

Initial REMS approved: 4/2014

Most recent modification: 07/2015

BLA STN-125431 TANZEUM®

(Albiglutide)

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

GlaxoSmithKline LLC

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

GlaxoSmithKline
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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 initial approval, and again at 1 year after

initial approval of this REMS. 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 upon request through the GSK Customer Response Center and from GSK sales and medical representatives for one year after approval of the most recent REMS modification.

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 initial approval of this REMS.

A REMS Factsheet will be made available to healthcare providers upon request through GSK sales and medical representatives for one year after approval of the most recent REMS modification.

3. REMS Website

The TANZEUM REMS website (www.TANZEUMREMS.com) will continue for 3 years after the initial approval of the REMS. The TANZEUM REMS website will include downloadable versions of the Prescribing Information and Medication Guide, REMS *Letter for Healthcare Providers*, and the REMS Factsheet. The TANZEUM website for healthcare professionals (www.gsksource.com/tanzeum) will include a prominent REMS-specific link to the TANZEUM REMS website. All website information will be updated within 60 days post approval of the most recent modification.

The following parts of the TANZEUM REMS revised with this modification are appended:

- The *REMS Letter for Healthcare Providers* (print)
- 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 (albiglutide):

Potential Risk of Medullary Thyroid Carcinoma (MTC)

- Carcinogenicity of albiglutide could not be assessed in rodents, but other glucagon-like peptide-1 (GLP-1) receptor agonists have caused thyroid C-cell tumors in rodents at clinically relevant exposures. It is unknown whether TANZEUM causes thyroid C-cell tumors, including MTC in humans.
- Cases of MTC in patients treated with liraglutide, another GLP-1 receptor agonist, have been reported in the postmarketing period. The data in these reports are insufficient to establish or exclude a causal relationship between MTC and GLP-1 receptor agonist use 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.

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.

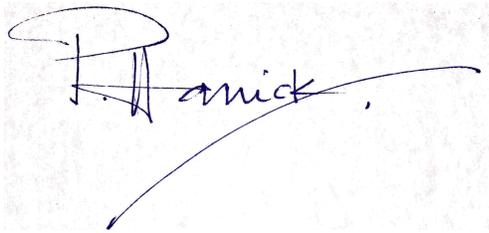
This letter does not contain the complete safety profile for TANZEUM. Please see the enclosed Prescribing Information and Medication Guide.

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 blue ink that reads "Philip Hornick". The signature is written in a cursive style with a large, stylized initial "P" and a long, sweeping underline.

Philip Hornick, MD, PhD, FESC
Medical Affairs Therapy Area Head/Vice President - CVM
Medical Affairs, North America

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*

- Carcinogenicity of albiglutide could not be assessed in rodents, but other glucagon-like peptide-1 (GLP-1) receptor agonists have caused thyroid C-cell tumors in rodents at clinically relevant exposures. Human relevance of GLP-1 receptor agonist induced C-cell tumors in rodents has not been determined. 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).
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- Cases of MTC in patients treated with liraglutide, another GLP-1 receptor agonist, have been reported in the postmarketing period. The data in these reports are insufficient to establish or exclude a causal relationship between MTC and GLP-1 receptor agonist use in humans.
 - **Counsel patients** regarding the potential risk for MTC and to report the symptoms of thyroid tumors (e.g., **a mass in the neck, dysphagia, dyspnea, persistent hoarseness**) to their healthcare provider.
 - 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 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 further evaluated.

* The information presented in this box does not represent the complete Boxed Warning. Please see the Prescribing Information.



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

- Carcinogenicity of albiglutide could not be assessed in rodents, but other glucagon-like peptide-1 (GLP-1) receptor agonists have caused thyroid C-cell tumors in rodents at clinically relevant exposures.
- Human relevance of GLP-1 receptor agonist induced C-cell tumors in rodents has not been determined. It is unknown whether TANZEUM causes thyroid C-cell tumors, including Medullary Thyroid Carcinoma (MTC) in humans.
- Cases of MTC in patients treated with liraglutide another GLP-1 receptor agonist, have been reported in the postmarketing period. The data in these reports are insufficient to establish or exclude a causal relationship between MTC and GLP-1 receptor agonist use in humans.
- Counsel patients about the risk of MTC and the symptoms of thyroid tumors.

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.

A rectangular box with a light beige background and a dark orange header. The header text reads "Materials for Healthcare Providers". Below the header, there are two entries, each with a small PDF icon to the left of the text. The first entry is "TANZEUM REMS Safety Information for Providers Factsheet" and the second is "REMS Letter to Healthcare Providers". Both text elements are underlined.

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.

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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/

JENNIFER R PIPPINS
07/27/2015