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

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 rodents. It is unknown whether Victoza causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as human relevance could not be determined by clinical or nonclinical studies (5.1)**.
- **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) (5.1).**

·····RECENT MAJOR CHANGES·····

Warnings and Precautions (5.3) 02/2015

·····INDICATIONS AND USAGE·····

Victoza is a glucagon-like peptide-1 (GLP-1) receptor agonist indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus (1).

Important Limitations of Use (1.1):

- Not recommended as first-line therapy for patients inadequately controlled on diet and exercise (5.1).
- Has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis (5.2).
- Not for treatment of type 1 diabetes mellitus or diabetic ketoacidosis.
- Has not been studied in combination with prandial insulin.

·····DOSAGE AND ADMINISTRATION·····

- Administer once daily at any time of day, independently of meals (2).
- Inject subcutaneously in the abdomen, thigh or upper arm (2).
- The injection site and timing can be changed without dose adjustment (2).
- Initiate at 0.6 mg per day for one week. This dose is intended to reduce gastrointestinal symptoms during initial titration, and is not effective for glycemic control. After one week, increase the dose 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 (2).

·····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) (3).

·····CONTRAINDICATIONS·····

Do not use in patients with a personal or family history of medullary thyroid carcinoma or in patients with Multiple Endocrine Neoplasia syndrome type 2 (4).

Do not use if history of serious hypersensitivity to Victoza or any product components (4).

·····WARNINGS AND PRECAUTIONS·····

- Thyroid C-cell tumors in animals: Counsel patients regarding the risk of medullary thyroid carcinoma and the symptoms of thyroid tumors (5.1).
- Pancreatitis: Postmarketing reports, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis. Discontinue promptly if pancreatitis is suspected. Do not restart if pancreatitis is confirmed. Consider other antidiabetic therapies in patients with a history of pancreatitis (5.2).
- Never share a Victoza pen between patients, even if the needle is changed (5.3).
- Serious hypoglycemia: Can occur when Victoza is used with an insulin secretagogue (e.g. a sulfonylurea) or insulin. Consider lowering the dose of the insulin secretagogue or insulin to reduce the risk of hypoglycemia (5.4).
- 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 Victoza in patients with renal impairment (5.5).
- Hypersensitivity: Postmarketing reports of serious hypersensitivity reactions (e.g., anaphylactic reactions and angioedema). The patient should discontinue Victoza and other suspect medications and promptly seek medical advice (5.6).
- Macrovascular outcomes: There have been no studies establishing conclusive evidence of macrovascular risk reduction with Victoza or any other antidiabetic drug (5.7).

·····ADVERSE REACTIONS·····

- The most common adverse reactions, reported in ≥5% of patients treated with Victoza and more commonly than in patients treated with placebo, are: headache, nausea, diarrhea and anti-liraglutide antibody formation (6).
- Immunogenicity-related events, including urticaria, were more common among Victoza-treated patients (0.8%) than among comparator-treated patients (0.4%) in clinical trials (6).

To report SUSPECTED ADVERSE REACTIONS, contact Novo Nordisk Inc. at 1-877-484-2869 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------

- Victoza delays gastric emptying. May impact absorption of concomitantly administered oral medications. Use caution (7).

·····USE IN SPECIFIC POPULATIONS·····

- Limited data in patients with renal or hepatic impairment. (8.6, 8.7).

See 17 for PATIENT COUNSELING INFORMATION and FDA-Approved Medication Guide.

Revised: 02/2015

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

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 human relevance could not be ruled out by clinical or nonclinical studies. 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). Based on the findings in rodents, monitoring with serum calcitonin or thyroid ultrasound was performed during clinical trials, but this may have increased the number of unnecessary thyroid surgeries. It is unknown whether monitoring with serum calcitonin or thyroid ultrasound will mitigate human risk of thyroid C-cell tumors. Patients should be counseled regarding the risk and symptoms of thyroid tumors *[see Contraindications (4), Warnings and Precautions (5.1) and Nonclinical Toxicology (13.1)]*.

