

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

125469Orig1s000

REMS

Initial REMS approval: 09/2014

BLA 125469 TRULICITY™
(Dulaglutide)
Glucagon-like Peptide-1 (GLP-1) Receptor Agonist

Eli Lilly and Company
Lilly Corporate Center, Indianapolis, Indiana 46285
Telephone: 317-276-2000

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOAL

The goal of the TRULICITY REMS is to mitigate the potential risk of medullary thyroid carcinoma and the risk of pancreatitis associated with the use of TRULICITY by:

- Informing healthcare providers (HCPs) about the potential risk of medullary thyroid carcinoma associated with TRULICITY.
- Informing HCPs about the risk of pancreatitis associated with TRULICITY.

II. REMS Elements

A. Communication Plan

Eli Lilly and Company (Lilly) will implement the following communication plan to HCPs likely to prescribe TRULICITY. The communication plan will include:

1. REMS Letters

Lilly will send a *REMS Letter for Healthcare Providers* and a *REMS Letter for Professional Societies* within 60 days of product approval and again after 12 months of product approval. The REMS Letters will address the potential risk of medullary thyroid carcinoma and the risk of pancreatitis.

Distribution of the REMS Letters will be via electronic mail (email). If the email or fax is marked as undeliverable, a follow-up hard copy of the REMS Letter will be sent within 30 days of the undeliverable date. For those HCPs who do not prefer to receive electronic communications and for those HCPs whose e-mail and/or fax communications fail, a direct mail REMS Letter will be sent.

A copy of (or a link to) the Prescribing Information (PI), Medication Guide, and REMS Factsheet will accompany the REMS Letters.

REMS Letter for Healthcare Providers

The intended audience for the *REMS Letter for Healthcare Providers* will be endocrinologists as well as those HCPs (including physicians in internal medicine and family practice, nurse practitioners, and physician assistants) who have prescribed a glucagon-like peptide-1 (GLP-1) receptor agonist in the 12 months prior to dissemination of the letter.

The *REMS Letter for Healthcare Providers* will also be available via a link from the TRULICITY REMS website, through The Lilly Answers Center, and from Eli Lilly sales and medical representatives for the duration of the REMS.

REMS Letter for Professional Societies

Lilly will send the *REMS Letter for Professional Societies* to the leadership of the following professional societies and organizations and will request that the letter or the content be provided to their membership:

- American College of Physicians
- American Medical Association
- American Academy of Family Physicians
- American College of Osteopathic Family Physicians
- American College of Clinical Pharmacy
- American Pharmacists Association
- American Society of Health-System Pharmacists
- American Academy of Nurse Practitioners
- American Association of Clinical Endocrinologists
- Endocrine Society
- American Diabetes Association
- American Association of Diabetes Educators
- American Academy of Physician Assistants
- Association of Managed Care Pharmacy
- National Association of Managed Care Physicians

2. REMS Factsheet

A REMS Factsheet for HCPs will be distributed with the REMS Letters and will be made available to HCPs through Lilly's sales and medical representatives during the initial product discussion of TRULICITY with all HCPs visited during the first 12 months after approval of this REMS.

The REMS Factsheet for HCPs is part of the REMS and is appended.

3. REMS Website

The TRULICITY REMS website for healthcare professionals (www.TRULICITYREMS.com) will continue for the duration of the REMS and will provide access to downloadable versions of all the REMS materials, the Prescribing Information, and Medication Guide. The TRULICITY product website will include a link to the TRULICITY REMS website.

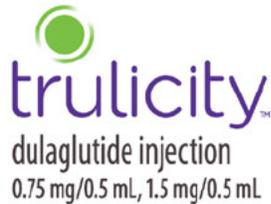
The following are part of the TRULICITY REMS and are appended:

- The *REMS Letter for Healthcare Providers* (print and email versions)
- The *REMS Letter for Professional Societies* (print and email versions)
- The REMS Factsheet
- The TRULICITY REMS Website

The TRULICITY REMS webpage is part of the REMS and is appended.

B. Timetable for Submission of Assessments

Lilly will submit REMS assessments to the Food and Drug Administration (FDA) at 18 months, 3 years, and 7 years from the date of the initial approval of the REMS. The reporting interval covered by each assessment will conclude no earlier than 60 days before the submission date for that assessment time interval. Lilly will submit each assessment so that it will be received by the FDA on or before the due date.



TRULICITY REMS

FDA Required REMS Safety Information

- **Potential Risk of Medullary Thyroid Carcinoma (MTC)**
- **Risk of Pancreatitis**

Important Safety Notice

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

- **Potential Risk of Medullary Thyroid Carcinoma (MTC).** Thyroid C-cell tumors have been observed in rodent studies with glucagon-like peptide (GLP-1) receptor agonists. It is unknown whether TRULICITY causes thyroid C-cell tumors, including MTC, in humans. Counsel patients regarding the risk of MTC and the symptoms of thyroid tumors.
- **Risk of Pancreatitis.** Pancreatitis has been reported with the use of GLP-1 receptor agonists. Cases of pancreatitis have been described in association with TRULICITY during clinical trials. Discontinue promptly if pancreatitis is suspected. Do not restart if pancreatitis is confirmed. Consider other antidiabetic therapies in patients with a history of pancreatitis.

