

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use TANZEUM safely and effectively. See full prescribing information for TANZEUM.

TANZEUM (albiglutide) for injection, for subcutaneous use  
Initial U.S. Approval: 2014

### WARNING: RISK OF THYROID C-CELL TUMORS

See full prescribing information for complete boxed warning.

- 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 (MTC), in humans. (5.1)
- 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). (4.1, 5.1)

### INDICATIONS AND USAGE

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. (1)

Limitations of Use:

- Not recommended as first-line therapy for patients inadequately controlled on diet and exercise. (1, 5.1)
- Has not been studied in patients with a history of pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis. (1, 5.2)
- Not for treatment of type 1 diabetes mellitus or diabetic ketoacidosis. (1)
- Not for patients with pre-existing severe gastrointestinal disease. (1)
- Has not been studied in combination with prandial insulin. (1)

### DOSAGE AND ADMINISTRATION

- Administer once weekly at any time of day, without regard to meals. (2.1)
  - Inject subcutaneously in the abdomen, thigh, or upper arm. (2.1)
  - Initiate at 30 mg subcutaneously once weekly. Dose can be increased to 50 mg once weekly in patients requiring additional glycemic control. (2.1)
  - If a dose is missed, administer within 3 days of missed dose. (2.1)
- See Full Prescribing Information and Patient Instructions for Use for reconstitution of lyophilized powder and administration. (2.4, 2.5, 17)

### DOSAGE FORMS AND STRENGTHS

For injection: 30 mg or 50 mg in a single-dose Pen. (3)

### CONTRAINDICATIONS

- Personal or family history of medullary thyroid carcinoma or in patients with Multiple Endocrine Neoplasia syndrome type 2. (4.1)
- History of serious hypersensitivity to albiglutide or any product components. (4.2, 5.4)

### WARNINGS AND PRECAUTIONS

- Pancreatitis: Discontinue promptly if suspected. Do not restart if confirmed. Consider other antidiabetic therapies in patients with a history of pancreatitis. (5.2)
- Hypoglycemia: Can occur when used in combination with insulin secretagogues (e.g., sulfonylureas) or insulin. Consider lowering sulfonylurea or insulin dosage when starting TANZEUM. (5.3)
- Hypersensitivity Reactions: Discontinue TANZEUM if suspected. Monitor and treat promptly per standard of care until signs and symptoms resolve. (5.4)
- Renal Impairment: Monitor renal function in patients with renal impairment reporting severe adverse gastrointestinal reactions. (5.5)
- Macrovascular Outcomes: There have been no clinical trials establishing conclusive evidence of macrovascular risk reduction with TANZEUM or any other antidiabetic drug. (5.6)

### ADVERSE REACTIONS

Adverse reactions, reported in  $\geq 10\%$  of patients treated with TANZEUM and more frequently than in patients on placebo, were upper respiratory tract infection, diarrhea, nausea, and injection site reaction. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact GlaxoSmithKline at 1-888-825-5249 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

### DRUG INTERACTIONS

TANZEUM delays gastric emptying. May impact absorption of concomitantly administered oral medications. (7)

### USE IN SPECIFIC POPULATIONS

- Pregnancy: TANZEUM may cause fetal harm; only use if potential benefit justifies potential risk to fetus. (8.1)
- Nursing Mothers: Discontinue nursing or discontinue TANZEUM. (8.3)
- Renal Impairment: No dosage adjustment recommended. Monitor renal function in patients with renal impairment reporting severe adverse gastrointestinal reactions. (5.5, 8.6)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 4/2014

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## FULL PRESCRIBING INFORMATION

### 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 (MTC), in humans [see *Warnings and Precautions* (5.1)].
- 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 [see *Contraindications* (4.1), *Warnings and Precautions* (5.1)].

## 1 INDICATIONS AND USAGE

TANZEUM is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus [see *Clinical Studies* (14)].

### Limitations of Use:

- TANZEUM is not recommended as first-line therapy for patients inadequately controlled on diet and exercise [see *Warnings and Precautions* (5.1)].
- TANZEUM has not been studied in patients with a history of pancreatitis [see *Warnings and Precautions* (5.2)]. Consider other antidiabetic therapies in patients with a history of pancreatitis.
- TANZEUM is not indicated in the treatment of patients with type 1 diabetes mellitus or for the treatment of patients with diabetic ketoacidosis. TANZEUM is not a substitute for insulin in these patients.
- TANZEUM has not been studied in patients with severe gastrointestinal disease, including severe gastroparesis. The use of TANZEUM is not recommended in patients with pre-existing severe gastrointestinal disease [see *Adverse Reactions* (6.1)].
- TANZEUM has not been studied in combination with prandial insulin.

## 2 DOSAGE AND ADMINISTRATION

### 2.1 Dosage

The recommended dosage of TANZEUM is 30 mg once weekly given as a subcutaneous injection in the abdomen, thigh, or upper arm region. The dosage may be increased to 50 mg once weekly if the glycemic response is inadequate.

TANZEUM may be administered at any time of day without regard to meals. Instruct patients to administer TANZEUM once a week on the same day each week. The day of

weekly administration may be changed if necessary as long as the last dose was administered 4 or more days before.

If a dose is missed, instruct patients to administer as soon as possible within 3 days after the missed dose. Thereafter, patients can resume dosing on their usual day of administration. If it is more than 3 days after the missed dose, instruct patients to wait until their next regularly scheduled weekly dose.

## **2.2 Concomitant Use with an Insulin Secretagogue (e.g., Sulfonylurea) or with Insulin**

When initiating TANZEUM, consider reducing the dosage of concomitantly administered insulin secretagogues (e.g., sulfonylureas) or insulin to reduce the risk of hypoglycemia [see Warnings and Precautions (5.3)].

## **2.3 Dosage in Patients with Renal Impairment**

No dose adjustment is needed in patients with mild, moderate, or severe renal impairment (eGFR 15 to 89 mL/min/1.73 m<sup>2</sup>). Use caution when initiating or escalating doses of TANZEUM in patients with renal impairment. Monitor renal function in patients with renal impairment reporting severe adverse gastrointestinal reactions [see Warning and Precautions (5.5), Use in Specific Populations (8.6)].

## **2.4 Reconstitution of the Lyophilized Powder**

The lyophilized powder contained within the Pen must be reconstituted prior to administration. See Patient Instructions for Use for complete administration instructions with illustrations. The instructions may also be found at [www.TANZEUM.com](http://www.TANZEUM.com). Instruct patients as follows:

### **Pen Reconstitution**

- a) Hold the Pen body with the clear cartridge pointing up to see the [1] in the number window.
- b) To reconstitute the lyophilized powder with the diluent in the Pen, twist the clear cartridge on the Pen in the direction of the arrow until the Pen is felt/heard to “click” into place and the [2] is seen in the number window. This mixes the diluent with the lyophilized powder.
- c) Slowly and gently rock the Pen side-to-side 5 times to mix the reconstituted solution of TANZEUM. Advise the patient to not shake the Pen hard to avoid foaming.
- d) Wait 15 minutes for the 30-mg Pen and 30 minutes for the 50-mg Pen to ensure that the reconstituted solution is mixed.

### **Preparing Pen for Injection**

- e) Slowly and gently rock the Pen side-to-side 5 additional times to mix the reconstituted solution.

f) Visually inspect the reconstituted solution in the viewing window for particulate matter. The reconstituted solution will be yellow in color. After reconstitution, use TANZEUM within 8 hours.

g) Holding the Pen upright, attach the needle to the Pen. Gently tap the clear cartridge to bring large bubbles to the top.

See *Dosage and Administration (2.5)* for important administration instructions, including the injection procedure.

### **Alternate Method of Reconstitution (Healthcare Professional Use Only)**

The Patient Instructions for Use provide directions for the patient to wait 15 minutes for the 30-mg Pen and 30 minutes for the 50-mg Pen after the lyophilized powder and diluent are mixed to ensure reconstitution.

Healthcare professionals may utilize the following alternate method of reconstitution. Because this method relies on appropriate swirling and visual inspection of the solution, it should only be performed by healthcare professionals.

a) Follow Step A (Inspect Your Pen and Twist Pen to Mix Your Medication) in the Instructions for Use. Make sure you have:

- Inspected the Pen for [1] in number window and expiration date.
- Twisted the clear cartridge until [2] appears in the number window and a “click” is heard. This combines the medicine powder and liquid in the clear cartridge.

b) Hold the Pen with the clear cartridge pointing up and maintain this orientation throughout the reconstitution.

c) Gently swirl the Pen in small circular motions for at least one minute. Avoid shaking as this can result in foaming, which may affect the dose.

d) Inspect the solution, and if needed, continue to gently swirl the Pen until all the powder is dissolved and you see a clear yellow solution that is free of particles. A small amount of foam, on top of the solution at the end of reconstitution, is normal.

- For 30-mg Pen: Complete dissolution usually occurs within 2 minutes but may take up to 5 minutes, as confirmed by visual inspection for a clear yellow solution free of particles.
- For 50-mg Pen: Complete dissolution usually occurs within 7 minutes but may take up to 10 minutes.

e) After reconstitution, continue to follow the steps in the Instructions for Use, starting at Step B: Attach the Needle.

## **2.5 Important Administration Instructions**

Instruct patients as follows:

- The pen should be used within 8 hours of reconstitution prior to attaching the needle.
  - After attaching the supplied needle, remove air bubbles by slowly twisting the Pen until you see the [3] in the number window. At the same time, the injection button will be automatically released from the bottom of the Pen.
  - Use immediately after the needle is attached and primed. The product can clog the needle if allowed to dry in the primed needle.
  - After subcutaneously inserting the needle into the skin in the abdomen, thigh, or upper arm region, press the injection button. Hold the injection button until you hear a “click” and then hold the button for 5 additional seconds to deliver the full dose.
- When using TANZEUM with insulin, instruct patients to administer as separate injections and to never mix the products. It is acceptable to inject TANZEUM and insulin in the same body region but the injections should not be adjacent to each other.
- When injecting in the same body region, advise patients to use a different injection site each week. TANZEUM must not be administered intravenously or intramuscularly.

### **3 DOSAGE FORMS AND STRENGTHS**

TANZEUM is supplied as follows:

- For injection: 30-mg lyophilized powder in a single-dose Pen (pen injector) for reconstitution.
- For injection: 50-mg lyophilized powder in a single-dose Pen (pen injector) for reconstitution.

### **4 CONTRAINDICATIONS**

#### **4.1 Medullary Thyroid Carcinoma**

TANZEUM is contraindicated in patients with a personal or family history of medullary thyroid carcinoma (MTC) or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2) [see *Warnings and Precautions* (5.1)].

#### **4.2 Hypersensitivity**

TANZEUM is contraindicated in patients with a prior serious hypersensitivity reaction to albiglutide or to any of the product components [see *Warnings and Precautions* (5.4)].

### **5 WARNINGS AND PRECAUTIONS**

#### **5.1 Risk of Thyroid C-cell Tumors**

Nonclinical studies in rodents of clinically relevant doses of GLP-1 receptor agonists showed dose-related and treatment-duration-dependent increases in the incidence of thyroid C-cell tumors (adenomas and carcinomas). Carcinogenicity studies could not be conducted with TANZEUM because drug-clearing, anti-drug antibodies develop in animals used for these types of studies [see *Nonclinical Toxicology* (13.1)]. It is unknown

whether GLP-1 receptor agonists are associated with thyroid C-cell tumors, including MTC in humans [see *Boxed Warning, Contraindications (4.1)*].

Across 8 Phase III clinical trials [see *Clinical Studies (14)*], MTC was diagnosed in 1 patient receiving TANZEUM and 1 patient receiving placebo. Both patients had markedly elevated serum calcitonin levels at baseline.

TANZEUM is contraindicated in patients with a personal or family history of MTC or in patients with MEN 2. Counsel patients regarding the risk for MTC with the use of TANZEUM and inform them of symptoms of thyroid tumors (e.g., a mass in the neck, dysphagia, dyspnea, persistent hoarseness). The clinical value of routine monitoring of serum calcitonin to diagnose MTC in patients at risk for MTC has not been established.

Elevated serum calcitonin is a biological marker of MTC. Patients with MTC usually have calcitonin values >50 ng/L. 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 referred to an endocrinologist for further evaluation.

## **5.2 Acute Pancreatitis**

In clinical trials, acute pancreatitis has been reported in association with TANZEUM.

Across 8 Phase III clinical trials [see *Clinical Studies (14)*], pancreatitis adjudicated as likely related to therapy occurred more frequently in patients receiving TANZEUM (6 of 2,365 [0.3%]) than in patients receiving placebo (0 of 468 [0%]) or active comparators (2 of 2,065 [0.1%]).

After initiation of TANZEUM, 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). If pancreatitis is suspected, promptly discontinue TANZEUM. If 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 pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.

## **5.3 Hypoglycemia with Concomitant Use of Insulin Secretagogues or Insulin**

The risk of hypoglycemia is increased when TANZEUM is used in combination with insulin secretagogues (e.g., sulfonylureas) or insulin. Therefore, patients may require a lower dose of sulfonylurea or insulin to reduce the risk of hypoglycemia in this setting [see *Adverse Reactions (6.1)*].

## **5.4 Hypersensitivity Reactions**

Across 8 Phase III clinical trials [see *Clinical Studies (14)*], a serious hypersensitivity reaction with pruritus, rash, and dyspnea occurred in a patient treated with TANZEUM. If hypersensitivity reactions occur, discontinue use of TANZEUM; treat promptly per standard of care and monitor until signs and symptoms resolve [see *Contraindications (4.2)*].

## **5.5 Renal Impairment**

In patients treated with GLP-1 receptor agonists, there have been postmarketing reports of acute renal failure and worsening of chronic renal failure, which may sometimes require hemodialysis. Some of these events were reported in patients without known underlying renal disease. A majority of reported events occurred in patients who had experienced nausea, vomiting, diarrhea, or dehydration. In a trial of TANZEUM in patients with renal impairment [see *Clinical Studies (14.3)*], the frequency of such gastrointestinal reactions increased as renal function declined [see *Use in Specific Populations (8.6)*]. Because these reactions may worsen renal function, use caution when initiating or escalating doses of TANZEUM in patients with renal impairment [see *Dosage and Administration (2.3)*, *Use in Specific Populations (8.6)*].

## **5.6 Macrovascular Outcomes**

There have been no clinical trials establishing conclusive evidence of macrovascular risk reduction with TANZEUM or any other antidiabetic drug.

# **6 ADVERSE REACTIONS**

The following serious reactions are described below or elsewhere in the labeling:

- Risk of Thyroid C-cell Tumors [see *Warnings and Precautions (5.1)*]
- Acute Pancreatitis [see *Warnings and Precautions (5.2)*]
- Hypoglycemia with Concomitant Use of Insulin Secretagogues or Insulin [see *Warnings and Precautions (5.3)*]
- Hypersensitivity Reactions [see *Warnings and Precautions (5.4)*]
- Renal Impairment [see *Warnings and Precautions (5.5)*]

## **6.1 Clinical Trials Experience**

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect the rates observed in practice.

