

Initial REMS approval: 01/2010

Most recent modification: 07/2015

NDA 22-341 VICTOZA[®] (liraglutide [rDNA origin] injection)

Novo Nordisk Inc.

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RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOAL

The goal of the VICTOZA[®] REMS is to mitigate the potential risk of medullary thyroid carcinoma and the risk of acute pancreatitis (including necrotizing pancreatitis) associated with VICTOZA[®] by:

- Informing healthcare providers about the potential risk of medullary thyroid carcinoma and the risk of acute pancreatitis (including necrotizing pancreatitis) associated with VICTOZA[®].

II. REMS ELEMENTS

A. Communication Plan

Novo Nordisk will implement the following elements of a communication plan to healthcare providers likely to prescribe VICTOZA[®]. The communication plan will include:

1. REMS Letters

Novo Nordisk will send a REMS Letter for Healthcare Providers and REMS Letter for Professional Societies within 60 days of approval of this REMS modification and again after 1 year after approval of REMS modification. The REMS Letters will address the potential risk of medullary thyroid tumors and the risk of acute pancreatitis. REMS Letters will be distributed by US mail.

On a quarterly basis, any newly identified healthcare providers who prescribed or are likely to prescribe VICTOZA[®] will be mailed the REMS Letter, Prescribing Information (PI) and the REMS Factsheet for the first 18 months after approval of the most recent REMS modification. In addition, Novo Nordisk will make the REMS Letter for Healthcare Providers available through Novo Nordisk's Medical Information Department and from Novo Nordisk sales and/or medical representatives upon request for one year after approval of the most recent REMS modification.

a. REMS Letter for Healthcare Providers

The intended audience for the REMS Letter for Healthcare Providers will be physicians, nurse practitioners, and physicians' assistants in the specialties of internal medicine and family practice.

b. REMS Letter for Professional Societies

Novo Nordisk will send the REMS Letter for Professional Societies to the leadership of the following professional societies and organizations requesting the letter be provided to their membership:

- American College of Physicians
- American Academy of Family Physicians
- American College of Osteopathic Family Physicians
- American Academy of Nurse Practitioners
- American Association of Diabetes Educators
- American Academy of Physician Assistants

2. REMS Factsheet

A REMS Factsheet will be made available for healthcare providers and distributed through Novo Nordisk sales representatives during a follow-up visit with healthcare providers detailed/visited for the first 18 months after approval of the most recent REMS modification.

3. REMS Slides

The REMS Slides will provide information about the potential risk of medullary thyroid carcinoma and the risk of acute pancreatitis (including necrotizing pancreatitis) associated with VICTOZA[®]. The REMS Slides will be part of a slide deck used at Novo Nordisk sponsored training/programs for the first 18 months after approval of the most recent REMS modification.

4. Dissemination of REMS information at scientific meetings

VICTOZA[®] REMS Factsheet will be prominently displayed and disseminated together with responses to medical information requests at all scientific meetings where Novo Nordisk Medical Information has a presence (e.g., booth) for the first 18 months after approval of the most recent REMS modification.

5. REMS Website

The VICTOZA[®] REMS website (www.victozapro.com/REMS) will continue for 7 years from the initial approval of the REMS. The VICTOZA[®] REMS website will include downloadable versions of the PI, REMS Letters, REMS Factsheet, and the REMS Slides. The VICTOZA[®] website for healthcare professionals (www.victozapro.com) will include a prominent REMS-specific link to the VICTOZA[®] REMS website. All website information will be updated within 60 days post approval of this modification.

The following are part of the REMS and are appended:

- The REMS Letter for Healthcare Providers (print version)
- The REMS Letter for Professional Societies (print version)
- The REMS Factsheet
- REMS Slides
- The VICTOZA[®] REMS Website (landing page)

B. Timetable for Submission of Assessments

Novo Nordisk will submit REMS Assessments to FDA at 1 year, 2 years, 3 years, 6 years and 7 years from the date of the approval of the initial REMS. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment. Novo Nordisk will submit each assessment so that it will be received by the FDA on or before the due date.