Because of these risks, TRULICITY is not recommended as first-line therapy for patients with type 2 diabetes mellitus inadequately controlled on diet and exercise.

A non-promotional factsheet, reviewed by the FDA, with more detailed safety information about these risks is enclosed.

Indication: TRULICITY is a GLP-1 receptor agonist indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Please visit www.TRULICITYREMS.com for more information.

This letter does not contain the complete safety information for TRULICITY. Please see the enclosed Prescribing Information and Medication Guide.

Reporting Adverse Events

You are encouraged to report negative side effects of prescription drugs to Eli Lilly and Company (the Sponsor) at 1-800-LillyRx (1-800-545-5979) and/or the FDA at www.fda.gov/medwatch, or call 1-800-FDA-1088.

Please contact The Lilly Answers Center at 1-800-545-5979 with any questions about the information in this letter or the safe and effective use of TRULICITY.

Sincerely,

Robert W. Baker, M.D.
Vice President, Global Patient Safety
Eli Lilly and Company



TRULICITY REMS

FDA Required REMS Safety Information

- **Potential Risk of Medullary Thyroid Carcinoma (MTC)**
- **Risk of Pancreatitis**

Important Safety Notice

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- **Potential Risk of Medullary Thyroid Carcinoma (MTC).** Thyroid C-cell tumors have been observed in rodent studies with glucagon-like peptide (GLP-1) receptor agonists. It is unknown whether TRULICITY causes thyroid C-cell tumors, including MTC, in humans. Counsel patients regarding the risk of MTC and the symptoms of thyroid tumors.
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Reporting Adverse Events

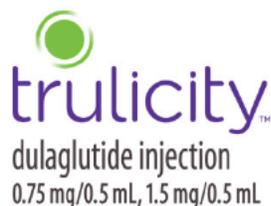
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Please contact The Lilly Answers Center at 1-800-545-5979 with any questions about the information in this letter or the safe and effective use of TRULICITY.

Sincerely,

Robert W. Baker, M.D.
Vice President, Global Patient Safety
Eli Lilly and Company

From: Eli Lilly and Company
To: Healthcare Providers
Subject: Potential Risk of Medullary Thyroid Carcinoma and Risk of Pancreatitis with Trulicity (Dulaglutide)



TRULICITY REMS

FDA Required REMS Safety Information

- Potential Risk of Medullary Thyroid Carcinoma (MTC)
- Risk of Pancreatitis

Important Safety Notice

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

- **Potential Risk of Medullary Thyroid Carcinoma (MTC).** Thyroid C-cell tumors have been observed in rodent studies with glucagon-like peptide (GLP-1) receptor agonists. It is unknown whether TRULICITY causes thyroid C-cell tumors, including MTC, in humans. Counsel patients regarding the risk of MTC and the symptoms of thyroid tumors.
- **Risk of Pancreatitis.** Pancreatitis has been reported with the use of GLP-1 receptor agonists. Cases of pancreatitis have been described in association with TRULICITY during clinical trials. Discontinue promptly if pancreatitis is suspected. Do not restart if pancreatitis is confirmed. Consider other antidiabetic therapies in patients with a history of pancreatitis.

Because of these risks, TRULICITY is not recommended as first-line therapy for patients with type 2 diabetes mellitus inadequately controlled on diet and exercise.

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Indication: TRULICITY is a GLP-1 receptor agonist indicated as 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 information for TRULICITY. To review the Prescribing Information and Medication Guide, see links below:

Prescribing Information	Medication Guide
Active link to be included in communication	Active link to be included in communication

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Sincerely,

Robert W. Baker, M.D.
Vice President, Global Patient Safety
Eli Lilly and Company

From: Eli Lilly and Company
To: Professional Society
Subject: Potential Risk of Medullary Thyroid Carcinoma and Risk of Pancreatitis with Trulicity (Dulaglutide)



TRULICITY REMS

FDA Required REMS Safety Information

- Potential Risk of Medullary Thyroid Carcinoma (MTC)
- Risk of Pancreatitis

Important Safety Notice

The FDA has required Eli Lilly and Company to distribute this safety notice to your organization as part of the TRULICITY REMS (Risk Evaluation and Mitigation Strategy) program.

We request that you inform your members about the following **serious risks of TRULICITY (dulaglutide)**:

- **Potential Risk of Medullary Thyroid Carcinoma (MTC).** Thyroid C-cell tumors have been observed in rodent studies with glucagon-like peptide (GLP-1) receptor agonists. It is unknown whether TRULICITY causes thyroid C-cell tumors, including MTC, in humans. Counsel patients regarding the risk of MTC and the symptoms of thyroid tumors.
- **Risk of Pancreatitis.** Pancreatitis has been reported with the use of GLP-1 receptor agonists. Cases of pancreatitis have been described in association with TRULICITY during clinical trials. Discontinue promptly if pancreatitis is suspected. Do not restart if pancreatitis is confirmed. Consider other antidiabetic therapies in patients with a history of pancreatitis.