### **Pool of Placebo-Controlled Trials**

The data in Table 1 are derived from 4 placebo-controlled trials. TANZEUM was used as monotherapy in 1 trial and as add-on therapy in 3 trials [see *Clinical Studies (14)*]. These data reflect exposure of 923 patients to TANZEUM and a mean duration of exposure to TANZEUM of 93 weeks. The mean age of participants was 55 years, 1% of participants

were 75 years or older and 53% of participants were male. The population in these studies was 48% white, 13% African/African American, 7% Asian, and 29% Hispanic/Latino. At baseline, the population had diabetes for an average of 7 years and had a mean HbA1c of 8.1%. At baseline, 17% of the population in these studies reported peripheral neuropathy and 4% reported retinopathy. Baseline estimated renal function was normal or mildly impaired (eGFR >60 mL/min/1.73 m<sup>2</sup>) in 91% of the study population and moderately impaired (eGFR 30 to 60 mL/min/1.73 m<sup>2</sup>) in 9%.

Table 1 shows common adverse reactions excluding hypoglycemia associated with the use of TANZEUM in the pool of placebo-controlled trials. These adverse reactions were not present at baseline, occurred more commonly on TANZEUM than on placebo, and occurred in at least 5% of patients treated with TANZEUM.

**Table 1. Adverse Reactions in Placebo-controlled Trials Reported in ≥5% of Patients Treated with TANZEUM<sup>a</sup>**

Adverse Reaction	Placebo (N = 468) %	TANZEUM (N = 923) %
Upper respiratory tract infection	13.0	14.2
Diarrhea	10.5	13.1
Nausea	9.6	11.1
Injection site reaction <sup>b</sup>	2.1	10.5
Cough	6.2	6.9
Back pain	5.8	6.7
Arthralgia	6.4	6.6
Sinusitis	5.8	6.2
Influenza	3.2	5.2

<sup>a</sup> Adverse reactions reported includes adverse reactions occurring with the use of glycemic rescue medications which included metformin (17% for placebo and 10% for TANZEUM) and insulin (24% for placebo and 14% for TANZEUM).

<sup>b</sup> See below for other events of injection site reactions reported.

### *Gastrointestinal Adverse Reactions*

In the pool of placebo-controlled trials, gastrointestinal complaints occurred more frequently among patients receiving TANZEUM (39%) than patients receiving placebo (33%). In addition to diarrhea and nausea (see Table 1), the following gastrointestinal adverse reactions also occurred more frequently in patients receiving TANZEUM: vomiting (2.6% versus 4.2% for placebo versus TANZEUM), gastroesophageal reflux disease (1.9% versus 3.5% for placebo versus TANZEUM), and dyspepsia (2.8% versus 3.4% for placebo versus TANZEUM). Constipation also contributed to the frequently reported reactions. In the group treated with TANZEUM, investigators graded the severity of GI reactions as “mild” in 56% of cases, “moderate” in 37% of cases, and “severe” in 7% of cases. Discontinuation due to GI adverse reactions occurred in 2% of individuals on TANZEUM or placebo.



## Injection Site Reactions

In the pool of placebo-controlled trials, injection site reactions occurred more frequently on TANZEUM (18%) than on placebo (8%). In addition to the term injection site reaction (see Table 1), the following other types of injection site reactions also occurred more frequently on TANZEUM: injection site hematoma (1.9% versus 2.1% for placebo versus TANZEUM), injection site erythema (0.4% versus, 1.7% for placebo versus TANZEUM), injection site rash (0% versus 1.4% for placebo versus TANZEUM), injection site hypersensitivity (0% versus 0.8% versus for placebo versus TANZEUM), and injection site hemorrhage (0.6% and 0.7% for placebo versus TANZEUM). Injection site pruritus also contributed to the frequently reported reactions. The majority of injection site reactions were judged as “mild” by investigators in both groups (73% for TANZEUM versus 94% for placebo). More patients on TANZEUM than on placebo: discontinued due to an injection site reaction (2% versus 0.2%), experienced more than 2 reactions (38% versus 20%), had a reaction judged by investigators to be “moderate” or “severe” (27% versus 6%) and required local or systemic treatment for the reactions (36% versus 11%).

## Pool of Placebo- and Active-controlled Trials

The occurrence of adverse reactions was also evaluated in a larger pool of patients with type 2 diabetes participating in 7 placebo- and active-controlled trials. These trials evaluated the use of TANZEUM as monotherapy, and as add-on therapy to oral antidiabetic agents, and as add-on therapy to basal insulin [see *Clinical Studies (14)*]. In this pool, a total of 2,116 patients with type 2 diabetes were treated with TANZEUM for a mean duration of 75 weeks. The mean age of patients treated with TANZEUM was 55 years, 1.5% of the population in these studies was 75 years or older and 51% of participants were male. Forty-eight percent of patients were white, 15% African/African American, 9% Asian, and 26% were Hispanic/Latino. At baseline, the population had diabetes for an average of 8 years and had a mean HbA1c of 8.2%. At baseline, 21% of the population reported peripheral neuropathy and 5% reported retinopathy. Baseline estimated renal function was normal or mildly impaired (eGFR >60 mL/min/1.73 m<sup>2</sup>) in 92% of the population and moderately impaired (eGFR 30 to 60 mL/min/1.73 m<sup>2</sup>) in 8% of the population.

In the pool of placebo- and active-controlled trials, the types and frequency of common adverse reactions excluding hypoglycemia were similar to those listed in Table 1.

## Other Adverse Reactions

### *Hypoglycemia*

The proportion of patients experiencing at least one documented symptomatic hypoglycemic episode on TANZEUM and the proportion of patients experiencing at least one severe hypoglycemic episode on TANZEUM in clinical trials [see *Clinical Studies (14)*] is shown in Table 2. Hypoglycemia was more frequent when TANZEUM was added to sulfonylurea or insulin [see *Warnings and Precautions (5.3)*].

294 Table 2. Incidence (%) of Hypoglycemia in Clinical Trials of TANZEUM<sup>a</sup>

<b>Monotherapy<sup>b</sup> (52 Weeks)</b>	<b>Placebo N = 101</b>	<b>TANZEUM 30 mg Weekly N = 101</b>
Documented symptomatic <sup>c</sup>	2%	2%
Severe <sup>d</sup>	-	-
<b>In Combination with Metformin Trial (104 Weeks)<sup>e</sup></b>	<b>Placebo N = 101</b>	<b>TANZEUM N = 302</b>
Documented symptomatic	4%	3%
Severe	-	-
<b>In Combination with Pioglitazone ± Metformin (52 Weeks)</b>	<b>Placebo N = 151</b>	<b>TANZEUM N = 150</b>
Documented symptomatic	1%	3%
Severe	-	1%
<b>In Combination with Metformin and Sulfonylurea (52 Weeks)</b>	<b>Placebo N = 115</b>	<b>TANZEUM N = 271</b>
Documented symptomatic	7%	13%
Severe	-	0.4%
<b>In Combination with Insulin Glargine (26 Weeks)</b>	<b>Insulin Lispro N = 281</b>	<b>TANZEUM N = 285</b>
Documented symptomatic	30%	16%
Severe	0.7%	-
<b>In Combination with Metformin ± Sulfonylurea (52 Weeks)</b>	<b>Insulin Glargine N = 241</b>	<b>TANZEUM N = 504</b>
Documented symptomatic	27%	17%
Severe	0.4%	0.4%
<b>In Combination with OADs in Renal Impairment (26 Weeks)</b>	<b>Sitagliptin N = 246</b>	<b>TANZEUM N = 249</b>
Documented symptomatic	6%	10%
Severe	0.8%	-

295 OAD = Oral antidiabetic agents.

296 <sup>a</sup> Data presented are to the primary endpoint and include only events occurring on-  
297 therapy with randomized medications and excludes events occurring after use of  
298 glycemic rescue medications (i.e., primarily metformin or insulin).

299 <sup>b</sup> In this trial, no documented symptomatic or severe hypoglycemia were reported for  
300 TANZEUM 50 mg and these data are omitted from the table.

301 <sup>c</sup> Plasma glucose concentration  $\leq 70$  mg/dL and presence of hypoglycemic symptoms.

302 <sup>d</sup> Event requiring another person to administer a resuscitative action.

303 <sup>e</sup> Rate of documented symptomatic hypoglycemia for active controls 18% (glimepiride)  
304 and 2% (sitagliptin).

305

306 *Pneumonia*

307 In the pool of 7 placebo- and active-controlled trials, the adverse reaction of pneumonia  
308 was reported more frequently in patients receiving TANZEUM (1.8%) than in patients in  
309 the all-comparators group (0.8%). More cases of pneumonia in the group receiving  
310 TANZEUM were serious (0.4% for TANZEUM versus 0.1% for all comparators).

311 *Atrial Fibrillation/Flutter*

312 In the pool of 7 placebo- and active-controlled trials, adverse reactions of atrial  
313 fibrillation (1.0%) and atrial flutter (0.2%) were reported more frequently for TANZEUM  
314 than for all comparators (0.5% and 0%, respectively). In both groups, patients with events  
315 were generally male, older, had underlying renal impairment or cardiac disease (e.g.,  
316 history of arrhythmia, palpitations, congestive heart failure, cardiomyopathy, etc.).

317 *Appendicitis*

318 In the pool of placebo- and active-controlled trials, serious events of appendicitis  
319 occurred in 0.3% patients treated with TANZEUM compared with 0% among all  
320 comparators.

321 *Immunogenicity*

322 In the pool of 7 placebo- and active-controlled trials, 116 (5.5%) of 2,098 patients  
323 exposed to TANZEUM tested positive for anti-albiglutide antibodies at any time during  
324 the trials. None of these antibodies were shown to neutralize the activity of albiglutide in  
325 an in vitro bioassay. Presence of antibody did not correlate with reduced efficacy as  
326 measured by HbA1c and fasting plasma glucose or specific adverse reactions.

327 Consistent with the high homology of albiglutide with human GLP-1, the majority of  
328 patients (approximately 79%) with anti-albiglutide antibodies also tested positive for anti-  
329 GLP-1 antibodies; none were neutralizing. A minority of patients (approximately 17%)  
330 who tested positive for anti-albiglutide antibodies also transiently tested positive for  
331 antibodies to human albumin.

332 The detection of antibody formation is highly dependent on the sensitivity and specificity  
333 of the assay. Additionally, the observed incidence of antibody (including neutralizing  
334 antibody) positivity in an assay may be influenced by several factors including assay  
335 methodology, sample handling, timing of sample collection, concomitant medications,  
336 and underlying disease. For these reasons, the incidence of antibodies to albiglutide  
337 cannot be directly compared with the incidence of antibodies of other products.

338 *Liver Enzyme Abnormalities*

339 In the pool of placebo- and active-controlled trials, a similar proportion of patients  
340 experienced at least one event of alanine aminotransferase (ALT) increase of 3-fold or  
341 greater above the upper limit of normal (0.9% and 0.9% for all comparators versus  
342 TANZEUM). Three subjects on TANZEUM and one subject in the all-comparator group  
343 experienced at least one event of ALT increase of 10-fold or greater above the upper limit  
344 of normal. In one of the 3 cases an alternate etiology was identified to explain the rise in

liver enzyme (acute viral hepatitis). In one case, insufficient information was obtained to establish or refute a drug-related causality. In the third case, elevation in ALT (10 times the upper limit of normal) was accompanied by an increase in total bilirubin (4 times the upper limit of normal) and occurred 8 days after the first dose of TANZEUM. The etiology of hepatocellular injury was possibly related to TANZEUM but direct attribution to TANZEUM was confounded by the presence of gallstone disease diagnosed on ultrasound 3 weeks after the event.

### *Gamma Glutamyltransferase (GGT) Increase*

In the pool of placebo-controlled trials, the adverse event of increased GGT occurred more frequently in the group treated with TANZEUM (0.9% and 1.5% for placebo versus TANZEUM).

### *Heart Rate Increase*

In the pool of placebo-controlled trials, mean heart rate in patients treated with TANZEUM was higher by an average of 1 to 2 bpm compared with mean heart rate in patients treated with placebo across study visits. The long-term clinical effects of the increase in heart rate have not been established [see *Warnings and Precautions (5.6)*].

## **7 DRUG INTERACTIONS**

TANZEUM did not affect the absorption of orally administered medications tested in clinical pharmacology studies to any clinically relevant degree [see *Clinical Pharmacology (12.3)*]. However, TANZEUM causes a delay of gastric emptying, and thereby has the potential to impact the absorption of concomitantly administered oral medications. Caution should be exercised when oral medications are concomitantly administered with TANZEUM.

## **8 USE IN SPECIFIC POPULATIONS**

### **8.1 Pregnancy**

#### Pregnancy Category C

There are no adequate and well-controlled studies of TANZEUM in pregnant women. Nonclinical studies have shown reproductive toxicity, but not teratogenicity, in mice treated with albiglutide at up to 39 times human exposure resulting from the maximum recommended dose of 50 mg/week, based on AUC [see *Nonclinical Toxicology (13.1, 13.3)*]. TANZEUM should not be used during pregnancy unless the expected benefit outweighs the potential risks.

Due to the long washout period for TANZEUM, consider stopping TANZEUM at least 1 month before a planned pregnancy.

There are no data on the effects of TANZEUM on human fertility. Studies in mice showed no effects on fertility [see *Nonclinical Toxicology (13.1)*]. The potential risk to human fertility is unknown.

### 8.3 Nursing Mothers

There are no adequate data to support the use of TANZEUM during lactation in humans.

It is not known if TANZEUM is excreted into human milk during lactation. Given that TANZEUM is an albumin-based protein therapeutic, it is likely to be present in human milk. Decreased body weight in offspring was observed in mice treated with TANZEUM during gestation and lactation [see *Nonclinical Toxicology* (13.3)]. A decision should be made whether to discontinue nursing or to discontinue TANZEUM, taking into account the importance of the drug to the mother and the potential risks to the infant.

### 8.4 Pediatric Use

Safety and effectiveness of TANZEUM have not been established in pediatric patients (younger than 18 years).

### 8.5 Geriatric Use

Of the total number of patients (N = 2,365) in 8 Phase III clinical trials who received TANZEUM, 19% (N = 444) were 65 years and older, and <3% (N = 52) were 75 years and older. No overall differences in safety or effectiveness were observed between these patients and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

### 8.6 Renal Impairment

Of the total number of patients (N = 2,365) in 8 Phase III clinical trials who received TANZEUM, 54% (N = 1,267) had mild renal impairment (eGFR 60 to 89 mL/min/1.73 m<sup>2</sup>), 12% (N = 275) had moderate renal impairment (eGFR 30 to 59 mL/min/1.73 m<sup>2</sup>) and 1% (N = 19) had severe renal impairment (eGFR 15 to <30 mL/min/1.73 m<sup>2</sup>).

No dosage adjustment is required in patients with mild (eGFR 60 to 89 mL/min/1.73 m<sup>2</sup>), moderate (eGFR 30 to 59 mL/min/1.73 m<sup>2</sup>), or severe (eGFR 15 to <30 mL/min/1.73 m<sup>2</sup>) renal impairment.