VICTOZA[®] REMS

FDA Required REMS Safety Information

- **Potential risk of medullary thyroid carcinoma**
- **Risk of acute pancreatitis associated with VICTOZA[®]**

Important Safety Notice

The FDA has required this notice as part of the VICTOZA[®] REMS (Risk Evaluation and Mitigation Strategy) to inform healthcare providers about the following serious risks:

Potential Risk of Medullary Thyroid Carcinoma

- 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.
- 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.

Risk of Acute Pancreatitis

- Based on spontaneous postmarketing reports, acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis has been observed in patients treated with VICTOZA[®].
- In clinical trials studying VICTOZA[®], there were more cases of pancreatitis in patients treated with VICTOZA[®] than in patients treated with comparators.

Because of these risks, VICTOZA is not recommended as a first-line therapy for patients inadequately controlled on diet and exercise.

A non-promotional factsheet, reviewed by the FDA, with more detailed safety information about these risks is enclosed. Please visit www.Victozaapro.com/REMS for more information about the VICTOZA[®] REMS program.

Indication: VICTOZA[®] (liraglutide [rDNA origin] injection) is an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

This letter does not contain the complete safety profile for VICTOZA[®]. Please see the Prescribing Information, including Boxed Warning, and Medication Guide, which are enclosed with this letter.

Reporting Adverse Events

You are encouraged to report negative side effects of prescription drugs to the FDA. Please contact Novo Nordisk at 1-877-4-VICTOZA (1-877-484-2869) or contact the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Sincerely,

Alan C. Moses, M.D.

Global Chief Medical Officer, Novo Nordisk

Enclosure: VICTOZA[®] REMS: FDA Required Safety Information

VICTOZA[®] Full Prescribing Information VICTOZA[®] Medication Guide

VICTOZA[®] REMS

FDA Required REMS Safety Information

- **Potential risk of medullary thyroid carcinoma**
- **Risk of acute pancreatitis associated with VICTOZA[®]**

Important Safety Notice

The FDA has required Novo Nordisk to distribute this safety notice to your organization as part of their VICTOZA[®] REMS (Risk Evaluation and Mitigation Strategy) program. We request that you provide the letter or the risk information included in this letter to your membership to inform your members about the following serious risks of VICTOZA[®]:

Potential Risk of Medullary Thyroid Carcinoma

- 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.
- 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.

Risk of Acute Pancreatitis

- Based on spontaneous postmarketing reports, acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis has been observed in patients treated with VICTOZA[®].
- In clinical trials studying VICTOZA[®], there were more cases of pancreatitis in patients treated with VICTOZA[®] than in patients treated with comparators.

Because of these risks, VICTOZA[®] is not recommended as a first-line therapy for patients inadequately controlled on diet and exercise.

A non-promotional factsheet, reviewed by the FDA, with more detailed safety information about these risks is enclosed. Please visit www.Victozaapro.com/REMS for more information about the VICTOZA[®] REMS program.

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Sincerely,

Alan C. Moses, M.D.

Global Chief Medical Officer, Novo Nordisk

Enclosure: VICTOZA® REMS: FDA Required Safety Information

VICTOZA® Full Prescribing Information VICTOZA® Medication Guide

VICTOZA[®] REMS (Risk Evaluation and Mitigation Strategy)

FDA Required REMS* Safety Information

- **Potential Risk of Medullary Thyroid Carcinoma**
- **Risk of Acute Pancreatitis**

Potential Risk of Medullary Thyroid Carcinoma

BOXED 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.
 - VICTOZA[®] is contraindicated in patients with a personal or family history of MTC and in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN2).
- 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.
 - **Counsel patients** regarding the potential risk of MTC with the use of Victoza and inform them of the symptoms of thyroid tumors (e.g., **mass in the neck, dysphagia, dyspnea or persistent hoarseness**). 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.