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

- Because of the uncertain relevance of the rodent thyroid C-cell tumor findings to humans, prescribe Victoza only to patients for whom the potential benefits are considered to outweigh the potential risk. Victoza is not recommended as first-line therapy for patients who have inadequate glycemic control on diet and exercise.

- 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

Do not use 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).

Do not use 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. A statistically significant increase in cancer was observed in rats receiving liraglutide at 8-times clinical exposure compared to controls. 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 could not be determined by clinical or nonclinical studies *[see Boxed Warning, Contraindications (4)]*.

In the clinical trials, there have been 6 reported cases of thyroid C-cell hyperplasia among Victoza-treated patients and 2 cases in comparator-treated patients (1.3 vs. 1.0 cases per 1000 patient-years). One comparator-treated patient with MTC had pre-treatment serum calcitonin concentrations >1000 ng/L suggesting pre-existing disease. All of these cases were diagnosed after thyroidectomy, which was prompted by abnormal results on routine, protocol-specified measurements of serum calcitonin. Five of the six Victoza-treated patients had elevated calcitonin concentrations at baseline and throughout the

trial. One Victoza and one non-Victoza-treated patient developed elevated calcitonin concentrations while on treatment.

Calcitonin, a biological marker of MTC, was measured throughout the clinical development program. The serum calcitonin assay used in the Victoza clinical trials had a lower limit of quantification (LLOQ) of 0.7 ng/L and the upper limit of the reference range was 5.0 ng/L for women and 8.4 ng/L for men. At Weeks 26 and 52 in the clinical trials, adjusted mean serum calcitonin concentrations were higher in Victoza-treated patients compared to placebo-treated patients but not compared to patients receiving active comparator. At these timepoints, the adjusted mean serum calcitonin values (~ 1.0 ng/L) were just above the LLOQ with between-group differences in adjusted mean serum calcitonin values of approximately 0.1 ng/L or less. Among patients with pre-treatment serum calcitonin below the upper limit of the reference range, shifts to above the upper limit of the reference range which persisted in subsequent measurements occurred most frequently among patients treated with Victoza 1.8 mg/day. In trials with on-treatment serum calcitonin measurements out to 5-6 months, 1.9% of patients treated with Victoza 1.8 mg/day developed new and persistent calcitonin elevations above the upper limit of the reference range compared to 0.8-1.1% of patients treated with control medication or the 0.6 and 1.2 mg doses of Victoza. In trials with on-treatment serum calcitonin measurements out to 12 months, 1.3% of patients treated with Victoza 1.8 mg/day had new and persistent elevations of calcitonin from below or within the reference range to above the upper limit of the reference range, compared to 0.6%, 0% and 1.0% of patients treated with Victoza 1.2 mg, placebo and active control, respectively. Otherwise, Victoza did not produce consistent dose-dependent or time-dependent increases in serum calcitonin.

Patients with MTC usually have calcitonin values >50 ng/L. In Victoza clinical trials, among patients with pre-treatment serum calcitonin <50 ng/L, one Victoza-treated patient and no comparator-treated patients developed serum calcitonin >50 ng/L. The Victoza-treated patient who developed serum calcitonin >50 ng/L had an elevated pre-treatment serum calcitonin of 10.7 ng/L that increased to 30.7 ng/L at Week 12 and 53.5 ng/L at the end of the 6-month trial. Follow-up serum calcitonin was 22.3 ng/L more than 2.5 years after the last dose of Victoza. The largest increase in serum calcitonin in a comparator-treated patient was seen with glimepiride in a patient whose serum calcitonin increased from 19.3 ng/L at baseline to 44.8 ng/L at Week 65 and 38.1 ng/L at Week 104. Among patients who began with serum calcitonin <20 ng/L, calcitonin elevations to >20 ng/L occurred in 0.7% of Victoza-treated patients, 0.3% of placebo-treated patients, and 0.5% of active-comparator-treated patients, with an incidence of 1.1% among patients treated with 1.8 mg/day of Victoza. The clinical significance of these findings is unknown.

