

## 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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1 **FULL PRESCRIBING INFORMATION**

2 **WARNING: RISK OF THYROID C-CELL TUMORS**

- 3 • **Thyroid C-cell tumors have been observed in rodent studies with glucagon-like**  
4 **peptide-1 (GLP-1) receptor agonists at clinically relevant exposures. It is**  
5 **unknown whether TANZEUM™ causes thyroid C-cell tumors, including**  
6 **medullary thyroid carcinoma (MTC), in humans [see Warnings and Precautions**  
7 **(5.1)].**
- 8 • **TANZEUM is contraindicated in patients with a personal or family history of**  
9 **MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN**  
10 **2). Routine serum calcitonin or thyroid ultrasound monitoring is of uncertain**  
11 **value in patients treated with TANZEUM. Patients should be counseled**  
12 **regarding the risk and symptoms of thyroid tumors [see Contraindications (4.1),**  
13 **Warnings and Precautions (5.1)].**

14 **1 INDICATIONS AND USAGE**

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

17 **Limitations of Use:**

- 18 • TANZEUM is not recommended as first-line therapy for patients inadequately  
19 controlled on diet and exercise [see *Warnings and Precautions (5.1)*].
- 20 • TANZEUM has not been studied in patients with a history of pancreatitis [see  
21 *Warnings and Precautions (5.2)*]. Consider other antidiabetic therapies in patients with  
22 a history of pancreatitis.
- 23 • TANZEUM is not indicated in the treatment of patients with type 1 diabetes mellitus  
24 or for the treatment of patients with diabetic ketoacidosis. TANZEUM is not a  
25 substitute for insulin in these patients.
- 26 • TANZEUM has not been studied in patients with severe gastrointestinal disease,  
27 including severe gastroparesis. The use of TANZEUM is not recommended in  
28 patients with pre-existing severe gastrointestinal disease [see *Adverse Reactions*  
29 *(6.1)*].
- 30 • TANZEUM has not been studied in combination with prandial insulin.

31 **2 DOSAGE AND ADMINISTRATION**

32 **2.1 Dosage**

33 The recommended dosage of TANZEUM is 30 mg once weekly given as a subcutaneous  
34 injection in the abdomen, thigh, or upper arm region. The dosage may be increased to  
35 50 mg once weekly if the glycemic response is inadequate.

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

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

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

## 44 **2.2 Concomitant Use with an Insulin Secretagogue (e.g., Sulfonylurea) or** 45 **with Insulin**

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

## 49 **2.3 Dosage in Patients with Renal Impairment**

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

## 55 **2.4 Reconstitution of the Lyophilized Powder**

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

### 60 **Pen Reconstitution**

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

### 71 **Preparing Pen for Injection**

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

- 74 f) Visually inspect the reconstituted solution in the viewing window for particulate  
75 matter. The reconstituted solution will be yellow in color. After reconstitution, use  
76 TANZEUM within 8 hours.
- 77 g) Holding the Pen upright, attach the needle to the Pen. Gently tap the clear cartridge to  
78 bring large bubbles to the top.
- 79 See *Dosage and Administration (2.5)* for important administration instructions, including  
80 the injection procedure.

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

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

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

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

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

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

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

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

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

105 • For 50-mg Pen: Complete dissolution usually occurs within 7 minutes  
106 but may take up to 10 minutes.

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

109 **2.5 Important Administration Instructions**

110 Instruct patients as follows:

- 111 • The pen should be used within 8 hours of reconstitution prior to attaching the needle.
- 112 • After attaching the supplied needle, remove air bubbles by slowly twisting the Pen
- 113 until you see the [3] in the number window. At the same time, the injection button
- 114 will be automatically released from the bottom of the Pen.
- 115 • Use immediately after the needle is attached and primed. The product can clog the
- 116 needle if allowed to dry in the primed needle.
- 117 • After subcutaneously inserting the needle into the skin in the abdomen, thigh, or
- 118 upper arm region, press the injection button. Hold the injection button until you hear a
- 119 “click” and then hold the button for 5 additional seconds to deliver the full dose.

120 When using TANZEUM with insulin, instruct patients to administer as separate  
121 injections and to never mix the products. It is acceptable to inject TANZEUM and insulin  
122 in the same body region but the injections should not be adjacent to each other.

123 When injecting in the same body region, advise patients to use a different injection site  
124 each week. TANZEUM must not be administered intravenously or intramuscularly.

### 125 **3 DOSAGE FORMS AND STRENGTHS**

126 TANZEUM is supplied as follows:

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

### 131 **4 CONTRAINDICATIONS**

#### 132 **4.1 Medullary Thyroid Carcinoma**

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

#### 136 **4.2 Hypersensitivity**

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

### 139 **5 WARNINGS AND PRECAUTIONS**

#### 140 **5.1 Risk of Thyroid C-cell Tumors**

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

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

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

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

156 Elevated serum calcitonin is a biological marker of MTC. Patients with MTC usually  
157 have calcitonin values >50 ng/L. Patients with thyroid nodules noted on physical  
158 examination or neck imaging should be referred to an endocrinologist for further  
159 evaluation. Routine monitoring of serum calcitonin or using thyroid ultrasound is of  
160 uncertain value for early detection of MTC in patients treated with TANZEUM. Such  
161 monitoring may increase the risk of unnecessary procedures, due to the low specificity of  
162 serum calcitonin testing for MTC and a high background incidence of thyroid disease. If  
163 serum calcitonin is measured and found to be elevated, the patient should be referred to  
164 an endocrinologist for further evaluation.

## 165 **5.2 Acute Pancreatitis**

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

167 Across 8 Phase III clinical trials [see *Clinical Studies (14)*], pancreatitis adjudicated as  
168 likely related to therapy occurred more frequently in patients receiving TANZEUM (6 of  
169 2,365 [0.3%]) than in patients receiving placebo (0 of 468 [0%]) or active comparators (2  
170 of 2,065 [0.1%]).