Efficacy of TANZEUM in patients with type 2 diabetes and renal impairment is described elsewhere [see *Clinical Studies* (14.3)]. There is limited clinical experience in patients with severe renal impairment (19 subjects). The frequency of GI events increased as renal function declined. For patients with mild, moderate, or severe impairment, the respective event rates were: diarrhea (6%, 13%, 21%), nausea (3%, 5%, 16%), and vomiting (1%, 2%, 5%). Therefore, caution is recommended when initiating or escalating doses of TANZEUM in patients with renal impairment [see *Dosage and Administration* (2.3), *Warnings and Precautions* (5.5), *Clinical Pharmacology* (12.3)].

## 10 OVERDOSAGE

No data are available with regard to overdosage in humans. Anticipated symptoms of an overdose may be severe nausea and vomiting.

In the event of an overdose, appropriate supportive treatment should be initiated as dictated by the patient's clinical signs and symptoms. A prolonged period of observation and treatment for these symptoms may be necessary, taking into account the half-life of TANZEUM (5 days).

## **11 DESCRIPTION**

TANZEUM is a GLP-1 receptor agonist, a recombinant fusion protein comprised of 2 tandem copies of modified human GLP-1 genetically fused in tandem to human albumin. The human GLP-1 fragment sequence 7 – 36 has been modified with a glycine substituted for the naturally-occurring alanine at position 8 in order to confer resistance to dipeptidylpeptidase IV (DPP-IV) mediated proteolysis. The human albumin moiety of the recombinant fusion protein, together with the DPP-IV resistance, extends the half-life allowing once-weekly dosing. TANZEUM has a molecular weight of 72,970 Daltons.

TANZEUM is produced by a strain of *Saccharomyces cerevisiae* modified to express the therapeutic protein.

TANZEUM 30-mg Pen for injection (for subcutaneous use) contains 40.3 mg lyophilized albiglutide and 0.65 mL Water for Injection diluent designed to deliver a dose of 30 mg in a volume of 0.5 mL after reconstitution.

TANZEUM 50-mg Pen for injection (for subcutaneous use) contains 67 mg lyophilized albiglutide and 0.65 mL Water for Injection diluent designed to deliver a dose of 50 mg in a volume of 0.5 mL after reconstitution.

The lyophilized powder of both dose strengths is white to yellow in color and the solvent is a clear and colorless solution. The reconstituted solution is yellow in color.

Inactive ingredients include 153 mM mannitol, 0.01% (w/w) polysorbate 80, 10 mM sodium phosphate, and 117 mM trehalose dihydrate. TANZEUM does not contain a preservative.

## **12 CLINICAL PHARMACOLOGY**

### **12.1 Mechanism of Action**

TANZEUM is an agonist of the GLP-1 receptor and augments glucose-dependent insulin secretion. TANZEUM also slows gastric emptying.

### **12.2 Pharmacodynamics**

TANZEUM lowers fasting glucose and reduces postprandial glucose excursions in patients with type 2 diabetes mellitus. The majority of the observed reduction in fasting plasma glucose occurs after a single dose, consistent with the pharmacokinetic profile of albiglutide. In a Phase II trial in Japanese patients with type 2 diabetes mellitus who received TANZEUM 30 mg, a reduction (22%) in postprandial glucose AUC<sub>(0-3 h)</sub> was observed at steady state (Week 16) compared with placebo following a mixed meal.

A single dose of TANZEUM 50 mg subcutaneous (SC) did not impair glucagon response to low glucose concentrations.

## Gastric Motility

TANZEUM slowed gastric emptying compared with placebo for both solids and liquids when albiglutide 100 mg (2 times the maximum approved dosage) was administered as a single dose in healthy subjects.

## Cardiac Electrophysiology

At doses up to the maximum recommended dose (50 mg), TANZEUM does not prolong QTc to any clinically relevant extent.

## **12.3 Pharmacokinetics**

### Absorption

Following SC administration of a single 30-mg dose to subjects with type 2 diabetes mellitus, maximum concentrations of albiglutide were reached at 3 to 5 days post-dosing. The mean peak concentration ( $C_{max}$ ) and mean area under the time-concentration curve (AUC) of albiglutide were 1.74 mcg/mL and 465 mcg.h/mL, respectively, following a single dose of 30 mg albiglutide in type 2 diabetes mellitus subjects. Steady-state exposures are achieved following 4 to 5 weeks of once-weekly administration. Exposures at the 30-mg and 50-mg dose levels were consistent with a dose-proportional increase. Similar exposure is achieved with SC administration of albiglutide in the abdomen, thigh, or upper arm. The absolute bioavailability of albiglutide following SC administration has not been evaluated.

### Distribution

The mean estimate of apparent volume of distribution of albiglutide following SC administration is 11 L. As albiglutide is an albumin fusion molecule, plasma protein binding has not been assessed.

### Metabolism

Albiglutide is a protein for which the expected metabolic pathway is degradation to small peptides and individual amino acids by ubiquitous proteolytic enzymes. Classical biotransformation studies have not been performed. Because albiglutide is an albumin fusion protein, it likely follows a metabolic pathway similar to native human serum albumin which is catabolized primarily in the vascular endothelium.

### Elimination

The mean apparent clearance of albiglutide is 67 mL/h with an elimination half-life of approximately 5 days, making albiglutide suitable for once-weekly administration.

### Specific Patient Populations

*Age, Gender, Race, and Body Weight:* Based on the population pharmacokinetic analysis with data collected from 1,113 subjects, age, gender, race, and body weight had no clinically relevant effect on the pharmacokinetics of albiglutide

*Pediatric:* No pharmacokinetic data are available in pediatric patients.

**Renal:** In a population pharmacokinetic analysis including a Phase III trial in patients with mild, moderate, and severe renal impairment, exposures were increased by approximately 30% to 40% in severe renal impairment compared with those observed in type 2 diabetic patients with normal renal function.

**Hepatic:** No clinical trials were conducted to examine the effects of mild, moderate, or severe hepatic impairment on the pharmacokinetics of albiglutide. Therapeutic proteins such as albiglutide are catabolized by widely distributed proteolytic enzymes, which are not restricted to hepatic tissue; therefore, changes in hepatic function are unlikely to have any effect on the elimination of albiglutide.

### Drug Interactions

In multiple-dose, drug-drug interaction trials no significant change in systemic exposures of the co-administered drugs were observed, except simvastatin (see Table 3). When albiglutide was co-administered with simvastatin,  $C_{max}$  of simvastatin and its active metabolite simvastatin acid was increased by approximately 18% and 98%, respectively. In the same trial, AUC of simvastatin decreased by 40% and AUC of simvastatin acid increased by 36%. Clinical relevance of these changes has not been established (see Table 3).

Additionally, no clinically relevant pharmacodynamic effects on luteinizing hormone, follicle-stimulating hormone, or progesterone were observed when albiglutide and a combination oral contraceptive were co-administered. Albiglutide did not significantly alter the pharmacodynamic effects of warfarin as measured by the international normalized ratio (INR).



517 **Table 3. Effect of Albiglutide on Systemic Exposure of Co-administered Drugs**

Co-administered Drug	Dose of Co-administered Drug <sup>a</sup>	Dose of TANZEUM	Geometric Mean Ratio (Ratio +/- Co-administered Drug) No Effect = 1		
			Analyte	AUC (90%CI) <sup>b</sup>	C <sub>max</sub> (90% CI)
No dose adjustments of co-administered drug required for the following:					
Simvastatin	80 mg	50 mg QW for 5 weeks	Simvastatin	0.60 (0.52 – 0.69)	1.18 (1.02 – 1.38)
			Simvastatin acid	1.36 (1.19 – 1.55)	1.98 (1.75 – 2.25)
Digoxin	0.5 mg	50 mg QW for 5 weeks	Digoxin	1.09 (1.01 – 1.18)	1.11 (0.98 – 1.26)
Oral contraceptive <sup>c</sup>	0.035 mg ethinyl estradiol and 0.5 mg norethindrone	50 mg QW for 4 weeks	Norethindrone	1.00 (0.96 – 1.04)	1.04 (0.98 – 1.10)
			Levonorgestrel	1.09 (1.06 – 1.14)	1.20 (1.11 – 1.29)
Warfarin	25 mg	50 mg QW for 5 weeks	R-Warfarin	1.02 (0.98 – 1.07)	0.94 (0.89 – 0.99)
			S-Warfarin	0.99 (0.95 – 1.03)	0.93 (0.87 – 0.98)

518 QW = Once weekly.

519 <sup>a</sup> Single dose unless otherwise noted.

520 <sup>b</sup> AUC<sub>inf</sub> for drugs given as a single dose and AUC<sub>24h</sub> for drugs given as multiple doses.

521 <sup>c</sup> Subjects received low-dose oral contraceptive for two 28-day treatment cycles  
522 (21 days active/7 days placebo).  
523

## 524 **13 NONCLINICAL TOXICOLOGY**

### 525 **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

526 As albiglutide is a recombinant protein, no genotoxicity studies have been conducted.

527 Carcinogenicity studies have not been performed with albiglutide because such studies  
528 are not technically feasible due to the rapid development of drug-clearing, anti-drug  
529 antibodies in rodents. Thyroid C-cell tumors were observed in 2-year rodent  
530 carcinogenicity studies with some GLP-1 receptor agonists. The clinical relevance of  
531 rodent thyroid findings observed with GLP-1 receptor agonists is unknown.

532 In a mouse fertility study, males were treated with SC doses of 5, 15, or 50 mg/kg/day for  
533 7 days prior to cohabitation with females, and continuing through mating. In a separate  
534 fertility study, females were treated with SC doses of 1, 5, or 50 mg/kg/day for 7 days  
535 prior to cohabitation with males, and continuing through mating. Reductions in estrous  
536 cycles were observed at 50 mg/kg/day, a dose associated with maternal toxicity (body  
537 weight loss and reduced food consumption). There were no effects on mating or fertility  
538 in either sex at doses up to 50 mg/kg/day (up to 39 times clinical exposure based on  
539 AUC).

### 13.3 Reproductive and Developmental Toxicity

In order to minimize the impact of the drug-clearing, anti-drug antibody response, reproductive and developmental toxicity assessments in the mouse were partitioned to limit the dosing period to no more than approximately 15 days in each study.

In pregnant mice given SC doses of 1, 5, or 50 mg/kg/day from gestation Day 1 to 6, there were no adverse effects on early embryonic development through implantation at 50 mg/kg/day (39 times clinical exposure based on AUC).

In pregnant mice given SC doses of 1, 5, or 50 mg/kg/day from gestation Day 6 through 15 (organogenesis), embryo-fetal lethality (post-implantation loss) and bent (wavy) ribs were observed at 50 mg/kg/day (39 times clinical exposure based on AUC), a dose associated with maternal toxicity (body weight loss and reduced food consumption).

Pregnant mice were given SC doses of 1, 5, or 50 mg/kg/day from gestation Day 6 to 17. Offspring of pregnant mice given 50 mg/kg/day (39 times clinical exposure based on AUC), a dose associated with maternal toxicity, had reduced body weight pre-weaning, dehydration and coldness, and a delay in balanopreputial separation.

Pregnant mice were given SC doses of 1, 5, or 50 mg/kg/day from gestation Day 15 to lactation Day 10. Increased mortality and morbidity were seen at all doses ( $\geq 1$  mg/kg/day) in lactating females in mouse pre- and postnatal development studies. Mortalities have not been observed in previous toxicology studies in non-lactating or non-pregnant mice, nor in pregnant mice. These findings are consistent with lactational ileus syndrome which has been previously reported in mice. Since the relative stress of lactation energy demands is lower in humans than mice and humans have large energy reserves, the mortalities observed in lactating mice are of questionable relevance to humans. The offspring had decreased pre-weaning body weight which reversed post-weaning in males but not females at  $\geq 5$  mg/kg/day (2.2 times clinical exposure based on AUC) with no other effects on development. Low levels of albiglutide were detected in plasma of offspring.

Lactating mice were given SC doses of 1, 5, or 50 mg/kg/day from lactation Day 7 to 21 (weaning) under conditions that limit the impact of lactational ileus (increased caloric intake and culling of litters). Doses  $\geq 1$  mg/kg/day (exposures below clinical AUC) caused reduced weight gain in the pups during the treatment period.

## 14 CLINICAL STUDIES

TANZEUM has been studied as monotherapy and in combination with metformin, metformin and a sulfonylurea, a thiazolidinedione (with and without metformin), and insulin glargine (with or without oral anti-diabetic drugs). The efficacy of TANZEUM was compared with placebo, glimepiride, pioglitazone, liraglutide, sitagliptin, insulin lispro, and insulin glargine.

Trials evaluated the use of TANZEUM 30 mg and 50 mg. Five of the 8 trials allowed optional uptitration of TANZEUM from 30 mg to 50 mg if glycemic response with 30 mg was inadequate.

In patients with type 2 diabetes mellitus, TANZEUM produced clinically relevant reduction from baseline in HbA1c compared with placebo. No overall differences in glycemic effectiveness or body weight were observed across demographic subgroups (age, gender, race/ethnicity, duration of diabetes).

#### 14.1 Monotherapy

The efficacy of TANZEUM as monotherapy was evaluated in a 52-week, randomized, double-blind, placebo-controlled, multicenter trial. In this trial, 296 patients with type 2 diabetes inadequately controlled on diet and exercise were randomized (1:1:1) to TANZEUM 30 mg SC once weekly, TANZEUM 30 mg SC once weekly uptitrated to 50 mg once weekly at Week 12, or placebo. The mean age of participants was 53 years, 55% of patients were men, the mean duration of diabetes was 4 years, and the mean baseline eGFR was 84 mL/min/1.73 m<sup>2</sup>. Primary and secondary efficacy results are presented in Table 4. Figure 1 shows the mean adjusted changes in HbA1c from baseline across study visits.

Compared with placebo, treatment with TANZEUM 30 mg or 50 mg resulted in statistically significant reductions in HbA1c from baseline at Week 52 (see Table 4). The adjusted mean change in weight from baseline did not differ significantly between TANZEUM (-0.4 to -0.9 kg) and placebo (-0.7 kg) at Week 52.