Because of these risks, TRULICITY is not recommended as first-line therapy for patients with type 2 diabetes mellitus inadequately controlled on diet and exercise.

A non-promotional factsheet, reviewed by the FDA, with more detailed safety information about these risks is available at www.TRULICITYREMS.com.

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Indication: TRULICITY is a GLP-1 receptor agonist indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

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Robert W. Baker, M.D.
Vice President, Global Patient Safety
Eli Lilly and Company



TRULICITY REMS (Risk Evaluation and Mitigation Strategy)

FDA Required TRULICITY REMS Safety Information

- **Potential Risk of Medullary Thyroid Carcinoma (MTC)**
- **Risk of Pancreatitis**

Potential Risk of Medullary Thyroid Carcinoma (MTC)

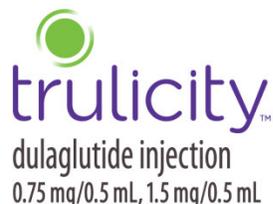
BOXED WARNING- Risk of Thyroid C-Cell Tumors

- Dulaglutide causes thyroid C-cell tumors in rats. It is unknown whether TRULICITY causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans as human relevance could not be determined from clinical or nonclinical studies.
- TRULICITY 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 and the symptoms of thyroid tumors (*e.g., a mass in the neck, dysphagia, dyspnea, or persistent hoarseness*).
- **Instruct patients** to contact their healthcare provider (HCP) promptly if these symptoms occur.
- **Refer patients** to an endocrinologist for further evaluation if thyroid nodules are noted upon physical examination or neck imaging.
- Routine monitoring of serum calcitonin (a biomarker of MTC) or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with TRULICITY. Such monitoring may increase the risk of unnecessary procedures, due to the low specificity of serum calcitonin testing for MTC and a high background incidence of thyroid disease. **Refer patients** to an endocrinologist for further evaluation if serum calcitonin is measured and found to be elevated.

Risk of Pancreatitis

- Pancreatitis has been reported with the use of glucagon-like peptide-1 (GLP-1) receptor agonists. Cases of pancreatitis have been described in association with TRULICITY during clinical trials.



- **Counsel patients** to contact their HCP promptly if they experience symptoms of pancreatitis (*e.g., persistent, severe abdominal pain sometimes radiating to the back, which may or may not be accompanied by vomiting*).
- **Immediately discontinue** TRULICITY if pancreatitis is suspected. Perform confirmatory tests, and initiate appropriate management. If pancreatitis is confirmed, TRULICITY should not be restarted.
- **Consider** other antidiabetic therapies for patients with a history of pancreatitis. TRULICITY has not been studied in patients with a history of pancreatitis to determine whether these patients are at increased risk for pancreatitis.

Indication

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

TRULICITY is not recommended as first-line therapy for patients with type 2 diabetes mellitus inadequately controlled on diet and exercise.

What is the TRULICITY 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 TRULICITY outweigh the potential risk of MTC and the risk of pancreatitis. This factsheet is required by the FDA as part of the TRULICITY REMS program.

Please visit www.TRULICITYREMS.com for further information.

Reporting Adverse Events

To report adverse events among patients taking TRULICITY, contact:

- Eli Lilly and Company at 1-800-LillyRx (1-800-545-5979) and/or
- FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please contact The Lilly Answers Center at 1-800-545-5979 with any questions about the information in this factsheet or the safe and effective use of TRULICITY.

This factsheet does not contain the complete safety information for TRULICITY. Please refer to the Prescribing Information, including Boxed Warning, for further information.



trulicity
dulaglutide injection
0.25 mg/0.5 mL, 1.5 mg/0.5 mL

[Prescribing Information including Boxed Warning](#)
[Medication Guide](#)

Trulicity™ REMS (Risk Evaluation and Mitigation Strategy)

What is the Trulicity REMS?

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

The purpose of the Trulicity REMS is to inform healthcare providers (HCPs) about the following risks of Trulicity:

- **Potential Risk of Medullary Thyroid Carcinoma**
 - Thyroid C-cell tumors have been observed in rodent studies with glucagon-like peptide-1 (GLP-1) receptor agonists.
 - It is unknown whether Trulicity causes thyroid C-cell tumors, including medullary thyroid carcinoma in humans.
 - Counsel patients regarding the risk of MTC and the symptoms of thyroid tumors.
- **Risk of Pancreatitis**
 - Pancreatitis has been reported with the use of GLP-1 receptor agonists. Cases of pancreatitis have been described in association with Trulicity during clinical trials.
 - Discontinue promptly if pancreatitis is suspected. Do not restart if pancreatitis is confirmed. Consider other anti-diabetic therapies in patients with a history of pancreatitis.

[A non-promotional fact sheet](#) reviewed by FDA, with more detailed safety information about these risks is available.

Materials for Healthcare Providers:

- » [Trulicity REMS Factsheet for Healthcare Providers](#)
- » [REMS Letters to Healthcare Providers](#)



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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/

MARY H PARKS
09/18/2014