

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 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).

RECENT MAJOR CHANGES

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)	03/2015

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

Victoza is contraindicated in patients with a personal or family history of medullary thyroid carcinoma or in patients with Multiple Endocrine Neoplasia syndrome type 2 (4).

Victoza is contraindicated in patients with a prior serious hypersensitivity reaction to Victoza or any of the product components (4).

WARNINGS AND PRECAUTIONS

- **Thyroid C-cell Tumors:** See Boxed Warning (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 $\geq 5\%$ 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: 03/2015

FULL PRESCRIBING INFORMATION: CONTENTS*

WARNING: RISK OF THYROID C-CELL TUMORS

1	INDICATIONS AND USAGE
	1.1 Important Limitations of Use
2	DOSAGE AND ADMINISTRATION
3	DOSAGE FORMS AND STRENGTHS
4	CONTRAINDICATIONS
5	WARNINGS AND PRECAUTIONS
	5.1 Risk of Thyroid C-cell Tumors
	5.2 Pancreatitis
	5.3 Never Share a Victoza Pen Between Patients
	5.4 Use with Medications Known to Cause Hypoglycemia
	5.5 Renal Impairment
	5.6 Hypersensitivity Reactions
	5.7 Macrovascular Outcomes
6	ADVERSE REACTIONS
	6.1 Clinical Trials Experience
	6.2 Post-Marketing Experience
7	DRUG INTERACTIONS
	7.1 Oral Medications
8	USE IN SPECIFIC POPULATIONS
	8.1 Pregnancy
	8.3 Nursing Mothers
	8.4 Pediatric Use
	8.5 Geriatric Use
	8.6 Renal Impairment
	8.7 Hepatic Impairment
	8.8 Gastroparesis

10	OVERDOSAGE
11	DESCRIPTION
12	CLINICAL PHARMACOLOGY
	12.1 Mechanism of Action
	12.2 Pharmacodynamics
	12.3 Pharmacokinetics
13	NONCLINICAL TOXICOLOGY
	13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
14	CLINICAL STUDIES
	14.1 Monotherapy
	14.2 Combination Therapy
16	HOW SUPPLIED/STORAGE AND HANDLING
	16.1 How Supplied
	16.2 Recommended Storage
17	PATIENT COUNSELING INFORMATION
	17.1 FDA-Approved Medication Guide
	17.2 Risk of Thyroid C-cell Tumors
	17.3 Dehydration and Renal Failure
	17.4 Pancreatitis
	17.5 Never Share a Victoza Pen Between Patients
	17.6 Hypersensitivity Reactions
	17.7 Instructions
	17.8 Laboratory Tests

*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 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), 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 calcitonin values >50 ng/L. If serum calcitonin is measured and found to be elevated, the patient should be further evaluated. Patients with thyroid nodules noted on physical examination or neck imaging should also be further evaluated.

5.2 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

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.