**Table 4. Results at Week 52 (LOCF<sup>a</sup>) in a Trial of TANZEUM as Monotherapy**

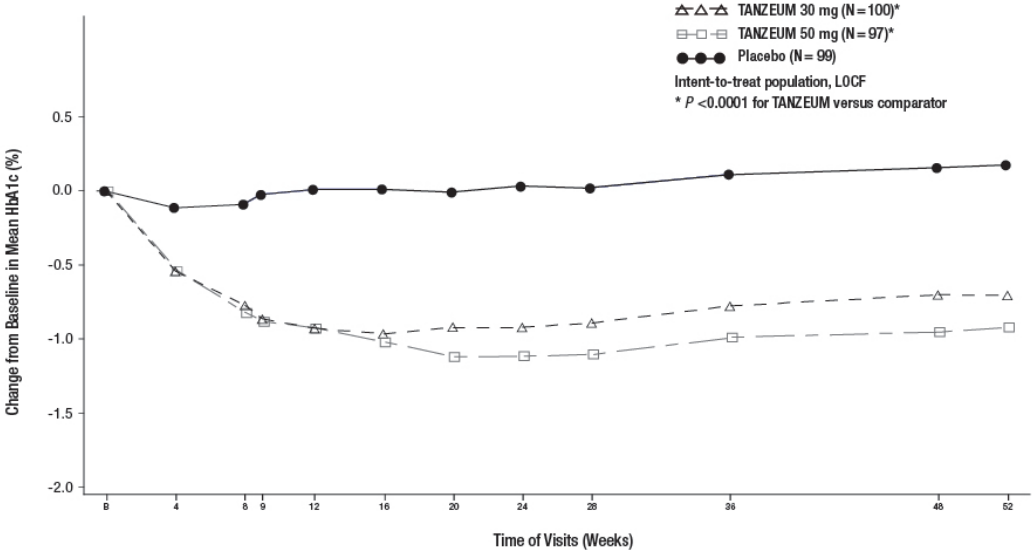
	Placebo	TANZEUM 30 mg Weekly	TANZEUM 50 mg Weekly
<b>ITT<sup>a</sup> (N)</b>	99	100	97
<b>HbA1c (%)</b>			
Baseline (mean)	8.0	8.1	8.2
Change at Week 52 <sup>b</sup>	+0.2	-0.7	-0.9
Difference from placebo <sup>b</sup> (95% CI)		-0.8 (-1.1, -0.6) <sup>c</sup>	-1.0 (-1.3, -0.8) <sup>c</sup>
Patients (%) achieving HbA1c <7%	21	49	40
<b>FPG (mg/dL)</b>			
Baseline (mean)	163	164	171
Change at Week 52 <sup>b</sup>	+18	-16	-25
Difference from placebo <sup>b</sup> (95% CI)		-34 (-46, -22) <sup>c</sup>	-43 (-55, -31) <sup>c</sup>

<sup>a</sup> Intent-to-treat population. Last observation carried forward (LOCF) was used to impute missing data. Data post-onset of rescue therapy are treated as missing. At Week 52, primary efficacy data was imputed for 63%, 34%, and 41% of individuals randomized to placebo, TANZEUM 30 mg, and TANZEUM 50 mg.

<sup>b</sup> Least squares mean adjusted for baseline value and stratification factors.

<sup>c</sup> *P* <0.0001 for treatment difference.

**Figure 1. Mean HbA1c Change from Baseline (ITT Population-LOCF) in a Trial of TANZEUM as Monotherapy**



**14.2 Combination Therapy**

**Add-on to Metformin**

The efficacy of TANZEUM was evaluated in a 104-week randomized, double-blind, multicenter trial in 999 patients with type 2 diabetes mellitus inadequately controlled on background metformin therapy ( $\geq 1,500$  mg daily). In this trial, TANZEUM 30 mg SC weekly (with optional uptitration to 50 mg weekly after a minimum of 4 weeks) was compared with placebo, sitagliptin 100 mg daily, or glimepiride 2 mg daily (with optional titration to 4 mg daily). The mean age of participants was 55 years, 48% of patients were men, the mean duration of type 2 diabetes was 6 years, and the mean baseline eGFR was 86 mL/min/1.73 m<sup>2</sup>. Results of the primary and secondary analyses are presented in Table 5. Figure 2 shows the mean adjusted changes in HbA1c across study visits.

Reduction in HbA1c from baseline achieved with TANZEUM was significantly greater than HbA1c reduction achieved with placebo, sitagliptin, and glimepiride at Week 104 (see Table 5). The difference in body weight change from baseline between TANZEUM and glimepiride was significant at Week 104.

**Table 5. Results at Week 104 (LOCF<sup>a</sup>) in a Trial Comparing TANZEUM with Placebo as Add-on Therapy in Patients Inadequately Controlled on Metformin**

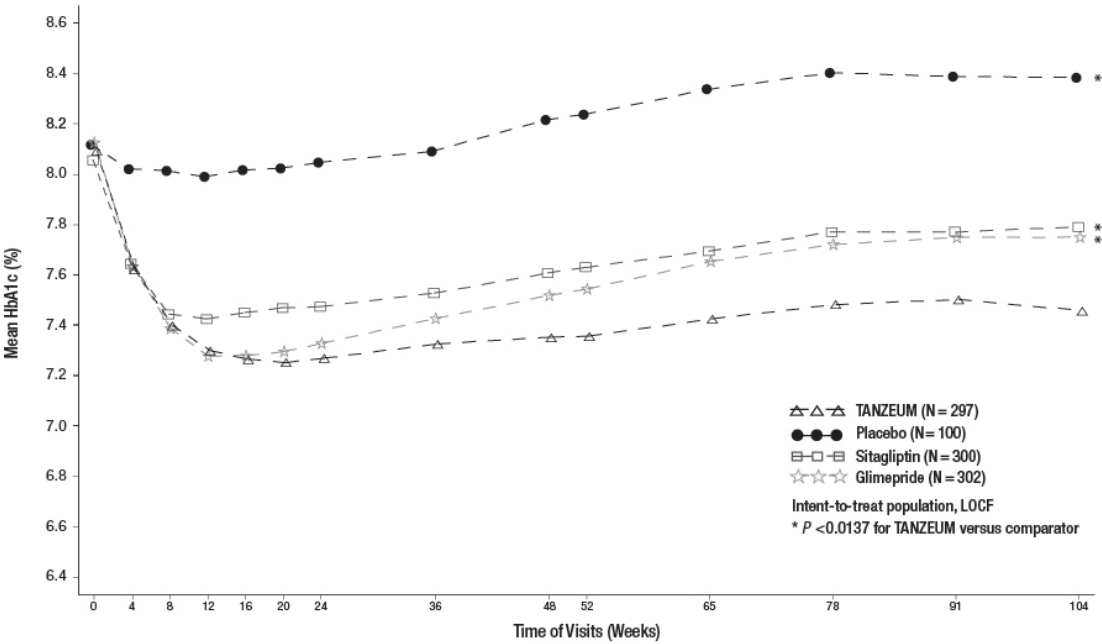
	<b>TANZEUM + Metformin</b>	<b>Placebo + Metformin</b>	<b>Sitagliptin + Metformin</b>	<b>Glimepiride + Metformin</b>
<b>ITT<sup>a</sup> (N)</b>	297	100	300	302
<b>HbA1c (%)</b>				
Baseline (mean)	8.1	8.1	8.1	8.1
Change at Week 104 <sup>b</sup>	-0.6	+0.3	-0.3	-0.4
Difference from placebo + metformin <sup>b</sup> (95% CI)	-0.9 (-1.16, -0.65) <sup>c</sup>			
Difference from sitagliptin + metformin <sup>b</sup> (95% CI)	-0.4 (-0.53, -0.17) <sup>c</sup>			
Difference from glimepiride + metformin <sup>b</sup> (95% CI)	-0.3 (-0.45, -0.09) <sup>c</sup>			
Proportion achieving HbA1c <7%	39	16	32	31
<b>FPG (mg/dL)</b>				
Baseline (mean)	165	162	165	168
Change at Week 104 <sup>b</sup>	-18	+10	-2	-8
Difference from placebo + metformin <sup>b</sup> (95% CI)	-28 (-39, -16) <sup>c</sup>			
Difference from sitagliptin + metformin <sup>b</sup> (95% CI)	-16 (-24, -8) <sup>c</sup>			
Difference from glimepiride + metformin <sup>b</sup> (95% CI)	-10 (-18, -2) <sup>c</sup>			
<b>Body Weight (kg)</b>				
Baseline (mean)	90	92	90	92
Change at Week 104 <sup>b</sup>	-1.2	-1.0	-0.9	+1.2
Difference from placebo + metformin <sup>b</sup> (95% CI)	-0.2 (-1.1, 0.7)			
Difference from sitagliptin + metformin <sup>b</sup> (95% CI)	-0.4 (-1.0, 0.3)			
Difference from glimepiride + metformin <sup>b</sup> (95% CI)	-2.4 (-3.0, -1.7) <sup>c</sup>			

<sup>a</sup> Intent-to-treat population. Last observation carried forward (LOCF) was used to impute missing data. Data post-onset of rescue therapy are treated as missing. At Week 104, primary efficacy data was imputed for 76%, 46%, 55%, and 51% of individuals randomized to placebo, TANZEUM, sitagliptin, and glimepiride, respectively.

<sup>b</sup> Least squares mean adjusted for baseline value and stratification factors.

<sup>c</sup>  $P < 0.0137$  for treatment difference.

**Figure 2. Mean HbA1c Over Time (ITT Population-LOCF) in a Trial Comparing TANZEUM with Placebo as Add-on Therapy in Patients Inadequately Controlled on Metformin**



# Add-on to Pioglitazone

The efficacy of TANZEUM was evaluated in a 52-week randomized, double-blind, multicenter trial in 299 patients with type 2 diabetes mellitus inadequately controlled on pioglitazone  $\geq 30$  mg daily (with or without metformin  $\geq 1,500$  mg daily). Patients were randomized to receive TANZEUM 30 mg SC weekly or placebo. The mean age of participants was 55 years, 60% of patients were men, the mean duration of type 2 diabetes was 8 years, and the mean baseline eGFR was 83 mL/min/1.73 m<sup>2</sup>. Results of the primary and secondary analyses are presented in Table 6.

Compared with placebo, treatment with TANZEUM resulted in a statistically significant reduction in HbA1c from baseline at Week 52 (see Table 6). The adjusted mean change from baseline in weight did not differ significantly between TANZEUM (+0.3 kg) and placebo (+0.5 kg) at Week 52.

**Table 6. Results at Week 52 (LOCF<sup>a</sup>) in a Trial Comparing TANZEUM with Placebo as Add-on Therapy in Patients Inadequately Controlled on Pioglitazone (with or without Metformin)**

	<b>TANZEUM + Pioglitazone (with or without Metformin)</b>	<b>Placebo + Pioglitazone (with or without Metformin)</b>
<b>ITT<sup>a</sup> (N)</b>	150	149
<b>HbA1c (%)</b>		
Baseline (mean)	8.1	8.1
Change at Week 52 <sup>b</sup>	-0.8	-0.1
Difference from placebo + pioglitazone <sup>b</sup> (95% CI)	-0.8 (-0.95, -0.56) <sup>c</sup>	
Proportion Achieving HbA1c <7%	44	15
<b>FPG (mg/dL)</b>		
Baseline (mean)	165	167
Change at Week 52 <sup>b</sup>	-23	+6
Difference from placebo + pioglitazone <sup>b</sup> (95% CI)	-30 (-39, -20) <sup>c</sup>	

<sup>a</sup> Intent-to-treat population. Last observation carried forward (LOCF) was used to impute missing data. Data post-onset of rescue therapy are treated as missing. At Week 52, primary efficacy data was imputed for 58% and 32% of individuals randomized to placebo and TANZEUM, respectively.

<sup>b</sup> Least squares mean adjusted for baseline value and stratification factors.

<sup>c</sup>  $P < 0.0001$  for treatment difference.

#### Add-on to Metformin Plus Sulfonylurea

The efficacy of TANZEUM was evaluated in a 52-week randomized, double-blind, multicenter trial in 657 patients with type 2 diabetes mellitus inadequately controlled on metformin ( $\geq 1,500$  mg daily) and glimepiride (4 mg daily). Patients were randomized to receive TANZEUM 30 mg SC weekly (with optional uptitration to 50 mg weekly after a minimum of 4 weeks), placebo, or pioglitazone 30 mg daily (with optional titration to 45 mg/day). The mean age of participants was 55 years, 53% of patients were men, the mean duration of type 2 diabetes was 9 years, and the mean baseline eGFR was 84 mL/min/1.73 m<sup>2</sup>. Results of the primary and main secondary analyses are presented in Table 7.

Treatment with TANZEUM resulted in statistically significant reductions in HbA1c from baseline compared with placebo (see Table 7). Treatment with TANZEUM did not meet the pre-specified, non-inferiority margin (0.3%) against pioglitazone. In this trial, TANZEUM provided less HbA1c reduction than pioglitazone and the treatment difference was statistically significant (see Table 7). The change from baseline in body weight for TANZEUM did not differ significantly from placebo but was significantly different compared with pioglitazone (see Table 7).

**Table 7. Results at Week 52 (LOCF<sup>a</sup>) in a Trial Comparing TANZEUM with Placebo as Add-on Therapy in Patients Inadequately Controlled on Metformin Plus Sulfonylurea**

	<b>TANZEUM + Metformin + Glimepiride</b>	<b>Placebo + Metformin + Glimepiride</b>	<b>Pioglitazone + Metformin + Glimepiride</b>
<b>ITT<sup>a</sup> (N)</b>	269	115	273
<b>HbA1c (%)</b>			
Baseline (mean)	8.2	8.3	8.3
Change at Week 52 <sup>b</sup>	-0.6	+0.3	-0.8
Difference from placebo + met + glim <sup>b</sup> (95% CI)	-0.9 (-1.07, -0.68) <sup>c</sup>		
Difference from pioglitazone + met + glim <sup>b</sup> (95% CI)	0.25 (0.10, 0.40) <sup>d</sup>		
Proportion achieving HbA1c <7%	30	9	35
<b>FPG (mg/dL)</b>			
Baseline (mean)	171	174	177
Change at Week 52 <sup>b</sup>	-12	+12	-31
Difference from placebo + met + glim <sup>b</sup> (95% CI)	-24 (-34, -14) <sup>c</sup>		
Difference from pioglitazone + met + glim <sup>b</sup> (95% CI)	19 (11, 27) <sup>c</sup>		
<b>Body Weight (kg)</b>			
Baseline (mean)	91	90	91
Change at Week 52 <sup>b</sup>	-0.4	-0.4	+4.4
Difference from placebo + met + glim <sup>b</sup> (95% CI)	-0.0 (-0.9, 0.8)		
Difference from pioglitazone + met + glim <sup>b</sup> (95% CI)	-4.9 (-5.5, -4.2) <sup>c</sup>		

<sup>a</sup> Intent-to-treat population. Last observation carried forward (LOCF) was used to impute missing data. Data post-onset of rescue therapy are treated as missing. At Week 52, primary efficacy data was imputed for 70%, 35%, and 34% of individuals randomized to placebo, TANZEUM, and pioglitazone.

<sup>b</sup> Least squares mean adjusted for baseline value and stratification factors.

<sup>c</sup>  $P < 0.0001$  for treatment difference.

<sup>d</sup> Did not meet non-inferiority margin of 0.3%.

#### Combination Therapy: Active-controlled Trial versus Liraglutide

The efficacy of TANZEUM was evaluated in a 32-week, randomized, open-label, liraglutide-controlled, non-inferiority trial in 805 patients with type 2 diabetes mellitus inadequately controlled on monotherapy or combination oral antidiabetic therapy (metformin, thiazolidinedione, sulfonylurea, or a combination of these). Patients were randomized to TANZEUM 30 mg SC weekly (with uptitration to 50 mg weekly at Week 6) or liraglutide 1.8 mg daily (titrated up from 0.6 mg at Week 1, and 1.2 mg at Week 1 to Week 2). The mean age of participants was 56 years, 50% of patients were men, the mean duration of type 2 diabetes was 8 years, and the mean baseline eGFR was 95 mL/min/1.73 m<sup>2</sup>. Results of the primary and main secondary analyses are presented in Table 8.