Risk of Acute Pancreatitis

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

- In clinical trials studying VICTOZA[®], there were more cases of pancreatitis in patients treated with VICTOZA[®] than in patients treated with comparators.
- After initiation of VICTOZA[®], and after dose increases, **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).**
- Discontinue VICTOZA[®] promptly if pancreatitis is suspected. Do not restart if pancreatitis is confirmed.
- Consider other antidiabetic therapies in patients with a history of pancreatitis.
- VICTOZA[®] has not been studied in patients with a history of pancreatitis.

Indication: VICTOZA[®] (liraglutide [rDNA origin] injection) is an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

VICTOZA is not recommended as a first-line therapy for patients inadequately controlled on diet and exercise.

* What is the VICTOZA REMS?

A REMS (Risk Evaluation and Mitigation Strategy) is a program required by the FDA to manage known or potential serious risks associated with a drug product. FDA has determined that a REMS is necessary to ensure that the benefits of VICTOZA[®] outweigh the potential risk of medullary thyroid carcinoma and the risk of acute pancreatitis. Novo Nordisk, Inc. has established an informational program for healthcare professionals to help minimize these risks. This factsheet is required by the FDA as part of the VICTOZA REMS program.

Please visit www.Victoza.com/REMS for further information.

Reporting Adverse Events:

To report adverse events contact:

- Novo Nordisk at 1-877-VICTOZA (1-877-484-2869) and/or
- FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

This factsheet does not contain the complete safety profile for Victoza. Please refer to the Prescribing Information, including Boxed Warning, for further information. If you have any questions about these materials, please call the Novo Nordisk Customer Care Center at 1-877-484-2869.

A REMS (Risk Evaluation and Mitigation Strategy) is a strategy required by the Food and Drug Administration (FDA) to manage known or potential serious risks associated with a drug product to ensure the benefits of a drug outweigh its risks.

The purpose of the VICTOZA[®] REMS is to inform healthcare providers about the following serious risks:

Potential Risk of Medullary Thyroid Carcinoma

- 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.
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- In clinical trials studying VICTOZA[®], there were more cases of pancreatitis in patients treated with VICTOZA[®] than in patients treated with comparators



Potential Risk of Thyroid C-Cell Tumors

Appropriate Patient Selection

- VICTOZA[®] is contraindicated in patients with a personal or family history of MTC and in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN2)
- VICTOZA[®] is not recommended as first-line therapy for patients who have inadequate glycemic control on diet and exercise

Patient Management

- 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 and to rule out thyroid C-cell tumor



Risk of Pancreatitis

Appropriate Patient Selection

Patient Management

- VICTOZA[®] has not been studied sufficiently in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis
- After initiation of VICTOZA[®], and after dose increases, 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)
- Discontinue promptly if pancreatitis is suspected
- Do not restart if pancreatitis is confirmed
- Consider other antidiabetic therapies in patients with a history of pancreatitis




VICTOZA[®]

liraglutide (rDNA origin) injection

VICTOZA[®] **REMS PROGRAM**

A REMS (**R**isk **E**valuation and **M**itigation **S**trategy) is a strategy required by the Food and Drug Administration (FDA) to manage known or potential serious risks associated with a drug product to ensure the benefits of a drug outweigh its risks.

The purpose of the VICTOZA[®] REMS is to inform healthcare providers about the following serious risks:

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Please see the non-promotional VICTOZA[®] REMS Factsheet for Prescribers, reviewed by the FDA, for further information on these risks.

**Materials for Healthcare
Providers**

[VICTOZA[®] REMS Factsheet for Prescribers](#)

[REMS Letter to Healthcare Providers](#)

[REMS Letter to Professional Societies](#)

[REMS Slides](#)

[VICTOZA[®] Medication Guide](#)

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/s/

JENNIFER R PIPPINS
07/01/2015