171 After initiation of TANZEUM, observe patients carefully for signs and symptoms of  
172 pancreatitis (including persistent severe abdominal pain, sometimes radiating to the back  
173 and which may or may not be accompanied by vomiting). If pancreatitis is suspected,  
174 promptly discontinue TANZEUM. If pancreatitis is confirmed, TANZEUM should not be  
175 restarted.

176 TANZEUM has not been studied in patients with a history of pancreatitis to determine  
177 whether these patients are at increased risk for pancreatitis. Consider other antidiabetic  
178 therapies in patients with a history of pancreatitis.

## 179 **5.3 Hypoglycemia with Concomitant Use of Insulin Secretagogues or** 180 **Insulin**

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

## 185 **5.4 Hypersensitivity Reactions**

186 Across 8 Phase III clinical trials [*see Clinical Studies (14)*], a serious hypersensitivity  
187 reaction with pruritus, rash, and dyspnea occurred in a patient treated with TANZEUM. If  
188 hypersensitivity reactions occur, discontinue use of TANZEUM; treat promptly per  
189 standard of care and monitor until signs and symptoms resolve [*see Contraindications*  
190 (4.2)].

## 191 **5.5 Renal Impairment**

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

## 202 **5.6 Macrovascular Outcomes**

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

## 205 **6 ADVERSE REACTIONS**

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

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

### 213 **6.1 Clinical Trials Experience**

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

#### 217 Pool of Placebo-Controlled Trials

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

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

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

233

234 **Table 1. Adverse Reactions in Placebo-controlled Trials Reported in ≥5% of**  
235 **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

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

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

240

#### 241 *Gastrointestinal Adverse Reactions*

242 In the pool of placebo-controlled trials, gastrointestinal complaints occurred more  
243 frequently among patients receiving TANZEUM (39%) than patients receiving placebo  
244 (33%). In addition to diarrhea and nausea (see Table 1), the following gastrointestinal  
245 adverse reactions also occurred more frequently in patients receiving TANZEUM:  
246 vomiting (2.6% versus 4.2% for placebo versus TANZEUM), gastroesophageal reflux  
247 disease (1.9% versus 3.5% for placebo versus TANZEUM), and dyspepsia (2.8% versus  
248 3.4% for placebo versus TANZEUM). Constipation also contributed to the frequently  
249 reported reactions. In the group treated with TANZEUM, investigators graded the  
250 severity of GI reactions as “mild” in 56% of cases, “moderate” in 37% of cases, and  
251 “severe” in 7% of cases. Discontinuation due to GI adverse reactions occurred in 2% of  
252 individuals on TANZEUM or placebo.

## 253 *Injection Site Reactions*

254 In the pool of placebo-controlled trials, injection site reactions occurred more frequently  
255 on TANZEUM (18%) than on placebo (8%). In addition to the term injection site  
256 reaction (see Table 1), the following other types of injection site reactions also occurred  
257 more frequently on TANZEUM: injection site hematoma (1.9% versus 2.1% for placebo  
258 versus TANZEUM ), injection site erythema (0.4% versus, 1.7% for placebo versus  
259 TANZEUM), injection site rash (0% versus 1.4% for placebo versus TANZEUM),  
260 injection site hypersensitivity (0% versus 0.8% versus for placebo versus TANZEUM),  
261 and injection site hemorrhage (0.6% and 0.7% for placebo versus TANZEUM). Injection  
262 site pruritus also contributed to the frequently reported reactions. The majority of  
263 injections site reactions were judged as “mild” by investigators in both groups (73% for  
264 TANZEUM versus 94% for placebo). More patients on TANZEUM than on placebo:  
265 discontinued due to an injection site reaction (2% versus 0.2%), experienced more than 2  
266 reactions (38% versus 20%), had a reaction judged by investigators to be “moderate” or  
267 “severe” (27% versus 6%) and required local or systemic treatment for the reactions  
268 (36% versus 11%).

## 269 Pool of Placebo- and Active-controlled Trials

270 The occurrence of adverse reactions was also evaluated in a larger pool of patients with  
271 type 2 diabetes participating in 7 placebo- and active-controlled trials. These trials  
272 evaluated the use of TANZEUM as monotherapy, and as add-on therapy to oral  
273 antidiabetic agents, and as add-on therapy to basal insulin [*see Clinical Studies (14)*]. In  
274 this pool, a total of 2,116 patients with type 2 diabetes were treated with TANZEUM for  
275 a mean duration of 75 weeks. The mean age of patients treated with TANZEUM was  
276 55 years, 1.5% of the population in these studies was 75 years or older and 51% of  
277 participants were male. Forty-eight percent of patients were white, 15% African/African  
278 American, 9% Asian, and 26% were Hispanic/Latino. At baseline, the population had  
279 diabetes for an average of 8 years and had a mean HbA1c of 8.2%. At baseline, 21% of  
280 the population reported peripheral neuropathy and 5% reported retinopathy. Baseline  
281 estimated renal function was normal or mildly impaired (eGFR >60 mL/min/1.73 m<sup>2</sup>) in  
282 92% of the population and moderately impaired (eGFR 30 to 60 mL/min/1.73 m<sup>2</sup>) in 8%  
283 of the population.