The between-treatment difference of 0.2% with 95% confidence interval (0.08, 0.34) between TANZEUM and liraglutide did not meet the pre-specified, non-inferiority margin (0.3%). In this trial, TANZEUM provided less HbA1c reduction than liraglutide and the treatment difference was statistically significant (see Table 8).

**Table 8. Results of Controlled Trial of TANZEUM versus Liraglutide at Week 32 (LOCF<sup>a</sup>)**

	<b>TANZEUM</b>	<b>Liraglutide</b>
<b>ITT<sup>a</sup> (N)</b>	402	403
<b>HbA1c (%)</b>		
Baseline (mean)	8.2%	8.2%
Change at Week 32 <sup>b</sup>	-0.8	-1.0
Difference from liraglutide <sup>b</sup> (95% CI)	0.2 (0.08, 0.34) <sup>c</sup>	
Proportion achieving HbA1c <7%	42%	52%
<b>FPG (mg/dL)</b>		
Baseline (mean)	169	167
Change at Week 32 <sup>b</sup>	-22	-30
Difference from liraglutide <sup>b</sup> (95% CI)	8 (3, 14) <sup>d</sup>	
<b>Body Weight (kg)</b>		
Baseline (mean)	92	93
Change at Week 32 <sup>b</sup>	-0.6	-2.2
Difference from liraglutide <sup>b</sup> (95% CI)	1.6 (1.1, 2.1) <sup>d</sup>	

<sup>a</sup> Intent-to-treat population. Last observation carried forward (LOCF) was used to impute missing data. Data post-onset of rescue therapy are treated as missing. At Week 32, primary efficacy data was imputed for 31% and 24% of individuals randomized to TANZEUM and liraglutide.

<sup>b</sup> Least squares mean adjusted for baseline value and stratification factors.

<sup>c</sup> Did not meet non-inferiority margin of 0.3%.

<sup>d</sup>  $P < 0.005$  for treatment difference in favor of liraglutide.

### Combination Therapy: Active-controlled Trial versus Basal Insulin

The efficacy of TANZEUM was evaluated in a 52-week, randomized (2:1), open-label, insulin glargine-controlled, non-inferiority trial in 735 patients with type 2 diabetes mellitus inadequately controlled on metformin  $\geq 1,500$  mg daily (with or without sulfonylurea). Patients were randomized to receive TANZEUM 30 mg SC weekly (with optional uptitration to 50 mg weekly) or insulin glargine (started at 10 units and titrated weekly per prescribing information). The primary endpoint was change in HbA1c from baseline compared with insulin glargine. The starting total daily dose of insulin glargine ranged between 2 and 40 units (median daily dose of 10 units) and ranged between 3 and 230 units (median daily dose of 30 units) at Week 52. Seventy-seven percent of patients treated with TANZEUM were uptitrated to 50 mg SC weekly. The mean age of

participants was 56 years, 56% of patients were men, the mean duration of type 2 diabetes was 9 years, and the mean baseline eGFR was 85 mL/min/1.73 m<sup>2</sup>. Results of the primary and main secondary analyses are presented in Table 9.

The between-treatment difference of 0.1% with 95% confidence interval (-0.04%, 0.27%) for TANZEUM and insulin glargine met the pre-specified, non-inferiority margin (0.3%). A mean decrease in body weight was observed for TANZEUM compared with a mean increase in body weight for insulin glargine, and the difference in weight change was statistically significant (see Table 9).

**Table 9. Results at Week 52 (LOCF<sup>a</sup>) in a Trial Comparing TANZEUM with Insulin Glargine as Add-on Therapy in Patients Inadequately Controlled on Metformin ± Sulfonylurea**

	<b>TANZEUM + Metformin (with or without Sulfonylurea)</b>	<b>Insulin Glargine + Metformin (with or without Sulfonylurea)</b>
<b>ITT<sup>a</sup> (N)</b>	496	239
<b>HbA1c (%)</b>		
Baseline (mean)	8.3	8.4
Change at Week 52 <sup>b</sup>	-0.7	-0.8
Difference from insulin glargine <sup>b</sup> (95% CI)	0.1 (-0.04, 0.27) <sup>c</sup>	
Proportion achieving HbA1c <7%	32	33
<b>FPG (mg/dL)</b>		
Baseline (mean)	169	175
Change at Week 52 <sup>b</sup>	-16	-37
Difference from insulin glargine <sup>b</sup> (95% CI)	21 (14, 29) <sup>d</sup>	
<b>Body Weight (kg)</b>		
Baseline (mean)	95	95
Change at Week 52 <sup>b</sup>	-1.1	1.6
Difference from insulin glargine <sup>b</sup> (95% CI)	-2.6 (-3.2, -2.0) <sup>e</sup>	

<sup>a</sup> Intent-to-treat population. Last observation carried forward (LOCF) was used to impute missing data. Data post-onset of rescue therapy are treated as missing. At Week 52, primary efficacy data was imputed for 41% and 36% of individuals randomized to TANZEUM and glargine.

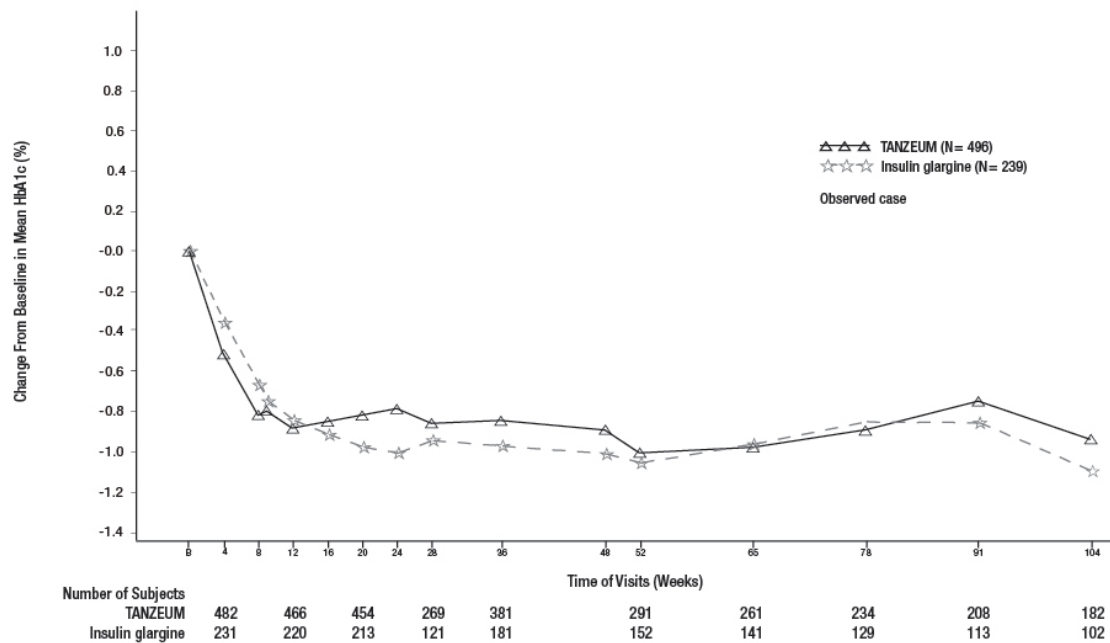
<sup>b</sup> Least squares mean adjusted for baseline value and stratification factors.

<sup>c</sup> Met non-inferiority margin of 0.3%.

<sup>d</sup> *P* <0.0001 in favor of insulin glargine.

<sup>e</sup> *P* <0.0001.

**Figure 3. Mean HbA1c Change from Baseline (Completers) in a Trial Comparing TANZEUM with Insulin Glargine as Add-on Therapy in Patients Inadequately Controlled on Metformin (with or without a Sulfonylurea)**



### Combination Therapy: Active-controlled Trial versus Prandial Insulin

The efficacy of TANZEUM was evaluated in a 26-week, randomized, open-label, multicenter, non-inferiority trial in 563 patients with type 2 diabetes mellitus inadequately controlled on insulin glargine (started at 10 units and titrated to  $\geq 20$  units per day). Patients were randomized to receive TANZEUM 30 mg SC once weekly (with uptitration to 50 mg if inadequately controlled after Week 8) or insulin lispro (administered daily at meal times, started according to standard of care and titrated to effect). At Week 26, the mean daily dose of insulin glargine was 53 IU for TANZEUM and 51 IU for insulin lispro. The mean daily dose of insulin lispro at Week 26 was 31 IU, and 69% of patients treated with TANZEUM were on 50 mg weekly. The mean age of participants was 56 years, 47% of patients were men, the mean duration of type 2 diabetes was 11 years, and the mean baseline eGFR was 91 mL/min/1.73 m<sup>2</sup>. Results of the primary and main secondary analyses are presented in Table 10. Figure 4 shows the mean adjusted changes in HbA1c from baseline across study visits.

The between-treatment difference of -0.2% with 95% confidence interval (-0.32%, 0.00%) between albiglutide and insulin lispro met the pre-specified non-inferiority margin (0.4%). Treatment with TANZEUM resulted in a mean weight loss for TANZEUM compared with a mean weight gain for insulin lispro, and the difference between treatment groups was statistically significant (see Table 10).

**Table 10. Results at Week 26 (LOCF<sup>a</sup>) in a Trial Comparing TANZEUM with Insulin Lispro as Add-On Therapy in Patients Inadequately Controlled on Insulin Glargine**

	<b>TANZEUM + Insulin Glargine</b>	<b>Insulin Lispro + Insulin Glargine</b>
<b>ITT<sup>a</sup> (N)</b>	282	281
<b>HbA<sub>1c</sub> (%)</b>		
Baseline (mean)	8.5	8.4
Change at Week 26 <sup>b</sup>	-0.8	-0.7
Difference from insulin lispro <sup>b</sup> (95% CI)	-0.2 (-0.32, 0.00) <sup>c</sup>	
Proportion achieving HbA <sub>1c</sub> <7%	30%	25%
<b>FPG (mg/dL)</b>		
Baseline (mean)	153	153
Change at Week 26 <sup>b</sup>	-18	-13
Difference from insulin lispro <sup>b</sup> (95% CI)	-5 (-13, 3)	
<b>Body Weight (kg)</b>		
Baseline (mean)	93	92
Change at Week 26 <sup>b</sup>	-0.7	+0.8
Difference from insulin lispro <sup>b</sup> (95% CI)	-1.5 (-2.1, -1.0) <sup>d</sup>	

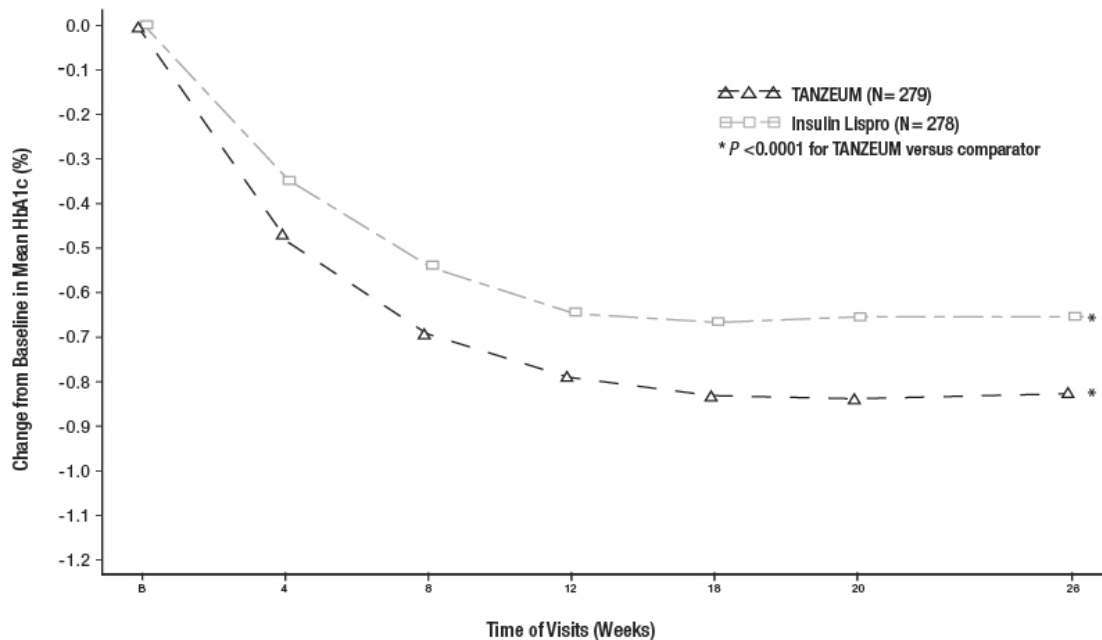
<sup>a</sup> Intent-to-treat population. Last observation carried forward (LOCF) was used to impute missing data. Data post-onset of rescue therapy are treated as missing. At Week 26, primary efficacy data was imputed for 29% and 29% of individuals randomized to TANZEUM and insulin lispro.

<sup>b</sup> Least squares mean adjusted for baseline value and stratification factors.

<sup>c</sup> Rules out a non-inferiority margin of 0.4%.

<sup>d</sup>  $P < 0.0001$  for treatment difference.

**Figure 4. Mean HbA1c Change from Baseline (ITT-LOCF population) in a Trial Comparing TANZEUM with Insulin Lispro as Add-On Therapy in Patients Inadequately Controlled on Insulin Glargine**



### 14.3 Type 2 Diabetes Mellitus Patients with Renal Impairment

The efficacy of TANZEUM was evaluated in a 26-week, randomized, double-blind, active-controlled trial in 486 patients with mild (n = 250), moderate (n = 200), and severe renal impairment (n = 36) inadequately controlled on a current regimen of diet and exercise or other antidiabetic therapy. Patients were randomized to receive TANZEUM 30 mg SC weekly (with uptitration to 50 mg weekly if needed as early as Week 4) or sitagliptin. Sitagliptin was dosed according to renal function (100 mg, 50 mg, and 25 mg daily in mild, moderate, and severe renal impairment, respectively). The mean age of participants was 63 years, 54% of patients were men, the mean duration of type 2 diabetes was 11 years, and the mean baseline eGFR was 60 mL/min/1.73 m<sup>2</sup>.

Results of the primary and main secondary analyses are presented in Table 11. Treatment with TANZEUM resulted in statistically significant reductions in HbA1c from baseline at Week 26 compared with sitagliptin (see Table 11).