Counsel patients regarding the risk for MTC and the symptoms of thyroid tumors (e.g. a mass in the neck, dysphagia, dyspnea or persistent hoarseness). It is unknown whether monitoring with serum calcitonin or thyroid ultrasound will mitigate the potential risk of MTC, and 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. Patients with thyroid nodules noted on physical examination or neck imaging obtained for other reasons should be referred to an endocrinologist for further evaluation. Although routine monitoring of serum calcitonin is of uncertain value in patients treated with Victoza, if serum calcitonin is measured and found to be elevated, the patient should be referred to an endocrinologist for further evaluation.

5.2 Pancreatitis

Based on spontaneous postmarketing reports, acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis, has been observed in patients treated with Victoza. After initiation of Victoza, observe patients carefully for signs and symptoms of pancreatitis (including persistent severe abdominal pain, sometimes radiating to the back and which may or may not be accompanied by vomiting). If pancreatitis is suspected, 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)]*.

5.6 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 Macrovascular Outcomes
There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with Victoza or any other antidiabetic drug.

6 ADVERSE REACTIONS
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 placebo.
- An open-label 26-week add-on to metformin and/or sulfonylurea trial compared Victoza 1.8 mg once-daily and exenatide 10 mcg twice-daily.
- An open-label 26-week add-on to metformin trial compared Victoza 1.2 mg once-daily, Victoza 1.8 mg once-daily, and sitagliptin 100 mg once-daily.
- 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 total) 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 insulin detemir or continued, unchanged treatment with Victoza 1.8 mg + metformin. During this randomized 26-week period, diarrhea was the only adverse reaction reported in ≥5% 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

	All Victoza N = 497	Glimepiride N = 248
Adverse Reaction	(%)	(%)
Nausea	28.4	8.5
Diarrhea	17.1	8.9
Vomiting	10.9	3.6
Constipation	9.9	4.8
Headache	9.1	9.3

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			
	All Victoza + Metformin N = 724	Placebo + Metformin N = 121	Glimepiride + Metformin N = 242
Adverse Reaction	(%)	(%)	(%)
Nausea	15.2	4.1	3.3
Diarrhea	10.9	4.1	3.7
Headache	9.0	6.6	9.5
Vomiting	6.5	0.8	0.4
Add-on to Glimepiride Trial			
	All Victoza + Glimepiride N = 695	Placebo + Glimepiride N = 114	Rosiglitazone + Glimepiride N = 231
Adverse Reaction	(%)	(%)	(%)
Nausea	7.5	1.8	2.6
Diarrhea	7.2	1.8	2.2
Constipation	5.3	0.9	1.7
Dyspepsia	5.2	0.9	2.6
Add-on to Metformin + Glimepiride			
	Victoza 1.8 + Metformin + Glimepiride N = 230	Placebo + Metformin + Glimepiride N = 114	Glargine + Metformin + Glimepiride N = 232
Adverse Reaction	(%)	(%)	(%)
Nausea	13.9	3.5	1.3
Diarrhea	10.0	5.3	1.3
Headache	9.6	7.9	5.6
Dyspepsia	6.5	0.9	1.7
Vomiting	6.5	3.5	0.4
Add-on to Metformin + Rosiglitazone			
	All Victoza + Metformin + Rosiglitazone N = 355	Placebo + Metformin + Rosiglitazone N = 175	
Adverse Reaction	(%)	(%)	
Nausea	34.6	8.6	
Diarrhea	14.1	6.3	
Vomiting	12.4	2.9	
Headache	8.2	4.6	
Constipation	5.1	1.1	

