Initial REMS approval: 12/2014

NDA 206321

SAXENDA® (liraglutide [rDNA origin] injection)

Novo Nordisk Inc.
800 Scudders Mill Road, Plainsboro, NJ 08536
Phone: 609-786-4690

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOAL

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

- Informing healthcare providers about the potential risk of medullary thyroid carcinoma associated with SAXENDA®
- Informing healthcare providers about the risk of acute pancreatitis (including necrotizing pancreatitis) associated with SAXENDA®

II. REMS ELEMENTS

A. Communication Plan

Novo Nordisk will implement the following communication plan to healthcare providers likely to prescribe SAXENDA®. The communication plan will include:

1. REMS Letters

Novo Nordisk will send a REMS Letter for Healthcare Providers and a REMS Letter for Professional Societies within 60 days of the REMS approval and again at 12 months after the REMS approval. The REMS Letters will address the potential risk of medullary thyroid carcinoma and the risk of acute pancreatitis. REMS Letters will be distributed by US mail. If a REMS Letter is undeliverable, Novo Nordisk will use available resources to obtain updated address information and send a second letter via US mail within 45 calendar days. If the proper

address cannot be obtained, the communication will not be sent again. A copy of the Prescribing Information (PI), Medication Guide, and REMS Factsheet will accompany the REMS Letters.

a) REMS Letter for Healthcare Providers.

The intended audience for the REMS Letter for Healthcare Providers is healthcare providers who are likely to prescribe SAXENDA® and includes general practitioners, family practitioners, internists, gynecologists, endocrinologists, gastroenterologists, cardiologists, nurse practitioners and physician assistants.

The REMS Letter for Healthcare Providers will also be available via a link from the SAXENDA® REMS website, through Novo Nordisk Customer Care center and from Novo Nordisk sales and medical representatives for the duration of the REMS.

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 or its content be provided to their membership:

- American Academy of Family Physicians (AAFP)
- American Academy of Nurse Practitioners (AANP)
- American Academy of Physicians Assistants (AAPA)
- American Association of Clinical Endocrinologists (AACE)
- American Association of Diabetic Educators (AADE)
- American Board of Physician Nutrition Specialists (ABPNS)
- American College of Cardiology (ACC)
- American College of Obstetricians and Gynecologists (ACOG)
- American College of Physicians (ACP)
- American College of Preventive Medicine (ACPM)
- American Diabetes Association (ADA)
- American Gastroenterological Association (AGA)
- American Heart Association (AHA)
- American Medical Association (AMA)
- American Osteopathic Association (AOA)

- American Pharmacists Association (APhA)
- American Society for Metabolic and Bariatric Surgery (ASMBS)
- American Society for Preventive Cardiology (ASPC)
- American Society of Bariatric Physicians (ASBP)
- The Endocrine Society (ENDO)
- The Obesity Society (TOS)

2) REMS Factsheet

A REMS Factsheet will be made available to healthcare providers and distributed through Novo Nordisk SAXENDA® field based sales or medical representatives during the initial healthcare provider discussion within the first 18 months after approval of this REMS. Novo Nordisk SAXENDA® field based sales or medical representatives will verbally review each risk message contained in the Factsheet.

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 SAXENDA®. The REMS Slides will be available at the SAXENDA® REMS website within 60 days of the REMS approval and will be part of a slide deck used at Novo Nordisk sponsored speaker training and promotional programs beginning 2015. The REMS Slides will be posted on the REMS website for the duration of the REMS.

4) Dissemination of REMS information at scientific meetings

The SAXENDA® 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 duration of the REMS.

5) REMS Website

The SAXENDA® REMS website for healthcare professionals (www.SAXENDA.com/REMS) will continue for the duration of the REMS. The REMS website will include the option to print versions of the PI, REMS Letter for Healthcare Providers, REMS Factsheet and the REMS

slides. The SAXENDA product website will include a prominent REMS-specific link to SAXENDA® REMS website. The following are part of the REMS and are appended:

- The REMS Letter for Healthcare Providers
- The REMS Letter for Professional Societies
- The REMS Factsheet
- REMS Slides
- The SAXENDA® REMS Website (landing page)

B. Timetable for Submission of Assessments

Novo Nordisk will submit REMS Assessments to FDA at 18 months, 3 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 will 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.

SAXENDA® REMS

FDA Required REMS Safety Information

- **Potential risk of medullary thyroid carcinoma**
- **Risk of acute pancreatitis**

Important Safety Notice

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

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 SAXENDA® causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as the human relevance of liraglutide-induced rodent thyroid C-cell tumors has not been determined.

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 liraglutide.
- In clinical trials studying SAXENDA®, there were more cases of pancreatitis in patients treated with SAXENDA® than in patients treated with placebo.

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

Indication: SAXENDA® (liraglutide [rDNA origin] injection) is indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adult patients with an initial body mass index (BMI) of:

- 30 kg/m^2 or greater (obese), or
- 27 kg/m^2 or greater (overweight) in the presence of at least one weight-related comorbid condition (e.g., hypertension, type 2 diabetes mellitus or dyslipidemia).

This letter does not contain the complete safety profile for SAXENDA®. 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 1-844-363-4448 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: SAXENDA® REMS: FDA Required Safety Information
SAXENDA® Full Prescribing Information SAXENDA® Medication Guide

SAXENDA® REMS

FDA Required REMS Safety Information

- **Potential risk of medullary thyroid carcinoma**
- **Risk of acute pancreatitis**

Important Safety Notice

The FDA has required Novo Nordisk to distribute this safety notice to your organization as part of their SAXENDA® 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 SAXENDA®:**

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 SAXENDA® causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as the human relevance of liraglutide-induced rodent thyroid C-cell tumors has not been determined.