**Table 11. Results at Week 26 (LOCF<sup>a</sup>) in a Trial Comparing TANZEUM with Sitagliptin in Patients with Renal Impairment**

	<b>TANZEUM</b>	<b>Sitagliptin</b>
<b>ITT<sup>a</sup> (N)</b>	246	240
<b>HbA1c (%)</b>		
Baseline (mean)	8.1	8.2
Change at Week 26 <sup>b</sup>	-0.8	-0.5
Difference from sitagliptin <sup>b</sup> (95% CI)	-0.3 (-0.49, -0.15) <sup>c</sup>	
Proportion achieving HbA1c <7%	43%	31%
<b>FPG (mg/dL)</b>		
Baseline (mean)	166	165
Change at Week 26 <sup>b</sup>	-26	-4
Difference from sitagliptin <sup>b</sup> (95% CI)	-22 (-31, -13) <sup>c</sup>	
<b>Body Weight (kg)</b>		
Baseline (mean)	84	83
Change at Week 26 <sup>b</sup>	-0.8	-0.2
Difference from sitagliptin <sup>b</sup> (95% CI)	-0.6 (-1.1, -0.1) <sup>d</sup>	

<sup>a</sup> Intent-to-treat population. Last observation carried forward (LOCF) was used to impute missing data. Data post-onset of rescue therapy are treated as missing. At Week 26 primary efficacy data was imputed for 17% and 25% of individuals randomized to TANZEUM and sitagliptin.

<sup>b</sup> Least squares mean adjusted for baseline value and stratification factors.

<sup>c</sup>  $P < 0.0003$  for treatment difference.

<sup>d</sup>  $P = 0.0281$  for treatment difference.

## **16 HOW SUPPLIED/STORAGE AND HANDLING**

### **16.1 How Supplied**

TANZEUM is available in the following strengths and package sizes:

30 mg single-dose Pen:

- carton of 1 (containing one 29-gauge, 5-mm, thinwall needle): NDC 0173-866-02
- carton of 4 (containing four 29-gauge, 5-mm, thinwall needles): NDC 0173-866-35

50 mg single-dose Pen:

- carton of 1 (containing one 29-gauge, 5-mm, thinwall needle): NDC 0173-867-02
- carton of 4 (containing four 29-gauge, 5-mm, thinwall needles): NDC 0173-867-35

### **16.2 Storage and Handling**

- Prior to dispensing: Store Pens in the refrigerator at 36°F to 46°F (2°C to 8°C). Pens may be stored refrigerated until the expiration date.

- 829 • Following dispensing: Store Pens in the refrigerator at 36°F to 46°F (2°C to 8°C).
- 830 Patients may store Pens at room temperature not to exceed 86°F (30°C) for up to
- 831 4 weeks prior to use. Store Pens in the original carton until use.
- 832 • Do not freeze.
- 833 • Do not use past the expiration date.
- 834 • Use within 8 hours after reconstitution.

## 835 **17 PATIENT COUNSELING INFORMATION**

836 See FDA-approved patient labeling (Medication Guide and Instructions for Use). The  
837 Medication Guide is contained in a separate leaflet that accompanies the product.

- 838 • Inform patients about self-management practices, including the importance of proper  
839 storage of TANZEUM, injection technique, timing of dosage of TANZEUM and  
840 concomitant oral drugs, and recognition and management of hypoglycemia.
- 841 • Inform patients that thyroid C-cell tumors have been observed in rodents treated with  
842 some GLP-1 receptor agonists, and the human relevance of this finding is unknown.  
843 Counsel patients to report symptoms of thyroid tumors to their physician [*see*  
844 *Warnings and Precautions (5.1)*].
- 845 • Advise patients that persistent, severe abdominal pain that may radiate to the back  
846 and which may (or may not) be accompanied by vomiting is the hallmark symptom of  
847 acute pancreatitis. Instruct patients to discontinue TANZEUM promptly and to  
848 contact their physician if persistent, severe abdominal pain occurs [*see Warnings and*  
849 *Precautions (5.2)*].
- 850 • The risk of hypoglycemia is increased when TANZEUM is used in combination with  
851 an agent that induces hypoglycemia, such as sulfonylurea or insulin. Instructions for  
852 hypoglycemia should be reviewed with patients and reinforced when initiating  
853 therapy with TANZEUM, particularly when concomitantly administered with a  
854 sulfonylurea or insulin [*see Warnings and Precautions (5.3)*].
- 855 • Advise patients on the symptoms of hypersensitivity reactions and instruct them to  
856 stop taking TANZEUM and seek medical advice promptly if such symptoms occur  
857 [*see Warnings and Precautions (5.4)*].
- 858 • Instruct patients to read the Instructions for Use before starting therapy. Instruct  
859 patients on proper use, storage, and disposal of the pen [*see How Supplied/Storage*  
860 *and Handling (16.2), Patient Instructions for Use*].
- 861 • Instruct patients to read the Medication Guide before starting TANZEUM and to read  
862 again each time the prescription is renewed. Instruct patients to inform their doctor or  
863 pharmacist if they develop any unusual symptom, or if any known symptom persists  
864 or worsens.
- 865 • Inform patients not to take an extra dose of TANZEUM to make up for a missed  
866 dose. If a dose is missed, instruct patients to take a dose as soon as possible within

867 3 days after the missed dose. Instruct patients to then take their next dose at their  
868 usual weekly time. If it has been longer than 3 days after the missed dose, instruct  
869 patients to wait and take TANZEUM at the next usual weekly time.

870

871 TANZEUM is a trademark of the GSK group of companies.



872

873 Manufactured by **GlaxoSmithKline LLC**

874 Wilmington, DE 19808

875 U.S. Lic. No. 1727

876 Marketed by **GlaxoSmithKline**

877 Research Triangle Park, NC 27709

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879 TNZ:XPI



**Medication Guide**  
**TANZEUM™ (TAN-zee-um)**  
**(albiglutide)**  
**for injection, for subcutaneous use**

Read this Medication Guide before you start taking TANZEUM and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

**What is the most important information I should know about TANZEUM?**

**Serious side effects may happen in people who take TANZEUM, including:**

- **Possible thyroid tumors, including cancer.** Tell your healthcare provider if you get a lump or swelling in your neck, hoarseness, trouble swallowing, or shortness of breath. These may be symptoms of thyroid cancer. In studies with rats and mice, medicines that work like TANZEUM caused thyroid tumors, including thyroid cancer. It is not known if TANZEUM will cause thyroid tumors or a type of thyroid cancer called medullary thyroid carcinoma in people.
- **Do not use TANZEUM if you** or your family have ever had a type of thyroid cancer called medullary thyroid carcinoma (MTC) or if you have an endocrine system cancer called Multiple Endocrine Neoplasia syndrome type 2 (MEN 2).

**What is TANZEUM?**

TANZEUM is an injectable prescription medicine that may improve blood sugar (glucose) in adults with type 2 diabetes mellitus, and should be used along with diet and exercise.

- TANZEUM is not recommended as the first choice of medicine for treating diabetes.
- It is not known if TANZEUM can be used in people who previously had pancreatitis.
- TANZEUM is not a substitute for insulin and is not for use in people with type 1 diabetes or people with diabetic ketoacidosis.
- TANZEUM is not recommended in people with severe stomach or intestinal problems.
- It is not known if TANZEUM can be used with short-acting or rapid-acting (mealtime) insulin.
- It is not known if TANZEUM is safe and effective in children under 18 years of age.

**Who should not use TANZEUM?**

**Do not use TANZEUM if:**

- you or your family have ever had a type of thyroid cancer called medullary thyroid carcinoma (MTC) or if you have an endocrine system cancer called Multiple Endocrine Neoplasia syndrome type 2 (MEN 2)
- you are allergic to albiglutide or any of the ingredients in TANZEUM.

**Before using TANZEUM, tell your healthcare provider about your medical conditions including, if you:**

- have or have had problems with your pancreas, kidneys, or liver
- have severe problems with your stomach, such as slowed emptying of your stomach (gastroparesis) or problems with digesting food
- are pregnant or plan to become pregnant. It is not known if TANZEUM will harm your unborn baby. Tell your healthcare provider if you become pregnant while using TANZEUM.
- are breastfeeding or plan to breastfeed. It is not known if TANZEUM passes into your breast milk. You and your healthcare provider should decide if you will use TANZEUM or breastfeed. You should not do both without talking with your healthcare provider first.
- are taking a new prescription or over-the-counter medicines, vitamins, or herbal supplements.

### How should I use TANZEUM?

- Read the **Instructions for Use** that comes with TANZEUM.
- Use TANZEUM exactly as your healthcare provider tells you to.
- **Use TANZEUM 1 time each week on the same day each week at any time of the day.**
- You may change your day of the week as long as your last dose was given **4** or more days before.
- If you miss a dose of TANZEUM, take the missed dose of TANZEUM within **3** days after your usual scheduled day. If more than **3** days have gone by since your missed dose, wait until your next regularly scheduled weekly dose.
- TANZEUM may be taken with or without food.
- **Do not mix insulin and TANZEUM together in the same injection.**
- **Do not share your pen or needles with another person.** You may give another person an infection or get an infection from them.

### What are the possible side effects of TANZEUM?

#### TANZEUM may cause serious side effects, including:

- **inflammation of your pancreas (pancreatitis).** Stop using TANZEUM and call your healthcare provider right away if you have severe pain in your stomach area (abdomen) that will not go away, with or without vomiting. You may feel pain that may go from your abdomen to your back.
- **low blood sugar (hypoglycemia).** Your risk is higher if you take TANZEUM with another medicine that can cause low blood sugar such as insulin or sulfonylurea. Signs and symptoms of low blood sugar may include:
  - dizziness or light-headedness
  - blurred vision
  - anxiety, irritability, or mood changes
  - sweating
  - slurred speech
  - hunger
  - confusion
  - shakiness
  - feeling jittery
  - headache
  - fast heart beat
- **allergic reactions.** Stop using TANZEUM and get medical help right away if you have any symptoms of an allergic reaction including itching, rash, or difficulty breathing.
- **kidney problems (kidney failure).** In people who have kidney problems, diarrhea, nausea, and vomiting may result in loss of fluids (dehydration) which may worsen kidney problems.

**Common side effects of TANZEUM may include** diarrhea, nausea, reactions at your injection site, cough, back pain, and cold or flu symptoms.

These are not all the possible side effects of TANZEUM. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

### General information about the safe and effective use of TANZEUM.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. You can ask your pharmacist or healthcare provider for information about TANZEUM that is written for health professionals. Do not use TANZEUM for a condition for which it was not prescribed. Do not give TANZEUM to other people, even if they have the same symptoms that you have. It may harm them.

### What are the ingredients in TANZEUM?

**Active Ingredient:** albiglutide

**Inactive Ingredients:** mannitol, polysorbate 80, sodium phosphate, and trehalose dihydrate. TANZEUM does not contain a preservative.

For more information, go to [www.TANZEUM.com](http://www.TANZEUM.com) or call 1-888-825-5249.

This Medication Guide has been approved by the U.S. Food and Drug Administration. Approved: April 2014



GlaxoSmithKline

Manufactured by **GlaxoSmithKline LLC**  
Wilmington, DE 19808  
U.S. Lic No. 1727  
Marketed by GlaxoSmithKline  
Research Triangle Park, NC 27709

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TNZ:XMG

## INSTRUCTIONS FOR USE

### TANZEUM™ (TAN-zee-um) (albiglutide)

for injection, for subcutaneous use

#### TANZEUM (albiglutide) Pen 30 mg

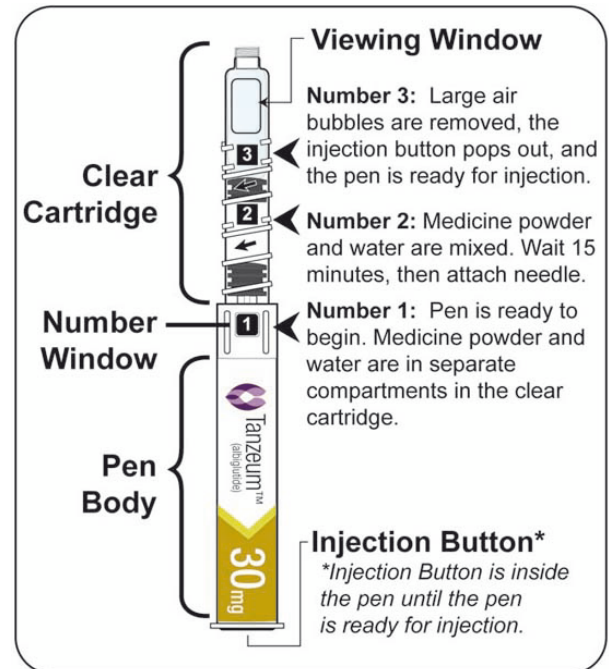
##### Use 1 Time Each Week

Read all the instructions and follow the steps below to mix the medicine and prepare the pen for injection.

**Failure to follow Steps A to C in the correct order may result in damage to your pen.**

##### Information About This Pen

- This medicine is injected **1** time each week.
- The pen has medicine powder in 1 compartment and water in another compartment. You will need to mix them together by twisting the pen, then wait for **15** minutes for the medicine and water to fully mix.



#### **CAUTION:**

**Do not allow the pen to freeze. Throw away the pen if frozen.**

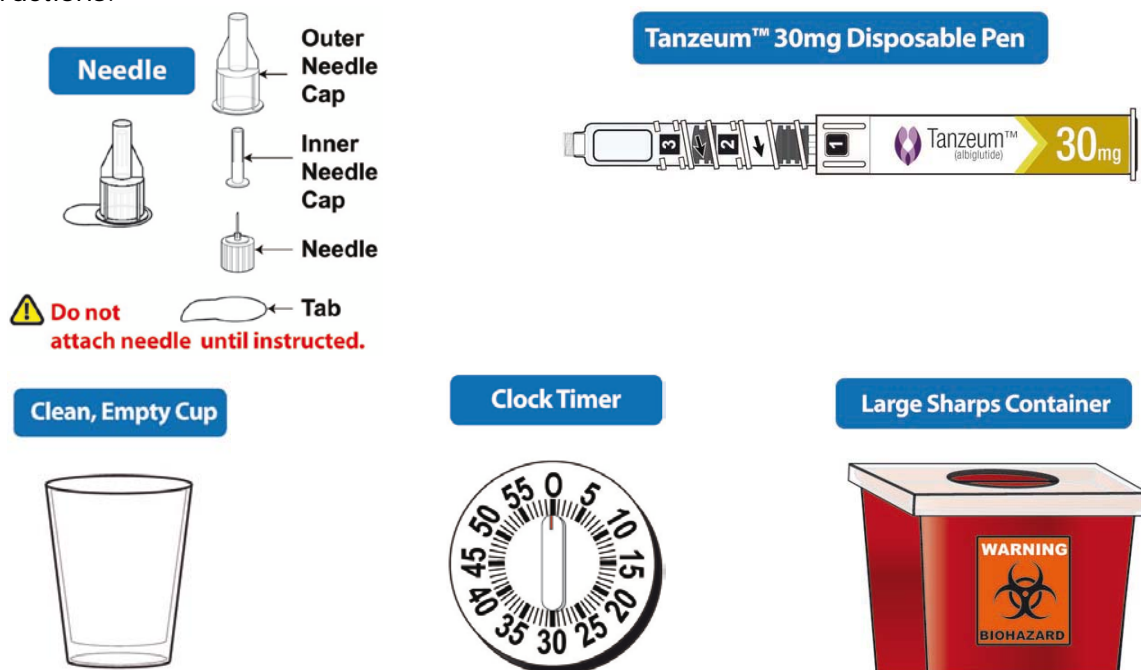
**If stored in refrigerator, allow to sit at room temperature for 15 minutes before starting Step A.**

**Dispose of the pen right away after injecting. Do not recap, remove, or reuse the needle.**

#### Before you Begin: Wash Your Hands, Gather and Inspect Your Supplies

- Wash your hands.
- Take a pen and new needle out of the box and check the label on your pen to make sure it is your prescribed dose of medicine.