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

	Victoza 1.8 mg once daily + metformin and/or sulfonylurea N = 235	**Exenatide 10 mcg twice daily + metformin and/or sulfonylurea** N = 232
Adverse Reaction	(%)	(%)
Nausea	25.5	28.0
Diarrhea	12.3	12.1
Headache	8.9	10.3
Dyspepsia	8.9	4.7
Vomiting	6.0	9.9
Constipation	5.1	2.6

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

	All Victoza + metformin N = 439	**Sitagliptin 100 mg/day + metformin** N = 219
Adverse Reaction	(%)	(%)
Nausea	23.9	4.6
Headache	10.3	10.0
Diarrhea	9.3	4.6
Vomiting	8.7	4.1

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. Among Victoza-treated antibody-negative patients, the most common category of adverse events was that of gastrointestinal events, which occurred in 43%, 18% and 19% of antibody-negative Victoza-treated, placebo-treated and active-control-treated patients, respectively. Antibody formation was not associated with reduced efficacy of Victoza when comparing mean HbA_{1c} of all antibody-positive and all antibody-negative patients. However, the 3 patients with the highest titers of anti-liraglutide antibodies had no reduction in HbA_{1c} with Victoza treatment.

In the five double-blind clinical trials of Victoza, events from a composite of adverse events potentially related to immunogenicity (e.g. urticaria, angioedema) occurred among 0.8% of Victoza-treated patients and among 0.4% of comparator-treated patients. Urticaria accounted for approximately one-half of the events in this composite for Victoza-treated patients. Patients who developed anti-liraglutide antibodies were not more likely to develop events from the immunogenicity events composite than were patients who did not develop anti-liraglutide antibodies.

Medication Guide
Victoza® (VIC-tow-za)
(liraglutide [rDNA origin])
Injection

Read this Medication Guide and Patient Instructions for Use that come with Victoza before you start using Victoza and each time you get a refill. There may be new information. This Medication Guide does not take the place of talking with your healthcare provider about your medical condition or your treatment. If you have questions about Victoza after reading this information, ask your healthcare provider or pharmacist.

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

Serious side effects may happen in people who take Victoza, including:

1. **Possible thyroid tumors, including cancer**. During the drug testing process, the medicine in Victoza caused rats and mice to develop tumors of the thyroid gland. Some of these tumors were cancers. It is not known if Victoza will cause thyroid tumors or a type of thyroid cancer called medullary thyroid cancer in people. If medullary thyroid cancer occurs, it may lead to death if not detected and treated early. If you develop tumors or cancer of the thyroid, your thyroid may have to be surgically removed.

    - Before you start taking Victoza, tell your healthcare provider if you or any of your family members have had thyroid cancer, especially medullary thyroid cancer, or Multiple Endocrine Neoplasia syndrome type 2. Do not take Victoza if you or any of your family members have medullary thyroid cancer, or if you have Multiple Endocrine Neoplasia syndrome type 2. People with these conditions already have a higher chance of developing medullary thyroid cancer in general and should not take Victoza.
    - While taking Victoza, 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.

2. **Inflammation of the pancreas** (**pancreatitis),** which may be severe and lead to death.

    Before taking Victoza, tell your healthcare provider if you have had:

    - pancreatitis
    - stones in your gallbladder (gallstones)
    - a history of alcoholism
    - high blood triglyceride levels

    These medical conditions can make you more likely to get pancreatitis in general. It is not known if having these conditions will lead to a higher chance of getting pancreatitis while taking Victoza.

While taking Victoza:

Stop taking Victoza and call your healthcare provider right away if you have pain in your stomach area (abdomen) that is severe and will not go away. The pain may happen with or without vomiting. The pain may be felt going from your abdomen through to your back. This type of pain may be a symptom of pancreatitis.

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.

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 medication for treating diabetes.
- Victoza is not a substitute for insulin.
- Victoza is not for use in people with type 1 diabetes or people with diabetic ketoacidosis.
- It is not known if Victoza is safe and effective in children. Victoza is not recommended for use in children.

Who should not use Victoza?