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

## 286 Other Adverse Reactions

### 287 *Hypoglycemia*

288 The proportion of patients experiencing at least one documented symptomatic  
289 hypoglycemic episode on TANZEUM and the proportion of patients experiencing at least  
290 one severe hypoglycemic episode on TANZEUM in clinical trials [*see Clinical Studies*  
291 (14)] is shown in Table 2. Hypoglycemia was more frequent when TANZEUM was  
292 added to sulfonylurea or insulin [*see Warnings and Precautions (5.3)*].  
293

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 ≤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

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

### 352 *Gamma Glutamyltransferase (GGT) Increase*

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

### 356 *Heart Rate Increase*

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

## 361 **7 DRUG INTERACTIONS**

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

## 368 **8 USE IN SPECIFIC POPULATIONS**

### 369 **8.1 Pregnancy**

#### 370 Pregnancy Category C

371 There are no adequate and well-controlled studies of TANZEUM in pregnant women.  
372 Nonclinical studies have shown reproductive toxicity, but not teratogenicity, in mice  
373 treated with albiglutide at up to 39 times human exposure resulting from the maximum  
374 recommended dose of 50 mg/week, based on AUC [*see Nonclinical Toxicology (13.1,*  
375 *13.3)*]. TANZEUM should not be used during pregnancy unless the expected benefit  
376 outweighs the potential risks.

377 Due to the long washout period for TANZEUM, consider stopping TANZEUM at least  
378 1 month before a planned pregnancy.

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

382 **8.3 Nursing Mothers**

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

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

390 **8.4 Pediatric Use**

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

393 **8.5 Geriatric Use**

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

399 **8.6 Renal Impairment**

400 Of the total number of patients (N = 2,365) in 8 Phase III clinical trials who received  
401 TANZEUM, 54% (N = 1,267) had mild renal impairment (eGFR 60 to  
402 89 mL/min/1.73 m<sup>2</sup>), 12% (N = 275) had moderate renal impairment (eGFR 30 to  
403 59 mL/min/1.73 m<sup>2</sup>) and 1% (N = 19) had severe renal impairment (eGFR 15 to  
404 <30 mL/min/1.73 m<sup>2</sup>).

405 No dosage adjustment is required in patients with mild (eGFR 60 to 89 mL/min/1.73 m<sup>2</sup>),  
406 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>)  
407 renal impairment.

408 Efficacy of TANZEUM in patients with type 2 diabetes and renal impairment is  
409 described elsewhere [*see Clinical Studies (14.3)*]. There is limited clinical experience in  
410 patients with severe renal impairment (19 subjects). The frequency of GI events increased  
411 as renal function declined. For patients with mild, moderate, or severe impairment, the  
412 respective event rates were: diarrhea (6%, 13%, 21%), nausea (3%, 5%, 16%), and  
413 vomiting (1%, 2%, 5%). Therefore, caution is recommended when initiating or escalating  
414 doses of TANZEUM in patients with renal impairment [*see Dosage and Administration*  
415 (2.3), *Warnings and Precautions (5.5)*, *Clinical Pharmacology (12.3)*].

416 **10 OVERDOSAGE**

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

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

## 423 **11 DESCRIPTION**

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

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

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

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

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

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

## 444 **12 CLINICAL PHARMACOLOGY**

### 445 **12.1 Mechanism of Action**

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

### 448 **12.2 Pharmacodynamics**

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

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

457 Gastric Motility

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

461 Cardiac Electrophysiology

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

464 **12.3 Pharmacokinetics**

465 Absorption

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

476 Distribution

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

480 Metabolism

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

486 Elimination

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

489 Specific Patient Populations

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

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

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

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

### 503 Drug Interactions

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

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

516

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)
			<b>No dose adjustments of co-administered drug required for the following:</b>		
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).

### 540 **13.3 Reproductive and Developmental Toxicity**

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

544 In pregnant mice given SC doses of 1, 5, or 50 mg/kg/day from gestation Day 1 to 6,  
545 there were no adverse effects on early embryonic development through implantation at  
546 50 mg/kg/day (39 times clinical exposure based on AUC).

547 In pregnant mice given SC doses of 1, 5, or 50 mg/kg/day from gestation Day 6 through  
548 15 (organogenesis), embryo-fetal lethality (post-implantation loss) and bent (wavy) ribs  
549 were observed at 50 mg/kg/day (39 times clinical exposure based on AUC), a dose  
550 associated with maternal toxicity (body weight loss and reduced food consumption).

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

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

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

## 571 **14 CLINICAL STUDIES**

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

577 Trials evaluated the use of TANZEUM 30 mg and 50 mg. Five of the 8 trials allowed  
578 optional uptitration of TANZEUM from 30 mg to 50 mg if glycemic response with  
579 30 mg was inadequate.

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

#### 584 **14.1 Monotherapy**

585 The efficacy of TANZEUM as monotherapy was evaluated in a 52-week, randomized,  
586 double-blind, placebo-controlled, multicenter trial. In this trial, 296 patients with type 2  
587 diabetes inadequately controlled on diet and exercise were randomized (1:1:1) to  
588 TANZEUM 30 mg SC once weekly, TANZEUM 30 mg SC once weekly uptitrated to  
589 50 mg once weekly at Week 12, or placebo. The mean age of participants was 53 years,  
590 55% of patients were men, the mean duration of diabetes was 4 years, and the mean  
591 baseline eGFR was 84 mL/min/1.73 m<sup>2</sup>. Primary and secondary efficacy results are  
592 presented in Table 4. Figure 1 shows the mean adjusted changes in HbA1c from baseline  
593 across study visits.

