

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

125431Orig1s000

REMS

Initial REMS approved: 4/2014

BLA STN-125431 TANZEUM™

(Albiglutide)

Glucagon-like Peptide-1 (GLP-1) Receptor Agonist

GlaxoSmithKline LLC

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

GlaxoSmithKline
5 Moore Drive, PO Box 13398
Research Triangle Park, NC 27709-3398, USA
Telephone: 1-888-825-5249

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOAL

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

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

II. REMS ELEMENTS

A. Communication Plan

GSK will implement the following elements of a communication plan to healthcare providers likely to prescribe TANZEUM. The communication plan will include:

1. REMS Letters

GSK will send the *REMS Letter for Healthcare Providers* and the *REMS Letter for Professional Societies* within 60 days of approval, and again at 1 year after approval. The REMS Letters will address the potential risk of medullary thyroid carcinoma and

the risk of acute pancreatitis.

Distribution of the REMS Letters will be via electronic mail (email) or by mail if no email contact information is available. If the first email is marked as unopened, a second email will be sent within one week. If the second email is marked as undeliverable or as unopened, a follow-up hard copy of the REMS Letter will be sent within 30 days. If a targeted healthcare provider's email address is not available or if an email is undeliverable, the letter will be sent through the mail.

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

REMS Letter for Healthcare Providers

The intended audience for the *REMS Letter for Healthcare Providers* are healthcare providers who are likely to prescribe TANZEUM, and includes physicians, nurse practitioners, and physician assistants in the specialties of endocrinology, internal medicine, and family practice.

The *REMS Letter for Healthcare Providers* will also be available via a link from the TANZEUM REMS website, through the GSK Customer Response Center and from GSK sales and medical representatives for the duration of the REMS.

GSK will provide an electronic copy of the *REMS Letter for Healthcare Providers* to the BLA and MedWatch prior to issuing.

REMS Letter for Professional Societies

GSK will send the *REMS Letter for Professional Societies* to the following professional societies and organizations. GSK will request the letter 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 will be made available to healthcare providers and distributed through GSK sales and medical representatives during the first product discussion for TANZEUM with healthcare providers during the first 12 months after approval of this REMS.

3. REMS Website

The TANZEUM REMS website for healthcare professionals (www.TANZEUMREMS.com) will continue for the duration of the REMS and will include a prominent REMS-specific link to downloadable versions of the Prescribing Information and Medication Guide, REMS *Letter for Healthcare Providers*, and the REMS Factsheet.

The following are part of the TANZEUM 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 TANZEUM REMS Website

B. Timetable for Submission of Assessments

GSK will submit REMS Assessments to FDA at 18 months, 3 years, and 7 years from the date of the approval. 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. GSK will submit each assessment so that it will be received by the FDA on or before the due date.



TANZEUM REMS

FDA Required REMS Safety Information

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

Important Safety Notice

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

- **Potential Risk of Medullary Thyroid Carcinoma (MTC).** Thyroid C-cell tumors have been observed in rodent studies with glucagon-like peptide-1 (GLP-1) receptor agonists at clinically relevant exposures. It is unknown whether TANZEUM causes thyroid C-cell tumors, including MTC in humans.
- **Acute Pancreatitis.** In clinical trials, there were more cases of acute pancreatitis among patients treated with TANZEUM than among patients treated with comparators.

Because of these risks, TANZEUM is not recommended as 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.

Indication: TANZEUM 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.TANZEUMREMS.com for more information.

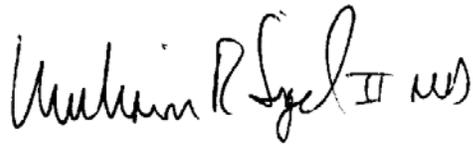
This letter does not contain the complete safety profile for TANZEUM. Please see the enclosed Prescribing Information and Medication Guide.

Reporting Adverse Events

You are encouraged to report negative side effects of prescription drugs to GlaxoSmithKline (the Sponsor) at 1-888-825-5249 and/or the FDA www.fda.gov/medwatch, or call 1-800-FDA-1088.

If you have any questions about the information contained in this letter or the use of TANZEUM, you may contact:

- US Medical Information Department at 1-877-356-8368

A handwritten signature in black ink that reads "William R Sigmund, II MD". The signature is written in a cursive style with a large initial 'W' and 'S'.

William R Sigmund, II, MD, MHS, FACC
Senior Vice President
Medical Affairs, North America



TANZEUM REMS

FDA Required REMS Safety Information

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

Important Safety Notice

The FDA has required GlaxoSmithKline to distribute this safety notice to your organization as part of their TANZEUM™ REMS (Risk Evaluation and Mitigation Strategy) program. We request that you provide the letter to your membership to inform your members about the following **serious risks of TANZEUM**:

- **Potential Risk of Medullary Thyroid Carcinoma (MTC).** Thyroid C-cell tumors have been observed in rodent studies with glucagon-like peptide-1 (GLP-1) receptor agonists at clinically relevant exposures. It is unknown whether TANZEUM causes thyroid C-cell tumors, including MTC in humans.
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Because of these risks, TANZEUM is not recommended as first-line therapy for patients inadequately controlled on diet and exercise.

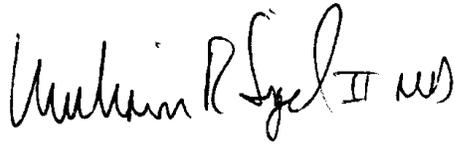
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William R Sigmund, II, MD, MHS, FACC
Senior Vice President
Medical Affairs, North America

From: GlaxoSmithKline
To: Healthcare Providers
Subject: Risk of Medullary Thyroid Carcinoma and Acute Pancreatitis with Tanzeum (albiglutide)



TANZEUM REMS

FDA Required REMS Safety Information

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

Important Safety Notice

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- **Acute Pancreatitis.** In clinical trials, there were more cases of acute pancreatitis among patients treated with TANZEUM than among patients treated with comparators.