Do not use Victoza if:

- you or any of your family members have a history of medullary thyroid cancer.
- you have Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). This is a disease where people have tumors in more than one gland in their body.
- you are allergic to liraglutide or any of the ingredients in Victoza. See the end of this Medication Guide for a complete list of ingredients in Victoza. Symptoms of a serious allergic reaction may include:

  o swelling of your face, lips, tongue, or throat

  o fainting or feeling dizzy

  o very rapid heartbeat

  o problems breathing or swallowing

  o severe rash or itching

Talk with your healthcare provider if you are not sure if you have any of these conditions.

What should I tell my healthcare provider before using Victoza?

Before taking Victoza, tell your healthcare provider if you:

- have any of the conditions listed in the section "What is the most important information I should know about Victoza?"
- are allergic to liraglutide or any of the other ingredients in Victoza. See the end of this Medication Guide for a list of ingredients in Victoza.
- have severe problems with your stomach, such as slowed emptying of your stomach (gastroparesis) or problems with digesting food.
- have or have had kidney or liver problems.
- 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 taking Victoza.
- are breastfeeding or plan to breastfeed. It is not known if Victoza passes into your breast milk. You and your healthcare provider should decide if you will take Victoza or breastfeed. You should not do both without talking with your healthcare provider first.

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

Know the medicines you take. Keep a list of them with you to show your healthcare provider and pharmacist each time you get a new medicine.

How should I use Victoza?

- Use Victoza exactly as prescribed by your healthcare provider. Your dose should be increased after using Victoza for one week. After that, do not change your dose unless your healthcare provider tells you to.
- Victoza is injected 1 time each day, at any time during the day.
- You can take Victoza with or without food.
- Victoza comes in a prefilled pen.
- Your healthcare provider must teach you how to inject Victoza before you use it for the first time. If you have questions or do not understand the instructions, talk to your healthcare provider or pharmacist. See the Patient Instructions for Use that come with this Medication Guide for detailed information about the right way to use your Victoza pen.

- Pen needles are not included. Use the Victoza pen with Novo Nordisk disposable needles. You may need a prescription to get pen needles from your pharmacist. Ask your healthcare provider which needle size is best for you. 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.
- When starting a new prefilled Victoza pen, you must follow the "First Time Use for Each New Pen" (see the detailed Patient Instructions for Use that comes with this Medication Guide). You only need to do this 1 time with each new pen. You should also do this if you drop your pen. If you do the "First Time Use for Each New Pen" before each injection, you will run out of medicine too soon.
- Inject your dose of Victoza under the skin (subcutaneous injection) in your stomach area (abdomen), upper leg (thigh), or upper arm, as instructed by your healthcare provider. **Do not inject into a vein or muscle.**
- If you also give yourself insulin injections in addition to Victoza, **never mix insulin and Victoza together**. Give yourself 2 separate injections. You may give both injections in the same body area (for example, your stomach area), but you should not give the injections right next to each other.
- If you take too much Victoza, call your healthcare provider right away. Too much Victoza may cause severe nausea and vomiting.
- If you miss your daily dose of Victoza, use Victoza as soon as you remember. Then take your next daily dose as usual on the following day. Do not take an extra dose of Victoza or increase your dose on the following day to make up for your missed dose. If you miss your dose of Victoza for **3 days or more**, call your healthcare provider to talk about how to restart your treatment.
- Follow your healthcare provider's instructions for diet, exercise, how often to test your blood sugar, and when to get your HbA_{1c} checked. If you stop using Victoza your blood sugar levels may increase. First talk to your healthcare provider if you want to stop taking Victoza.
- Your dose of diabetes medicines may need to be changed if your body is under certain types of stress. Tell your healthcare provider if you:
    - have fever
    - have trauma
    - have an infection
    - plan to have or have had surgery
- **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.

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?"