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

598

599 **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>

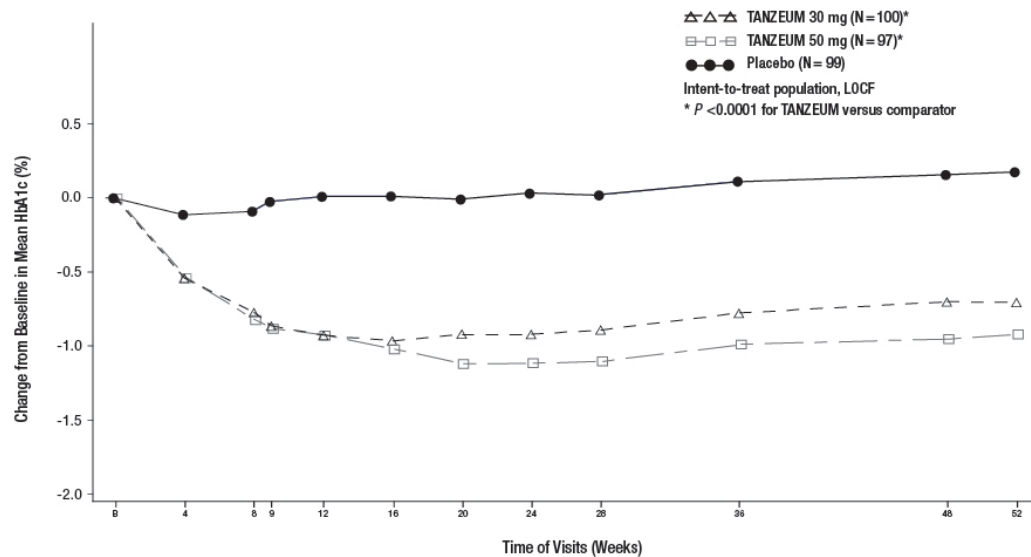
600 <sup>a</sup> Intent-to-treat population. Last observation carried forward (LOCF) was used to  
601 impute missing data. Data post-onset of rescue therapy are treated as missing. At  
602 Week 52, primary efficacy data was imputed for 63%, 34%, and 41% of individuals  
603 randomized to placebo, TANZEUM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

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

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

606

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



609  
610

## 611 14.2 Combination Therapy

### 612 Add-on to Metformin

613 The efficacy of TANZEUM was evaluated in a 104-week randomized, double-blind,  
614 multicenter trial in 999 patients with type 2 diabetes mellitus inadequately controlled on  
615 background metformin therapy ( $\geq 1,500$  mg daily). In this trial, TANZEUM 30 mg SC  
616 weekly (with optional uptitration to 50 mg weekly after a minimum of 4 weeks) was  
617 compared with placebo, sitagliptin 100 mg daily, or glimepiride 2 mg daily (with optional  
618 titration to 4 mg daily). The mean age of participants was 55 years, 48% of patients were  
619 men, the mean duration of type 2 diabetes was 6 years, and the mean baseline eGFR was  
620 86 mL/min/1.73 m<sup>2</sup>. Results of the primary and secondary analyses are presented in  
621 Table 5. Figure 2 shows the mean adjusted changes in HbA1c across study visits.

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

626

627 **Table 5. Results at Week 104 (LOCF<sup>a</sup>) in a Trial Comparing TANZEUM with**  
628 **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>			

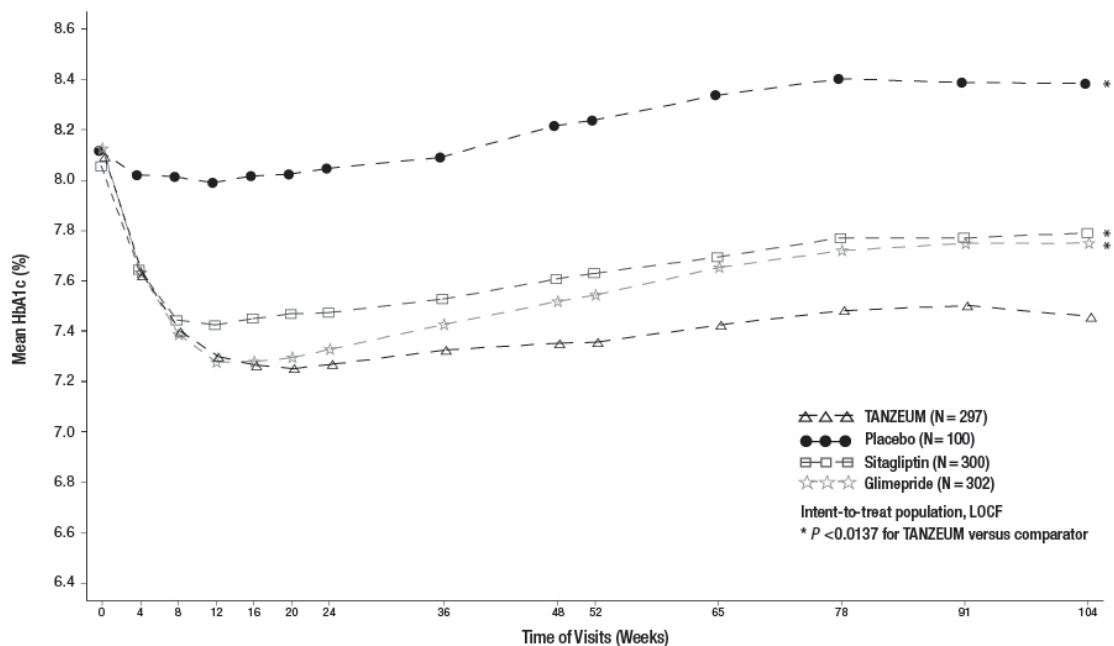
629 <sup>a</sup> Intent-to-treat population. Last observation carried forward (LOCF) was used to  
630 impute missing data. Data post-onset of rescue therapy are treated as missing. At  
631 Week 104, primary efficacy data was imputed for 76%, 46%, 55%, and 51% of  
632 individuals randomized to placebo,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

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

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

636

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



640

641

#### 642 Add-on to Pioglitazone

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

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

654

655 **Table 6. Results at Week 52 (LOCF<sup>a</sup>) in a Trial Comparing TANZEUM with**  
656 **Placebo as Add-on Therapy in Patients Inadequately Controlled on Pioglitazone**  
657 **(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>	

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

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

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

664

#### 665 Add-on to Metformin Plus Sulfonylurea

666 The efficacy of TANZEUM was evaluated in a 52-week randomized, double-blind,  
667 multicenter trial in 657 patients with type 2 diabetes mellitus inadequately controlled on  
668 metformin (≥1,500 mg daily) and glimepiride (4 mg daily). Patients were randomized to  
669 receive TANZEUM 30 mg SC weekly (with optional uptitration to 50 mg weekly after a  
670 minimum of 4 weeks), placebo, or pioglitazone 30 mg daily (with optional titration to  
671 45 mg/day). The mean age of participants was 55 years, 53% of patients were men, the  
672 mean duration of type 2 diabetes was 9 years, and the mean baseline eGFR was  
673 84 mL/min/1.73 m<sup>2</sup>. Results of the primary and main secondary analyses are presented in  
674 Table 7.