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 liraglutide.
- In clinical trials studying SAXENDA®, there were more cases of pancreatitis in patients treated with SAXENDA® than in patients treated with placebo.

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

Indication: SAXENDA® (liraglutide [rDNA origin] injection) is indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adult patients with an initial body mass index (BMI) of:

- 30 kg/m^2 or greater (obese), or
- 27 kg/m^2 or greater (overweight) in the presence of at least one weight-related comorbid condition (e.g., hypertension, type 2 diabetes mellitus, or dyslipidemia).

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

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Sincerely,

Alan C. Moses, M.D.
Global Chief Medical Officer, Novo Nordisk

Enclosure: SAXENDA® REMS: FDA Required Safety Information
SAXENDA® Full Prescribing Information SAXENDA® Medication Guide

Saxenda®
liraglutide (rDNA origin) injection

SAXENDA® 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 SAXENDA® causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as the human relevance of liraglutide-induced rodent thyroid C-cell tumors has not been determined.
- SAXENDA® is contraindicated in patients with a personal or family history of MTC and in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN2).

- **Counsel patients** regarding the risk for MTC and inform them of symptoms of thyroid tumors (e.g., **mass in the neck, dysphagia, dyspnea, persistent hoarseness**). Patients with thyroid nodules noted on physical examination or neck imaging should also be further evaluated.
- Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with SAXENDA®. If serum calcitonin is measured and found to be elevated, the patient should be further evaluated.

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 liraglutide.
- In clinical trials studying SAXENDA®, there were more cases of pancreatitis in patients treated with SAXENDA® than in patients treated with placebo.
- SAXENDA® has not been studied sufficiently in patients with a history of pancreatitis.
- After initiation of SAXENDA®, and after dose increases, **observe patients carefully for signs and symptoms of pancreatitis.**
- **Counsel patients** to contact their healthcare provider promptly if they experience symptoms of pancreatitis **(e.g., 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.

Indication: SAXENDA® is indicated as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adult patients with an initial body mass index (BMI) of:

- 30 kg/m^2 or greater (obese), or
- 27 kg/m^2 or greater (overweight) in the presence of at least one weight-related comorbid conditions (e.g., hypertension, type 2 diabetes mellitus, or dyslipidemia).

* What is the SAXENDA® 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 SAXENDA® outweigh the potential risk of medullary thyroid carcinoma and the risk of acute pancreatitis. This factsheet is required by the FDA as part of the SAXENDA® REMS program.

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

Reporting Adverse Events:

To report adverse events, contact:

- Novo Nordisk at 1-844-363-4448 and/or
- FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

This factsheet does not contain the complete safety profile for SAXENDA®. 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 1-844-363-4448.

SAXENDA® REMS: Risk Evaluation and Mitigation Strategy

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 SAXENDA REMS is to inform healthcare providers of the following serious risks associated with SAXENDA:

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

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Please see Important Safety Information in this presentation.
Please see Prescribing Information.

Saxenda®
liraglutide (rDNA origin) injection

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 SAXENDA® causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as the human relevance of liraglutide-induced rodent thyroid C-cell tumors has not been determined.

Potential Risk of Medullary Thyroid Carcinoma (2)

Appropriate Patient Selection

- SAXENDA® is contraindicated in patients with a personal or family history of MTC and in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN2).

Patient Management

- **Counsel patients** regarding the risk for MTC and inform them of symptoms of thyroid tumors (e.g., **mass in the neck, dysphagia, dyspnea, persistent hoarseness**).
- **Instruct patients** to contact their healthcare provider promptly if these symptoms occur.
- Patients with thyroid nodules noted on physical examination or neck imaging should be further evaluated.

Potential Risk of Medullary Thyroid Carcinoma (3)

Patient Management

- Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value in patients treated with SAXENDA®. If serum calcitonin is measured and found to be elevated, the patient should be further evaluated.

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 liraglutide.
- In clinical trials studying SAXENDA®, there were more cases of pancreatitis in patients treated with SAXENDA® than in patients treated with placebo.

Risk of Acute Pancreatitis (2)

Appropriate Patient Selection

- SAXENDA® has not been studied sufficiently in patients with a history of pancreatitis.

Patient Management

- After initiation of SAXENDA®, and after dose increases, **observe patients** carefully for signs and symptoms of pancreatitis.
- Counsel patients to contact their healthcare provider promptly if they experience 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.

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Please see Important Safety Information in this presentation.
Please see Prescribing Information.

Saxenda®
liraglutide (rDNA origin) injection

Saxenda®
liraglutide (rDNA origin) injection

SAXENDA® 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 SAXENDA® REMS is to inform healthcare providers about the following serious risks:

Potential Risk of Medullary Thyroid Carcinoma

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Materials for Healthcare Providers

SAXENDA® REMS Factsheet for Prescribers

REMS Letter to Healthcare Providers

REMS Letter to Professional Societies

REMS Slides

SAXENDA® Medication Guide

Please see the non-promotional *SAXENDA® REMS* Factsheet for Prescribers, reviewed by the FDA, for further information on these risks

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This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

JAMES P SMITH
12/23/2014