- Gather a **clean, empty cup** to hold the pen while the medicine mixes, a **clock timer** to measure the time while the medicine mixes, and a large **sharps container** for pen disposal. See “**Disposing of Your Used Pens and Needles**” at the end of these instructions.



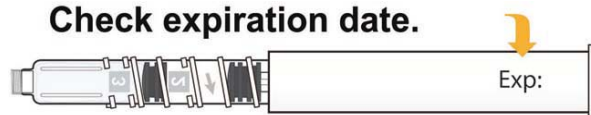
## STEP A

### Inspect Your Pen and Mix Your Medicine

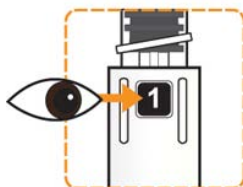
#### Inspect Your Pen

- Make sure that you have all of the supplies listed above (pen, needle, cup, timer, sharps container).
- Check the expiration date on the pen. **Do not** use if expired.

#### Check expiration date.

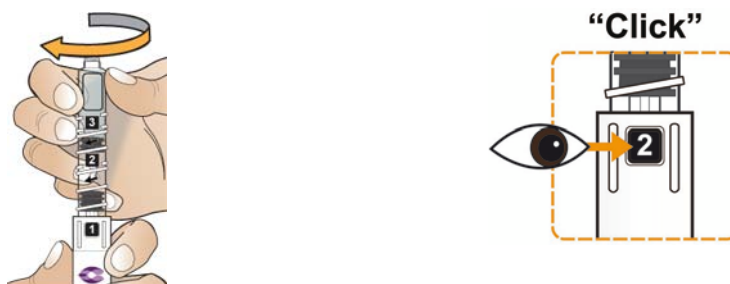


- Check that the pen has a **[1]** in the number window. **Do not** use if the **[1]** is not showing.



### Twist Pen to Mix Your Medicine

- Hold the pen body with the clear cartridge pointing up so that you **see the [1] in the number window**.
- With your other hand, twist the clear cartridge several times in the direction of the arrow (clockwise) until you feel and hear the pen “click” into place and you **see the [2] in the number window**. This will mix the medicine powder and liquid in the clear cartridge.



- Slowly and gently rock the pen side to side (like a windshield wiper) **5 times** to mix the medicine. **Do not** shake the pen hard to avoid foaming; it may affect your dose.



### Wait for Medicine to Dissolve

- Place the pen into the clean, empty cup to keep the clear cartridge pointing up.
- **Set the clock timer for 15 minutes.**



You must wait 15 minutes for the medicine to dissolve before continuing to Step B.

## STEP B

### Attach the Needle and Prepare the Pen for Injection

After the 15 minute wait, wash your hands and finish the rest of the steps right away.

### Inspect Your Dissolved Medicine

- Again, slowly and gently rock the pen side to side (like a windshield wiper) **5 times** to mix your medicine again. **Do not** shake the pen hard to avoid foaming; it may affect your dose.



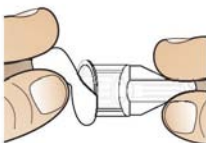
- Look through the viewing window to check that the liquid in the cartridge is clear and free of solid particles.



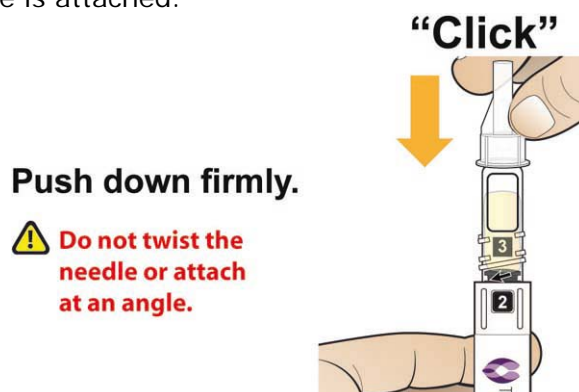
- The liquid will have a yellow color and there will be **large air bubbles** on top of the liquid.

### Attach the Needle

- Peel the tab from the outer needle cap.



- Hold the pen with the clear cartridge pointing up and push the needle straight down onto the clear cartridge until you hear a “click” and feel the needle “snap” down into place. This means the needle is attached.



### Tap for Air Bubbles

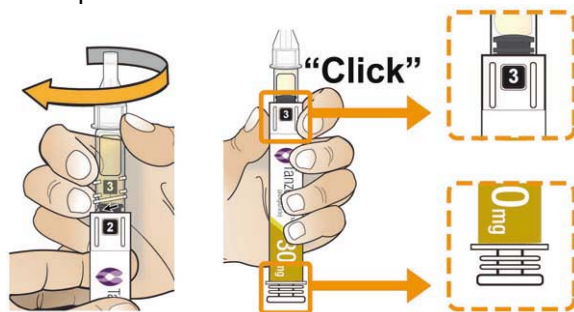
- With the needle point up, gently tap the clear cartridge **2 to 3** times to bring large air bubbles to the top.



**Small bubbles are okay and do not need to rise to the top.**

### Twist Pen to Prime the Needle

- Twist the clear cartridge several times in the direction of the arrow (clockwise) until you feel and hear the pen “click” and you **see the [3] in the number window**. This removes the large air bubbles from the clear cartridge. The injection button will also pop out from the bottom of the pen.



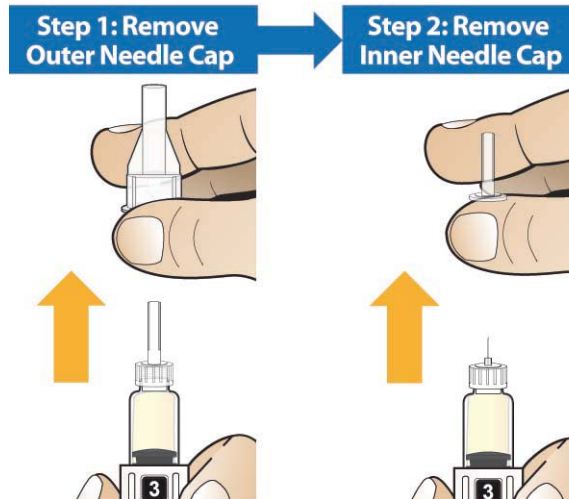


## STEP C

### Remove Both Needle Caps and Inject Your Medicine

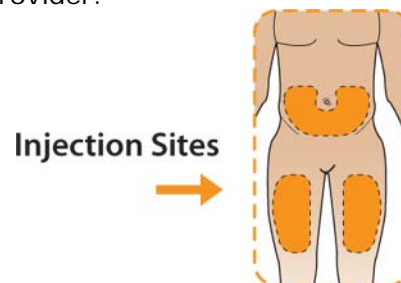
#### Remove Needle Caps

- Carefully remove the outer needle cap, then the inner needle cap. **A few drops of liquid may come out of the needle. This is normal.**



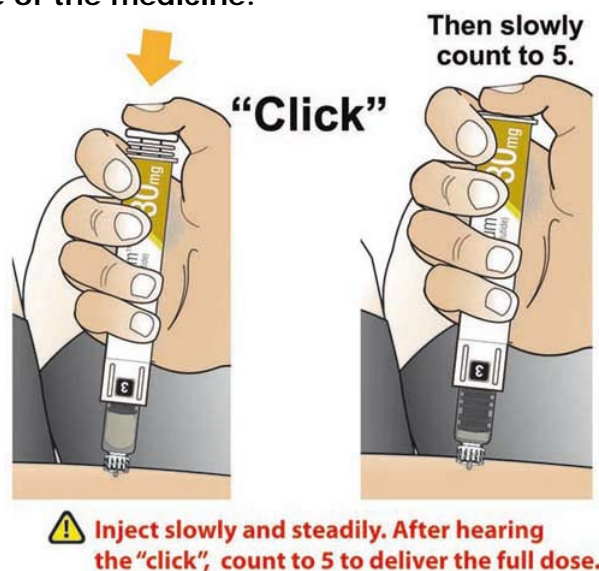
#### Inject the Medicine

- Insert the needle into the skin on your abdomen, thigh, or upper arm and inject as shown to you by your healthcare provider.





- With your thumb, press the injection button slowly and steadily to inject your medicine. The slower you press the button, the less pressure you will feel.
- Keep the injection button pressed down until you hear a “click”. **After hearing the click, continue holding your thumb down on the button and then slowly count to 5 to deliver the full dose of the medicine.**



- After hearing the “click” and then slowly counting to **5**, pull the needle out of your skin.

### Disposing of Your Used Pens and Needles

- **Do not** recap the needle or remove needle from the pen.
- Put your used needles and pens in a FDA-cleared sharps disposal container right away after use. **Do not throw away (dispose of) loose needles and pens in your household trash.**



## General Information About the Safe and Effective Use of TANZEUM

- Take **1** time each week. You can take your medicine at any time of day, with or without meals.
- **Your healthcare provider will teach you how to mix and inject TANZEUM before you use it for the first time.** If you have questions or do not understand the **Instructions for Use**, talk to your healthcare provider.
- **Use TANZEUM exactly as your healthcare provider tells you. Do not** change your dose or stop TANZEUM without talking to your healthcare provider.
- **Change (rotate) your injection site with each injection (weekly).**
- TANZEUM is injected under the skin (subcutaneously) in your stomach area (abdomen), upper leg (thigh), or upper arm.
- **Do not** inject TANZEUM into a vein or muscle.
- If you use TANZEUM with insulin, you should inject your TANZEUM and insulin separately. **Do not mix insulin and TANZEUM together.** You can inject TANZEUM and insulin in the same body area (for example, your stomach area), but you should not give the injections right next to each other.
- Keep pens and needles out of the reach of children.
- Always use a new needle for each injection.
- Do not share pens or needles.

## Frequently Asked Questions

### Medicine Dosing

#### What if I need to take my medicine on a different day of the week?

- You may take your next dose of medicine on a different day as long as it has been at least **4** days since your last dose.

#### What if I forget to take the medicine on the day I am supposed to?

- Take your missed dose of medicine within **3** days after your scheduled day, then return to your scheduled day for your next dose. If more than **3** days have passed since your usual scheduled day, wait until your next regularly scheduled day to take the injection of TANZEUM.

### Storage

#### How should I store my medicine?

- Store your pens in the refrigerator between 36°F to 46°F (2°C to 8°C).
- You may store your pen in the box at room temperature below 86°F (30°C) for up to **4** weeks before you are ready to use the pen.
- Store pens in the carton they came in.

- **Do not** freeze pens. If the liquid in the pen is frozen, throw away the pen and use another pen.

## **Number Window**

### **Are the Numbers 1, 2, and 3 used to select my dose of medicine?**

- No, you do not have to select your dose. The numbers are to help you prepare and give your medicine.

**Number 1:** Pen is ready to begin. Medicine powder and water are in separate compartments in the clear cartridge. If you don't see a number **1** in the window, throw away the pen.

**Number 2:** Medicine powder and water are mixed and then gently rocked. Wait **15** minutes, then attach needle.

**Number 3:** Large air bubbles are removed, the injection button pops out, and the pen is ready for injection.

### **What if I do not hear the “click” when the 2 or 3 are moved into the Number Window?**

- If you do not hear a “click” when **2 or 3** are moved into the number window, you may not have the number fully centered in the window. Twist the clear cartridge slightly in the direction of the arrow to complete the “click” and center the number in the window. Do not turn the clear cartridge in the opposite direction from the arrows.

## **Step A: Inspect Your Pen and Mix Your Medicine**

### **What if I do not wait 15 minutes after turning the pen to the Number 2?**

- If you do not wait the full **15** minutes the medicine may not be mixed with the water the right way. This can result in particles floating in the clear cartridge, not getting your full dose, or a blocked needle. Waiting the full **15** minutes ensures that the medicine powder and water are mixed the right way, even though it may look like it is mixed sooner than that.

### **What if I leave my pen for more than 15 minutes after turning the pen to the Number 2 in Step A?**

- As long as the needle has not been attached, the pen can be used for up to **8** hours from the time **Step A** was started. If it has been more than **8** hours since the medicine was mixed in **Step A**, throw away the pen and use another pen.
- If you have attached the needle, TANZEUM should be used right away.

## **Step B: Attach the Needle and Prepare Pen for Injection**

**What if I leave my pen with the needle attached at Step B, and come back later to finish Step C?**

- This can cause your needle to block, you should continue from **Step B** to **Step C** right away.

**What if I do not attach the needle at Step B?**

- If the needle is attached at **Step A**, some of the medicine may be lost during mixing. Throw away the pen and use another pen.
- If the needle is not attached in **Step B**, and you go to **Step C** to turn the pen from Position **2 to 3**, this can damage the pen.

## **Step C: Remove Both Needle Caps and Inject Your Medicine**

**After I turn the pen to Number 3 (Step C), there are still some small air bubbles remaining. Can I still use the pen?**

- Seeing small air bubbles remaining is normal and you can still use the pen.

**After I give my medicine, there is some liquid still seen in the clear cartridge.**

- This is normal. If you have heard or felt the injection button “click” and slowly counted to **5** before pulling the needle out of your skin, you should have received the full dose of your medicine.

**How should I dispose of the pen?**

- **Do not** recap the needle or remove needle from the pen.
- Put your used needles and pens in a FDA-cleared sharps disposal container right away after use. **Do not throw away (dispose of) loose needles and pens in your household trash.**
- If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:
  - made of a heavy-duty plastic,
  - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
  - upright and stable during use,
  - leak-resistant, and
  - properly labeled to warn of hazardous waste inside the container.
- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and pens. For more information about safe sharps disposal, and for specific information

about sharps disposal in the state that you live in, go to the FDA's website at:

<http://www.fda.gov/safesharpsdisposal>.


- **Do not** dispose of your used sharps disposal container in your household trash unless your community guidelines permit this. **Do not** recycle your used sharps disposal container.



**Please make sure you are using the right dose.  
These instructions are for the 30 mg dose.**

This Instructions for Use has been approved by the U.S. Food and Drug Administration.