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

682

683 **Table 7. Results at Week 52 (LOCF<sup>a</sup>) in a Trial Comparing TANZEUM with**  
684 **Placebo as Add-on Therapy in Patients Inadequately Controlled on Metformin Plus**  
685 **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>		

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

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

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

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

693

694 **Combination Therapy: Active-controlled Trial versus Liraglutide**

695 The efficacy of TANZEUM was evaluated in a 32-week, randomized, open-label,  
696 liraglutide-controlled, non-inferiority trial in 805 patients with type 2 diabetes mellitus  
697 inadequately controlled on monotherapy or combination oral antidiabetic therapy  
698 (metformin, thiazolidinedione, sulfonylurea, or a combination of these). Patients were  
699 randomized to TANZEUM 30 mg SC weekly (with uptitration to 50 mg weekly at  
700 Week 6) or liraglutide 1.8 mg daily (titrated up from 0.6 mg at Week 1, and 1.2 mg at  
701 Week 1 to Week 2). The mean age of participants was 56 years, 50% of patients were  
702 men, the mean duration of type 2 diabetes was 8 years, and the mean baseline eGFR was  
703 95 mL/min/1.73 m<sup>2</sup>. Results of the primary and main secondary analyses are presented in  
704 Table 8.

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

709

710 **Table 8. Results of Controlled Trial of TANZEUM versus Liraglutide at Week 32**  
711 **(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>	

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

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

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

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

719

720 **Combination Therapy: Active-controlled Trial versus Basal Insulin**

721 The efficacy of TANZEUM was evaluated in a 52-week, randomized (2:1), open-label,  
722 insulin glargine-controlled, non-inferiority trial in 735 patients with type 2 diabetes  
723 mellitus inadequately controlled on metformin  $\geq$ 1,500 mg daily (with or without  
724 sulfonylurea). Patients were randomized to receive TANZEUM 30 mg SC weekly (with  
725 optional uptitration to 50 mg weekly) or insulin glargine (started at 10 units and titrated  
726 weekly per prescribing information). The primary endpoint was change in HbA1c from  
727 baseline compared with insulin glargine. The starting total daily dose of insulin glargine  
728 ranged between 2 and 40 units (median daily dose of 10 units) and ranged between 3 and  
729 230 units (median daily dose of 30 units) at Week 52. Seventy-seven percent of patients  
730 treated with TANZEUM were uptitrated to 50 mg SC weekly. The mean age of

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

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

739

740 **Table 9. Results at Week 52 (LOCF<sup>a</sup>) in a Trial Comparing TANZEUM with**  
741 **Insulin Glargine as Add-on Therapy in Patients Inadequately Controlled on**  
742 **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>	

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

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

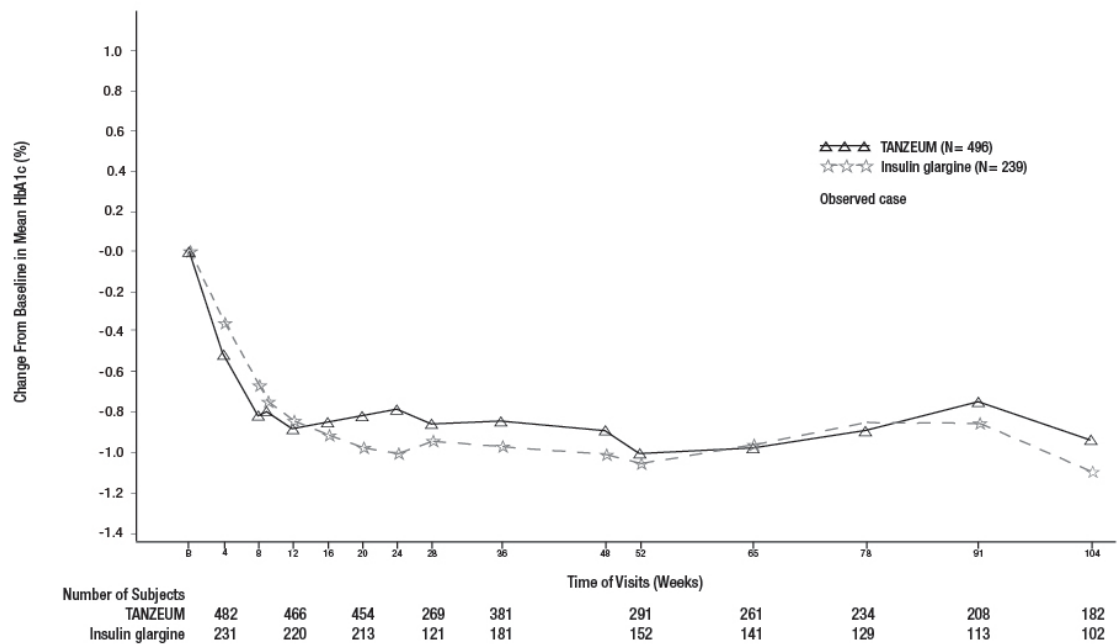
748 <sup>c</sup> Met non-inferiority margin of 0.3%.