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Indication:

TANZEUM 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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[Prescribing Information](#)

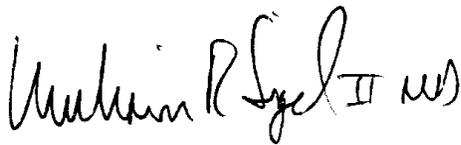
[Medication Guide](#)

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William R Sigmund, II, MD, MHS, FACC
Senior Vice President
Medical Affairs, North America

GlaxoSmithKline Response Center
1-888-825-5249

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From: GlaxoSmithKline
To: Professional Societies
Subject: Risk of Medullary Thyroid Carcinoma and Acute Pancreatitis with Tanzeum (albiglutide)



TANZEUM REMS

FDA Required REMS Safety Information

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

Important Safety Notice

The FDA has required GlaxoSmithKline to distribute this safety notice to your organization as part of their TANZEUM REMS (Risk Evaluation and Mitigation Strategy) program.

We request that you inform your members about the following **serious risks of TANZEUM**:

- **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 at clinically relevant exposures. It is unknown whether TANZEUM causes thyroid C-cell tumors, including MTC in humans.
- **Acute Pancreatitis.** In clinical trials, there were more cases of acute pancreatitis among patients treated with TANZEUM than among patients treated with comparators.



Because of these risks, TANZEUM is not recommended as 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 available at www.TANZEUMREMS.com

Indication:

TANZEUM 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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[Prescribing Information](#)

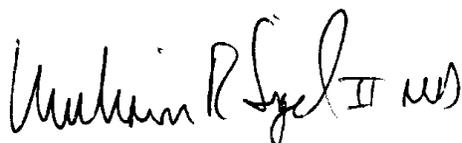
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William R Sigmund, II, MD, MHS, FACC
Senior Vice President
Medical Affairs, North America

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Tanzeum REMS (Risk Evaluation and Mitigation Strategy)

FDA Required REMS Safety Information

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

Potential Risk of Medullary Thyroid Carcinoma

BOXED WARNING: Risk of Thyroid C-Cell Tumors

- Thyroid C-cell tumors have been observed in rodent studies with glucagon-like peptide-1 (GLP-1) receptor agonists at clinically relevant exposures. It is unknown whether TANZEUM causes thyroid C-cell tumors, including medullary thyroid carcinoma in humans.
 - TANZEUM is contraindicated in patients with a personal or family history of MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Routine serum calcitonin or thyroid ultrasound monitoring is of uncertain value in patients treated with TANZEUM. Patients should be counseled regarding the risk and symptoms of thyroid tumors
- **Counsel patients** regarding the potential risk for MTC and the symptoms of thyroid tumors (**e.g., a mass in the neck, dysphagia, dyspnea, persistent hoarseness**). Patients should be instructed to contact their Healthcare Provider (HCP) promptly in the event of symptoms. Patients with thyroid nodules noted on physical examination or neck imaging should be referred to an endocrinologist for further evaluation.
 - 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 TANZEUM. 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. 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

- In clinical trials, there were more cases of acute pancreatitis among patients treated with TANZEUM than among patients treated with comparators.



- **Counsel patients** to contact their HCP promptly in the event of characteristic symptoms of acute pancreatitis: **persistent, severe abdominal pain** sometimes radiating to the back, which may or may not be accompanied by vomiting.
- If acute pancreatitis is suspected, TANZEUM should promptly be discontinued. If acute pancreatitis is confirmed, TANZEUM should not be restarted.
- TANZEUM has not been studied in patients with a history of pancreatitis to determine whether these patients are at increased risk for acute pancreatitis. Consider other anti-diabetic therapies in patients with a history of pancreatitis.

Indication

TANZEUM 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.

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

What is the Tanzeum 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 TANZEUM 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 TANZEUM REMS program. Please visit www.tanzeumrems.com for further information.

Adverse Events

To report adverse events among patients taking TANZEUM, contact:

- GlaxoSmithKline (the Sponsor) at 1-888-825-5249 and/or
- FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

Please contact our Medical Information department at 1-888-825-5249 if you have any questions about this factsheet or the safe and effective use of TANZEUM.





Prescribing Information including Boxed Warning Medication Guide

TANZEUM REMS (Risk Evaluation and Mitigation Strategy)

What is the TANZEUM REMS?

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

The purpose of the TANZEUM REMS is to inform healthcare providers about the following risks of TANZEUM:

- Potential Risk of Medullary Thyroid Carcinoma
 - Thyroid C-cell tumors have been observed in rodent studies with glucagon-like peptide (GLP-1) receptor agonists at clinically relevant exposures. It is unknown whether TANZEUM causes thyroid C-cell tumors, including Medullary Thyroid Carcinoma in humans.
- Risk of Acute Pancreatitis
 - In clinical trials, there were more cases of acute pancreatitis among patients treated with TANZEUM than among patients treated with comparators.

A non-promotional factsheet, reviewed by the FDA, with more detailed safety information about these risks is available in the box to the right.

Materials for Healthcare Providers

 [TANZEUM REMS Safety Information for Providers Factsheet](#)

 [REMS Letter to Healthcare Providers](#)

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/s/

CURTIS J ROSEBRAUGH
04/15/2014