- **Low blood sugar (hypoglycemia).** Your risk for getting low blood sugar is higher if you take Victoza with another medicine that can cause low blood sugar, such as a sulfonylurea or insulin. In some people, the blood sugar may get so low that they need another person to help them. The dose of your sulfonylurea medicine or insulin may need to be lowered while you use Victoza. Signs and symptoms of low blood sugar may include:
  - shakiness
  - sweating
  - headache
  - drowsiness
  - weakness
  - dizziness
  - confusion
  - irritability
  - hunger
  - fast heartbeat
  - feeling jittery

Talk to your healthcare provider about how to recognize and treat low blood sugar. Make sure that your family and other people who are around you a lot know how to recognize and treat low blood sugar.

- **Kidney problems (kidney failure).** Victoza may cause nausea, vomiting or diarrhea leading to loss of fluids (dehydration). Dehydration may cause kidney failure which can lead to the need for dialysis. This can happen in people who have never had kidney problems before. Drinking plenty of fluids may reduce your chance of dehydration.

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

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

Common side effects of Victoza include:
- headache
- nausea
- diarrhea

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

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

These are not all the side effects with Victoza. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store Victoza?

Before use:

- Store your new, unused Victoza pen in the refrigerator at 36ºF to 46ºF (2ºC to 8ºC).
- 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 either at 59ºF to 86ºF (15ºC to 30ºC), or in a refrigerator at 36ºF to 46ºF (2°C to 8°C).
- When carrying the pen away from home, store the pen at a temperature between 59ºF to 86ºF (15ºC to 30ºC) and keep it dry.
- If Victoza has been exposed to temperatures above 86ºF (30ºC), 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 your Victoza pen within 30 days after the first day it is stored outside the refrigerator. After these 30 days, throw away your Victoza pen even if some medicine is left in the pen.
- Do not use Victoza after the expiration date printed on the carton.

Do not store the Victoza pen with the needle attached. Always safely remove and safely throw away the needle after each injection. This may help prevent contamination, infection and leakage. It also helps to make sure that you get the correct dose of Victoza. See the Patient Instructions for Use for information about how to dispose of used pen needles and used Victoza pens.

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

General information about 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 you have. It may harm them.

This Medication Guide summarizes the most important information you should know about using 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

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

For information about Victoza contact:
Novo Nordisk Inc.
800 Scudders Mill Road
Plainsboro, NJ 08536
1-877-484-2869

Issued: February 2015
Version: X

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

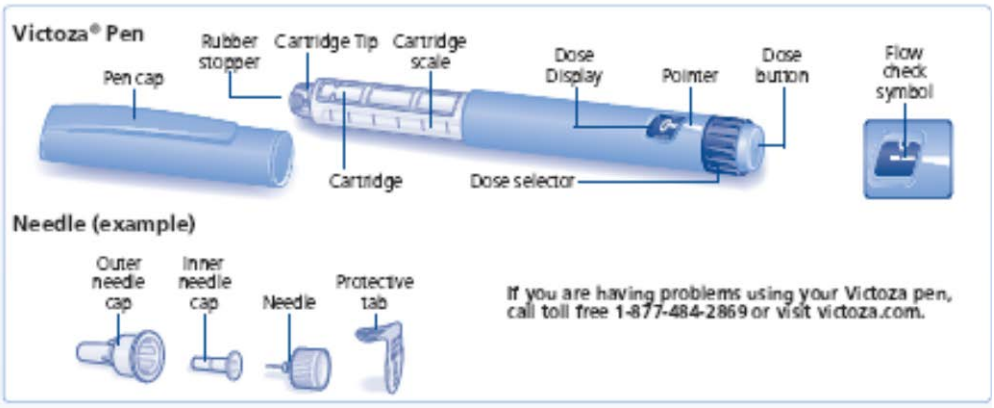
Victoza® is a registered trademark of Novo Nordisk A/S.

Victoza® is covered by US Patent Nos. 6,268,343, 6,458,924, 7,235,627, 8,114,833 and other patents pending.

Victoza® pen is covered by US Patent Nos. 6,004,297, RE 43,834, RE 41,956 and other patents pending.

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.