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

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

751

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



755

756

757 **Combination Therapy: Active-controlled Trial versus Prandial Insulin**

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

771 The between-treatment difference of -0.2% with 95% confidence interval (-0.32%,  
 772 0.00%) between albiglutide and insulin lispro met the pre-specified non-inferiority  
 773 margin (0.4%). Treatment with TANZEUM resulted in a mean weight loss for  
 774 TANZEUM compared with a mean weight gain for insulin lispro, and the difference  
 775 between treatment groups was statistically significant (see Table 10).

776

777 **Table 10. Results at Week 26 (LOCF<sup>a</sup>) in a Trial Comparing TANZEUM with**  
 778 **Insulin Lispro as Add-On Therapy in Patients Inadequately Controlled on Insulin**  
 779 **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>	

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

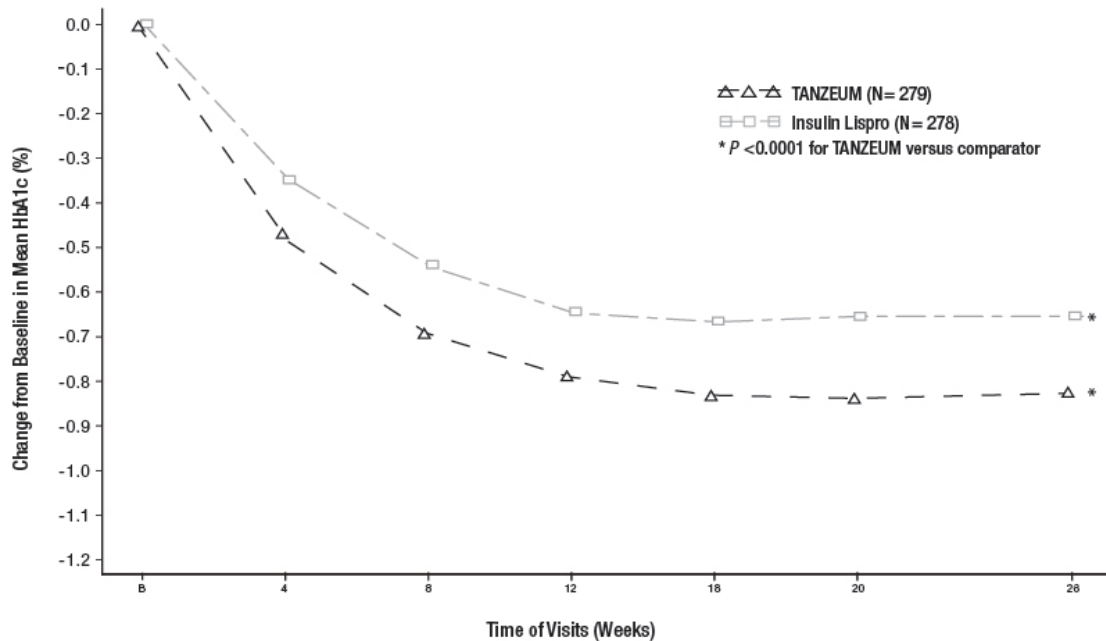
784 <sup>b</sup> Least squares mean adjusted for baseline value and stratification factors.

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

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

787

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



791

792

### 793 **14.3 Type 2 Diabetes Mellitus Patients with Renal Impairment**

794 The efficacy of TANZEUM was evaluated in a 26-week, randomized, double-blind,  
795 active-controlled trial in 486 patients with mild (n = 250), moderate (n = 200), and severe  
796 renal impairment (n = 36) inadequately controlled on a current regimen of diet and  
797 exercise or other antidiabetic therapy. Patients were randomized to receive TANZEUM  
798 30 mg SC weekly (with up titration to 50 mg weekly if needed as early as Week 4) or  
799 sitagliptin. Sitagliptin was dosed according to renal function (100 mg, 50 mg, and 25 mg  
800 daily in mild, moderate, and severe renal impairment, respectively). The mean age of  
801 participants was 63 years, 54% of patients were men, the mean duration of type 2  
802 diabetes was 11 years, and the mean baseline eGFR was 60 mL/min/1.73 m<sup>2</sup>.

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

806

807 **Table 11. Results at Week 26 (LOCF<sup>a</sup>) in a Trial Comparing TANZEUM with**  
808 **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>	

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

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

814 <sup>c</sup> *P* <0.0003 for treatment difference.

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

816

## 817 **16 HOW SUPPLIED/STORAGE AND HANDLING**

### 818 **16.1 How Supplied**

819 TANZEUM is available in the following strengths and package sizes:

820 30 mg single-dose Pen:

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

823 50 mg single-dose Pen:

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

### 826 **16.2 Storage and Handling**

- 827 • Prior to dispensing: Store Pens in the refrigerator at 36°F to 46°F (2°C to 8°C). Pens  
828 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.

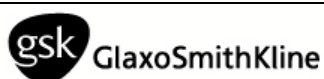
### What are the ingredients in TANZEUM?