Approved: April 2014

 <b>GlaxoSmithKline</b>	Manufactured by <b>GlaxoSmithKline LLC</b> Wilmington, DE 19808 U.S. Lic No. 1727 Marketed by GlaxoSmithKline Research Triangle Park, NC 27709	TANZEUM is a trademark of the GSK group of companies. ©2014, the GSK group of companies. All rights reserved. TNZ: XIFU-30
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## INSTRUCTIONS FOR USE

### TANZEUM™ (TAN-zee-um) (albiglutide) for injection, for subcutaneous use

#### TANZEUM (albiglutide) Pen 50 mg

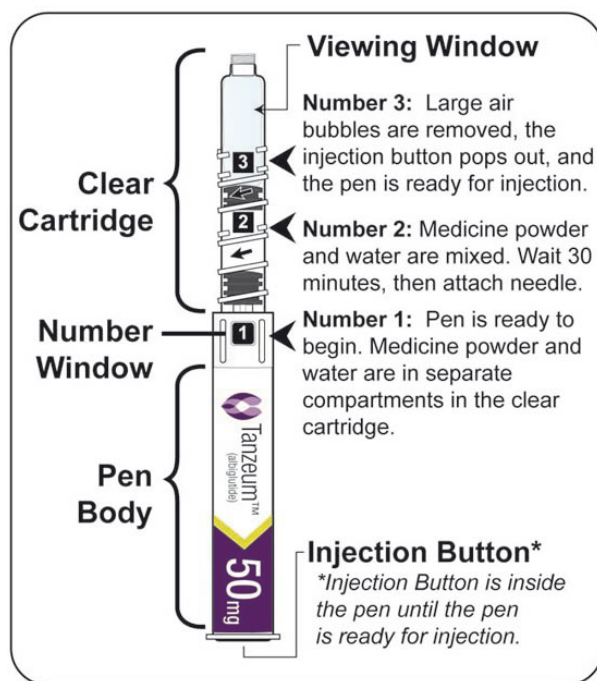
##### Use 1 Time Each Week

Read all the instructions and follow the steps below to mix the medicine and prepare the pen for injection.

**Failure to follow Steps A to C in the correct order may result in damage to your pen.**

##### Information About This Pen

- This medicine is injected **1** time each week.
- The pen has medicine powder in 1 compartment and water in another compartment. You will need to mix them together by twisting the pen, then wait for **30** minutes for the medicine and water to fully mix.



#### **CAUTION:**

**Do not allow the pen to freeze. Throw away the pen if frozen.**

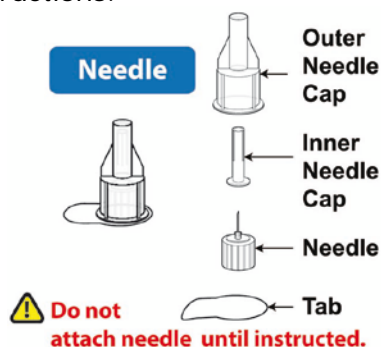
**If stored in refrigerator, allow to sit at room temperature for 15 minutes before starting Step A.**

**Dispose of the pen right away after injecting. Do not recap, remove, or reuse the needle.**

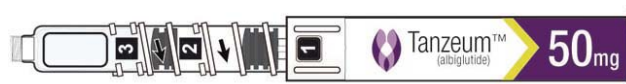
#### Before you Begin: Wash Your Hands, Gather and Inspect Your Supplies

- Wash your hands.
- Take a pen and new needle out of the box and check the label on your pen to make sure it is your prescribed dose of medicine.

- Gather a **clean, empty cup** to hold the pen while the medicine mixes, a **clock timer** to measure the time while the medicine mixes, and a large **sharps container** for pen disposal. See “**Disposing of Your Used Pens and Needles**” at the end of these instructions.



#### Tanzeum™ 50mg Disposable Pen



This TANZEUM 50 mg pen needs **30 minutes** to let the medicine powder and water mix in Step A. This is different from the TANZEUM 30 mg pen you may have used before.

#### Clean, Empty Cup



#### Clock Timer



#### Large Sharps Container



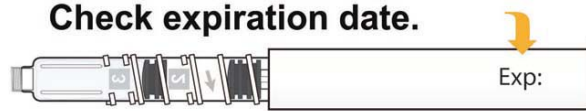
## STEP A

### Inspect Your Pen and Mix Your Medicine

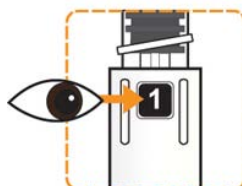
#### Inspect Your Pen

- Make sure that you have all of the supplies listed above (pen, needle, cup, timer, sharps container).
- Check the expiration date on the pen. **Do not** use if expired.

#### Check expiration date.



- Check that the pen has a **[1]** in the number window. **Do not** use if the **[1]** is not showing.



### Twist Pen to Mix Your Medicine

- Hold the pen body with the clear cartridge pointing up so that you **see the [1] in the window**.
- With your other hand, twist the clear cartridge several times in the direction of the arrow (clockwise) until you feel and hear the pen “click” into place and you **see the [2] in the number window**. This will mix the medicine powder and liquid in the clear cartridge.



- Slowly and gently rock the pen side to side (like a windshield wiper) **5 times** to mix the medicine. **Do not** shake the pen hard to avoid foaming; it may affect your dose.



### Wait for Medicine to Dissolve

- Place the pen into the clean, empty cup to keep the clear cartridge pointing up.
- **Set the clock timer for 30 minutes.**



You must wait 30 minutes for the medicine to dissolve before continuing to Step B.



## STEP B

### Attach the Needle and Prepare the Pen for Injection

After the 30 minute wait, wash your hands and finish the rest of the steps right away.

### Inspect Your Dissolved Medicine

- Again, slowly and gently rock the pen side to side (like a windshield wiper) **5 times** to mix the medicine again. **Do not** shake the pen hard to avoid foaming; it may affect your dose.



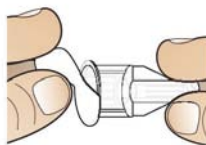
- Look through the viewing window to check that the liquid in the cartridge is clear and free of solid particles.



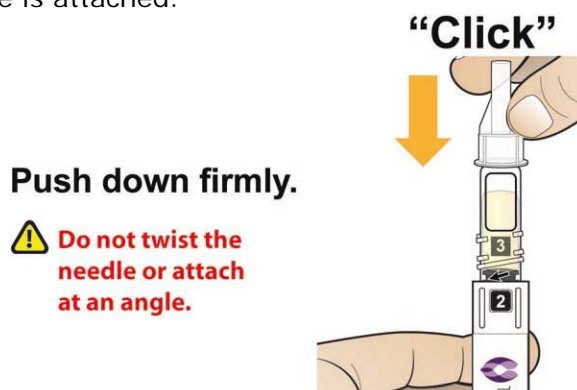
- The liquid will have a yellow color and there will be **large air bubbles** on top of the liquid.

### Attach the Needle

- Peel the tab from the outer needle cap.



- Hold the pen with the clear cartridge pointing up and push the needle straight down onto the clear cartridge until you hear a “click” and feel the needle “snap” down into place. This means the needle is attached.



### Tap for Air Bubbles

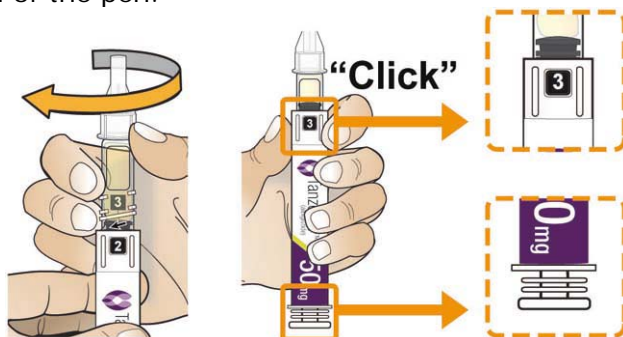
- With the needle point up, gently tap the clear cartridge **2 to 3** times to bring large air bubbles to the top.



**Small bubbles are okay and do not need to rise to the top.**

### Twist Pen to Prime the Needle

- Twist the clear cartridge several times in the direction of the arrow (clockwise) until you feel and hear the pen “click” and you **see the [3] in the number window**. This removes the large air bubbles from the clear cartridge. The injection button will also pop out from the bottom of the pen.

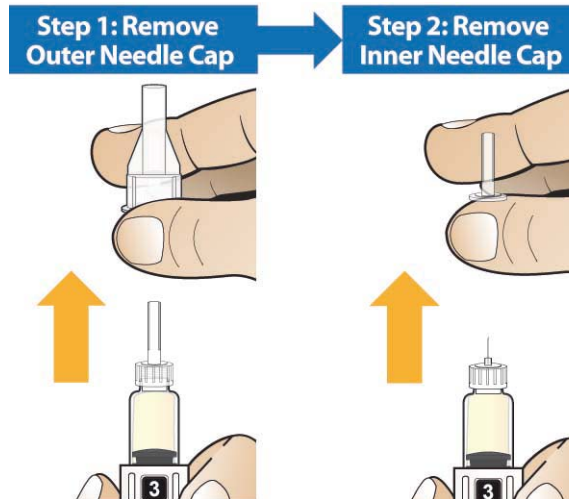


## STEP C

### Remove Both Needle Caps and Inject Your Medicine

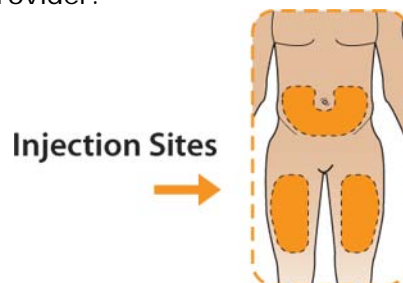
#### Remove Needle Caps

- Carefully remove the outer needle cap, then the inner needle cap. **A few drops of liquid may come out of the needle. This is normal.**



#### Inject the Medicine

- Insert the needle into the skin on your abdomen, thigh, or upper arm and inject as shown to you by your healthcare provider.



- With your thumb, press the injection button slowly and steadily to inject your medicine. The slower you press the button, the less pressure you will feel.

- Keep the injection button pressed down until you hear a “click”. **After hearing the click, continue holding your thumb down on the button and then slowly count to 5 to deliver the full dose of the medicine.**



**⚠ Inject slowly and steadily. After hearing the “click”, count to 5 to deliver the full dose.**

- After hearing the “click” and then slowly counting to 5, pull the needle out of your skin.

### **Disposing of Your Used Pens and Needles**

- **Do not** recap the needle or remove needle from the pen.
- Put your used needles and pens in a FDA-cleared sharps disposal container right away after use. **Do not throw away (dispose of) loose needles and pens in your household trash.**



## General Information About the Safe and Effective Use of TANZEUM

- Take **1** time each week. You can take your medicine at any time of day, with or without meals.
- **Your healthcare provider will teach you how to mix and inject TANZEUM before you use it for the first time.** If you have questions or do not understand the **Instructions for Use**, talk to your healthcare provider.
- **Use TANZEUM exactly as your healthcare provider tells you. Do not** change your dose or stop TANZEUM without talking to your healthcare provider.
- **Change (rotate) your injection site with each injection (weekly).**
- TANZEUM is injected under the skin (subcutaneously) in your stomach area (abdomen), upper leg (thigh), or upper arm.
- **Do not** inject TANZEUM into a vein or muscle.
- If you use TANZEUM with insulin, you should inject your TANZEUM and insulin separately. **Do not mix insulin and TANZEUM together.** You can inject TANZEUM and insulin in the same body area (for example, your stomach area), but you should not give the injections right next to each other.
- Keep pens and needles out of the reach of children.
- Always use a new needle for each injection.
- Do not share pens or needles.

## Frequently Asked Questions

### Medicine Dosing

#### What if I need to take my medicine on a different day of the week?

- You may take your next dose of medicine on a different day as long as it has been at least **4** days since your last dose.

#### What if I forget to take the medicine on the day I am supposed to?

- Take your missed dose of medicine within **3** days after your scheduled day, then return to your scheduled day for your next dose. If more than **3** days have passed since your usual scheduled day, wait until your next regularly scheduled day to take the injection of TANZEUM.

### Storage

#### How should I store my medicine?

- Store your pens in the refrigerator between 36°F to 46°F (2°C to 8°C).
- You may store your pen in the box at room temperature below 86°F (30°C) for up to **4** weeks before you are ready to use the pen.
- Store pens in the carton they came in.

- **Do not** freeze pens. If the liquid in the pen is frozen, throw away the pen and use another pen.

## **Number Window**

### **Are the Numbers 1, 2, and 3 used to select my dose of medicine?**

- No, you do not have to select your dose. The numbers are to help you prepare and give your medicine.

**Number 1:** Pen is ready to begin. Medicine powder and water are in separate compartments in the clear cartridge. If you don't see a number **1** in the window, throw away the pen.

**Number 2:** Medicine powder and water are mixed and then gently rocked. Wait **30** minutes, then attach needle.

**Number 3:** Large air bubbles are removed, the injection button pops out, and the pen is ready for injection.

### **What if I do not hear the “click” when the 2 or 3 are moved into the Number Window?**

- If you do not hear a “click” when **2 or 3** are moved into the number window, you may not have the number fully centered in the window. Twist the clear cartridge slightly in the direction of the arrow to complete the “click” and center the number in the window. Do not turn the clear cartridge in the opposite direction from the arrows.

## **Step A: Inspect Your Pen and Mix Your Medicine**

### **What if I do not wait 30 minutes after turning the pen to the Number 2?**

- If you do not wait the full **30** minutes the medicine may not be mixed with the water the right way. This can result in particles floating in the clear cartridge, not getting your full dose, or blocked needle. Waiting the full **30** minutes ensures that the medicine powder and water are mixed the right way, even though it may look like it is mixed sooner than that.

### **What if I leave my pen for more than 30 minutes after turning the pen to the Number 2 in Step A?**

- As long as the needle has not been attached, the pen can be used for up to **8** hours from the time **Step A** was started. If it has been more than **8** hours since the medicine was mixed in **Step A**, throw away the pen and use another pen.
- If you have attached the needle, TANZEUM should be used right away.

## **Step B: Attach the Needle and Prepare Pen for Injection**

**What if I leave my pen with the needle attached at Step B, and come back later to finish Step C?**

- This can cause your needle to block, you should continue from **Step B** to **Step C** right away.

**What if I do not attach the needle at Step B?**

- If the needle is attached at **Step A**, some of the medicine may be lost during mixing. Throw away the pen and use another pen.
- If the needle is not attached in **Step B**, and you go to **Step C** to turn the pen from Position **2 to 3**, this can damage the pen.

## **Step C: Remove Both Needle Caps and Inject Your Medicine**

**After I turn the pen to Number 3 (Step C), there are still some small air bubbles remaining. Can I still use the pen?**

- Seeing small air bubbles remaining is normal and you can still use the pen.

**After I give my medicine, there is some liquid still seen in the clear cartridge.**

- This is normal. If you have heard and felt the injection button “click” and slowly counted to **5** before pulling the needle out of your skin, you should have received the full dose of your medicine.

**How should I dispose of the pen?**

- **Do not** recap the needle or remove needle from the pen.
- Put your used needles and pens in a FDA-cleared sharps disposal container right away after use. **Do not throw away (dispose of) loose needles and pens in your household trash.**
- If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:
  - made of a heavy-duty plastic,
  - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
  - upright and stable during use,
  - leak-resistant, and
  - properly labeled to warn of hazardous waste inside the container.
- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and pens. For more information about safe sharps disposal, and for specific information

about sharps disposal in the state that you live in, go to the FDA's website at:

<http://www.fda.gov/safesharpsdisposal>.

- **Do not** dispose of your used sharps disposal container in your household trash unless your community guidelines permit this. **Do not** recycle your used sharps disposal container.



**Please make sure you are using the right dose.  
These instructions are for the 50 mg dose.**

This Instructions for Use has been approved by the U.S. Food and Drug Administration.

Approved: April 2014

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