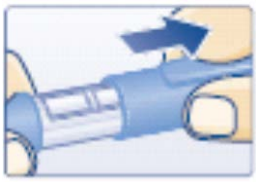
Important Information

- 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

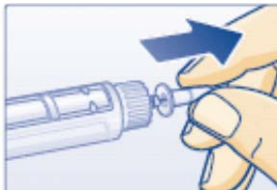


- Take your new Victoza pen out of the refrigerator.
- Wash hands with soap and water before use.
- Check pen label before each use to make sure it is your Victoza pen.
- Pull off pen cap.
- Check Victoza in the cartridge. The liquid should be clear, colorless and free of particles. If not, do not use.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

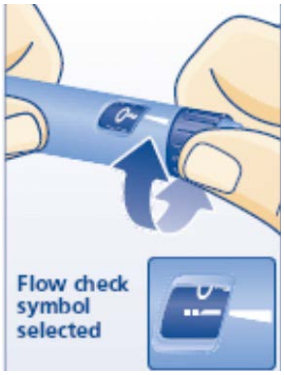
- Pull off outer needle cap. Do not throw away.



- 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

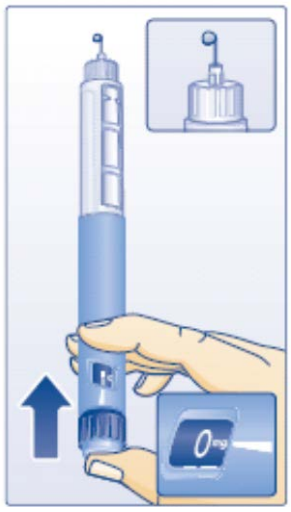
This step is done only ONCE for each new pen and is ONLY required the first time you use a new pen.



- 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.

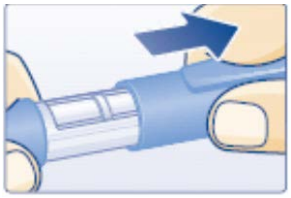


If you still see no drop of Victoza, use a new pen and contact Novo Nordisk at 1-877-484-2869.

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

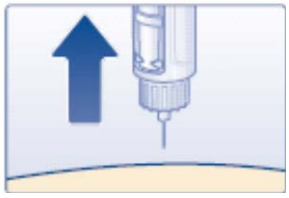
backwards or forwards until the correct dose lines up with the pointer. Be careful not to press the dose button when turning the dose selector. This may cause Victoza to come out.

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.

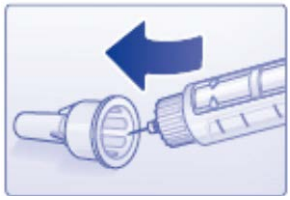
- Keep the dose button pressed down and make sure that you keep the needle under the skin for a full count of 6 seconds to make sure the full dose is injected. Keep your thumb on the injection button until you remove the needle from your skin.
- Change (rotate) your injection sites within the area you choose for each dose. **Do not** use the same injection site for each injection.

Step I. Withdraw Needle



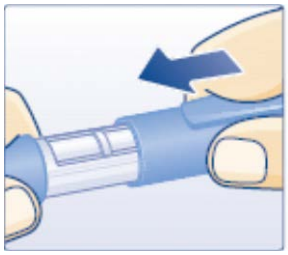
- You may see a drop of Victoza at the needle tip. This is normal and it does not affect the dose you just received. If blood appears after you take the needle out of your skin, apply light pressure, but **do not rub the area**.

Step J. Remove and Dispose of the Needle



- Carefully put 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:
  - 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. 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 36ºF to 46ºF (2ºC to 8ºC).
- 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 59ºF to 86ºF (15ºC to 30ºC), or in a refrigerator at 36ºF to 46ºF (2°C to 8°C).
- When carrying the pen away from home, store the pen at a temperature between 59ºF to 86ºF (15ºC to 30ºC).
- If Victoza has been exposed to temperatures above 86ºF (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.