**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



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

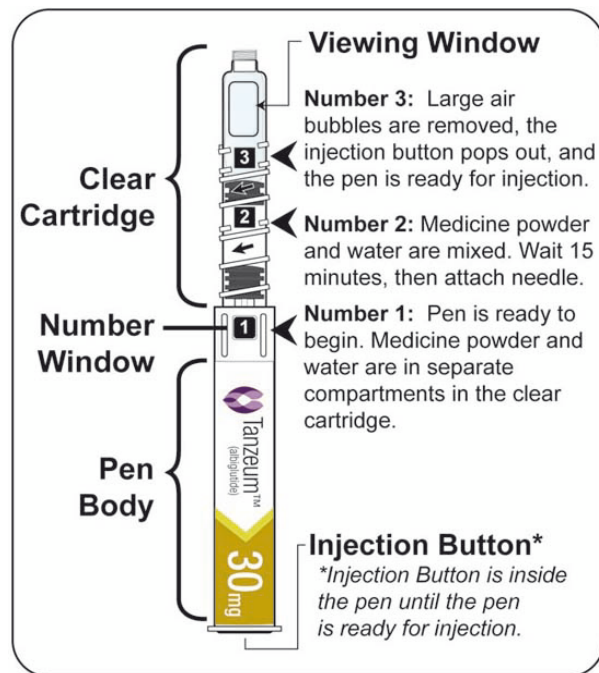
##### Use 1 Time Each Week

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.**

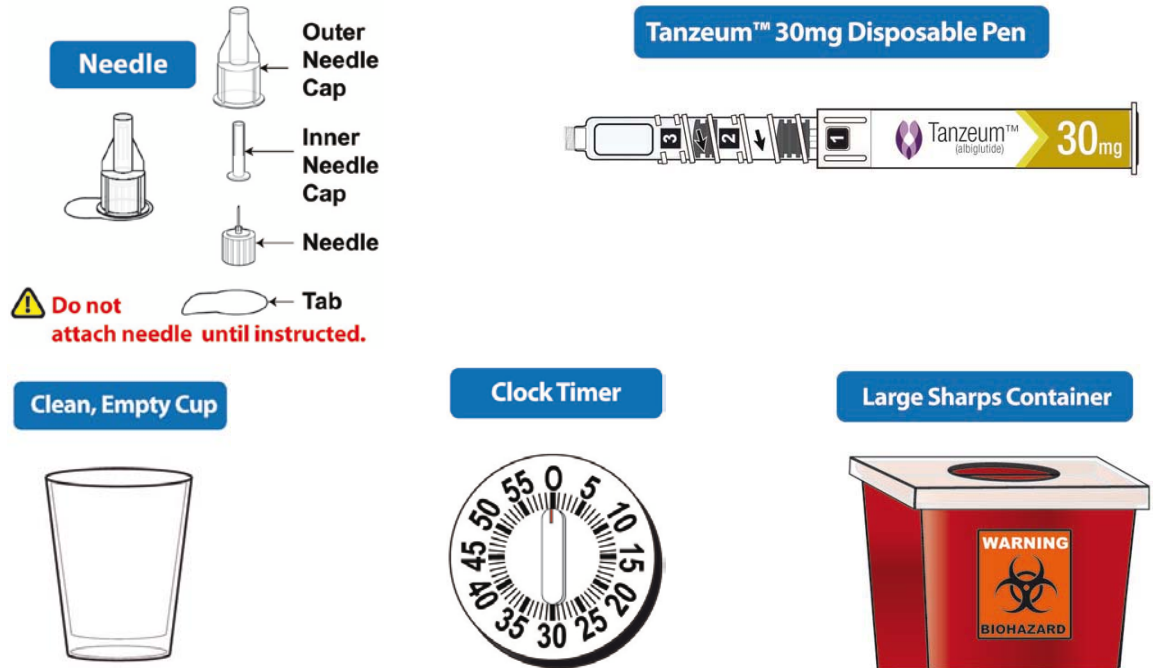
**If stored in refrigerator, allow to sit at room temperature for 15 minutes before starting Step A.**

**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.

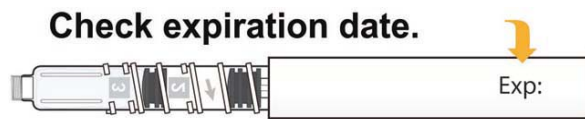


## STEP A

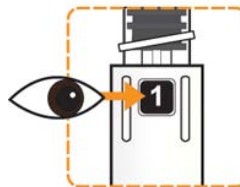
### Inspect Your Pen and Mix Your Medicine

#### 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.

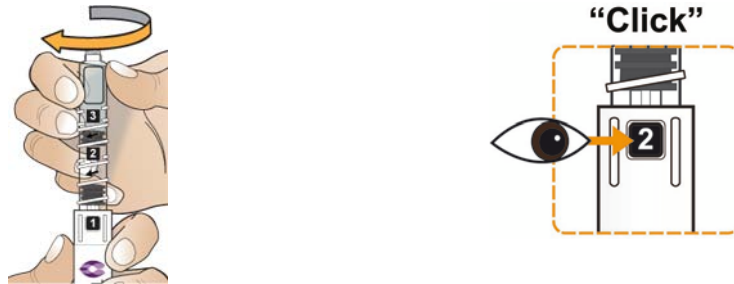


- Check that the pen has a **[1]** in the number window. **Do not** use if the **[1]** is not showing.



### 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

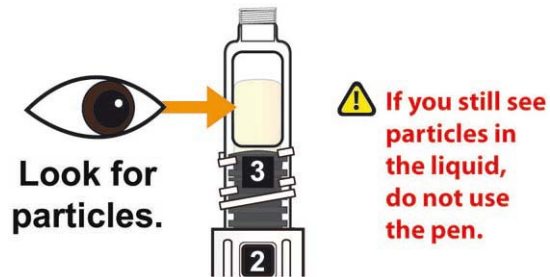
After the 15 minute wait, wash your hands and finish the rest of the steps right away.

#### 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.



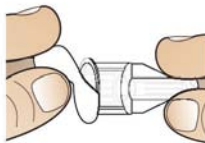
- Look through the viewing window to check that the liquid in the cartridge is clear and free of solid particles.



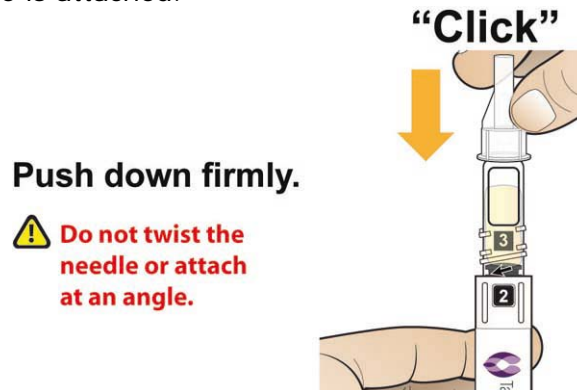
- The liquid will have a yellow color and there will be **large air bubbles** on top of the liquid.

