen.
- Pull off pen cap.
- Check Victoza® in the cartridge. The liquid should be clear, colorless and free of particles. If not, do not use.
- Wipe the rubber stopper with an alcohol swab.

Step B. Attach the Needle
- Remove protective tab from outer needle cap.
- Push outer needle cap containing the needle straight onto the pen, then screw needle on until secure.
- Pull off outer needle cap. Do not throw away.
- Pull off inner needle cap and throw away. A small drop of liquid may appear. This is normal.

Step C. Dial to the Flow Check Symbol
This step is done only ONEC for each new pen and is ONLY required the first time you use a new pen.
- Turn dose selector until flow check symbol (—) lines up with pointer. The flow check symbol does not administer the dose as prescribed by your healthcare provider.
- To select the dose prescribed by your healthcare provider, continue to Step G under “Routine Use”.

Step D. Prepare the Pen
- Hold pen with needle pointing up.
- Tap cartridge gently with your finger a few times to bring any air bubbles to the top of the cartridge.
- Keep needle pointing up and press dose button until 0 mg lines up with pointer. Repeat steps C and D, up to 6 times, until a drop of Victoza® appears at the needle tip.

If you still see no drop of Victoza®, use a new pen and contact Novo Nordisk at 1-877-484-2869.

Continue to Step G under “Routine Use” ←

Routine Use

Step E. Check the Pen
- Take your Victoza® pen from where it is stored.
- Wash hands with soap and water before use.
- Check pen label before each use to make sure it is your Victoza® pen.
- Pull off pen cap.
- Check Victoza® in the cartridge. The liquid should be clear, colorless and free of particles. If not, do not use.
- Wipe the rubber stopper with an alcohol swab.

Step F. Attach the Needle
- Remove protective tab from outer needle cap.
- Push outer needle cap containing the needle straight onto the pen, then screw needle on until secure.
- Pull off outer needle cap. Do not throw away.
- Pull off inner needle cap and throw away. A small drop of liquid may appear. This is normal.

Step G. Dial the Dose
- Victoza® pen can give a dose of 0.6 mg (starting dose), 1.2 mg or 1.8 mg. Be sure that you know the dose of Victoza® that is prescribed for you.
- Turn the dose selector until your needed dose lines up with the pointer (0.6 mg, 1.2 mg or 1.8 mg).
- 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.
- If you select a wrong dose, change it by turning the dose selector backwards or forwards until the correct dose lines up with the pointer.
- Be careful not to press the dose button when turning the dose selector. This may cause Victoza® to come out.

Step H. Injecting the Dose
- Insert needle into your skin in the stomach, thigh or upper arm. Use the injection technique shown to you by your healthcare provider. Do not inject Victoza® into a vein or muscle.
- Press down on the center of the dose button to inject until 0 mg lines up with the pointer.
- Be careful not to touch the dose display with your other fingers. This may block the injection.
- Keep the dose button pressed down and make sure that you keep the needle under the skin for a full count of 6 seconds to make sure the full dose is injected. Keep your thumb on the injection button until you remove the needle from your skin.
- Change (rotate) your injection sites within the area you choose for each dose. Do not use the same injection site for each injection.

Step I. Withdraw Needle
- You may see a drop of Victoza® at the needle tip. This is normal and it does not affect the dose you just received. If blood appears after you take the needle out of your skin, apply light pressure, but do not rub the area.

Step J. Remove and Dispose of the Needle
- Carefully pull the outer needle cap over the needle. Unscrew the needle.
- Safely remove the needle from your Victoza® pen after each use.
- Put your used VICTOZA® pen and needles in a FDA-cleared sharps disposal container right away after use. Do not throw away (dispose of) loose needles and pens in your household trash.
- If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:
  o made of a heavy-duty plastic
  o can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out
  o upright and stable during use
  o leak-resistant
  o 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. Do not reuse or share your needles with other people. 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.

Caring for your Victoza® pen
- After removing the needle, put the pen cap on your Victoza® pen and store your Victoza® pen without the needle attached.
- Do not try to refill your Victoza® pen – it is prefilled and is disposable.
- Do not try to repair your pen or pull it apart.
- Keep your Victoza® pen away from dust, dirt and liquids.
- If cleaning is needed, wipe the outside of the pen with a clean, damp cloth.
How should I store Victoza®?

**Before use:**
- Store your new, unused Victoza® pen in the refrigerator at 36°F to 46°F (2°C to 8°C).
- If Victoza® is stored outside of refrigeration (by mistake) prior to first use, it should be used or thrown away within 30 days.
- Do not freeze Victoza® or use Victoza® if it has been frozen. Do not store Victoza® near the refrigerator cooling element.

**Pen in use:**
- Store your Victoza® pen 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).
- When carrying the pen away from home, store the pen at a temperature between 59°F to 86°F (15°C to 30°C).
- If Victoza® has been exposed to temperatures above 86°F (30°C), it should be thrown away.
- Protect your Victoza® pen from heat and sunlight.
- Keep the pen cap on when your Victoza® pen is not in use.
- Use a Victoza® pen for only 30 days. Throw away a used Victoza® pen after 30 days, even if some medicine is left in the pen.