#### 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

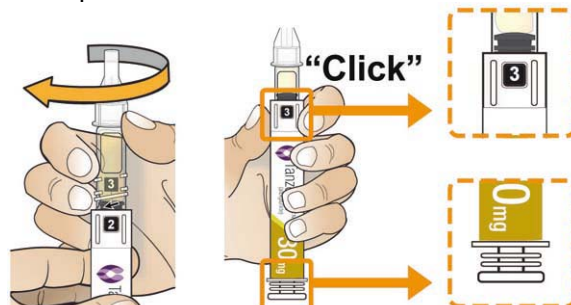
- With the needle point up, gently tap the clear cartridge **2 to 3** times to bring large air bubbles to the top.



**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.

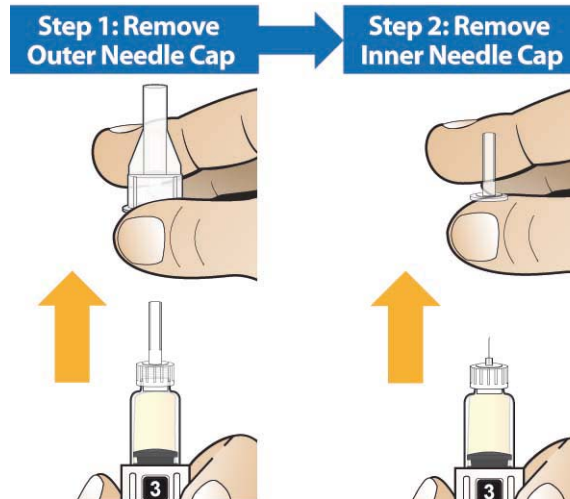


## STEP C

### Remove Both Needle Caps and Inject Your Medicine

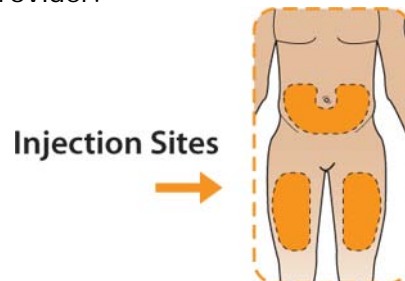
#### Remove Needle Caps

- 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.**

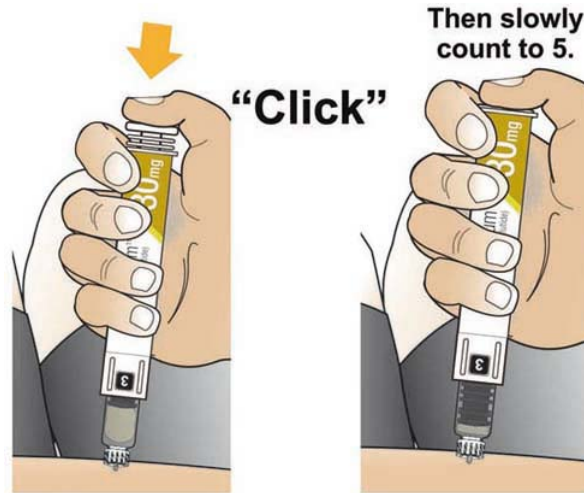


#### Inject the Medicine

- 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.**



**⚠ 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 **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

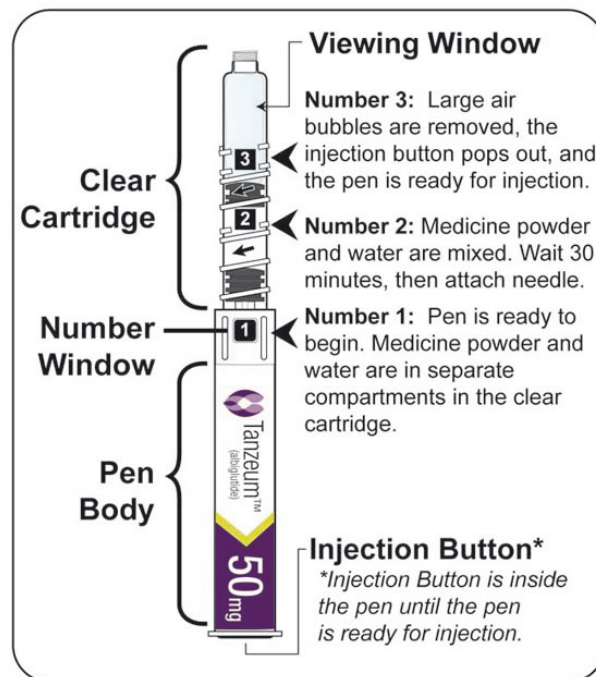
##### Use 1 Time Each Week

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.**

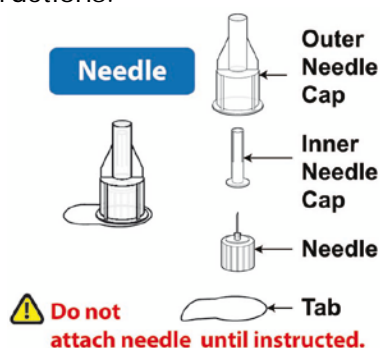
**If stored in refrigerator, allow to sit at room temperature for 15 minutes before starting Step A.**

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

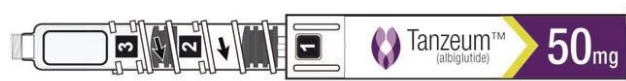
#### **Before you Begin: Wash Your Hands, Gather and Inspect Your Supplies**

- 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



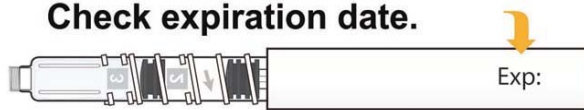
## STEP A

### Inspect Your Pen and Mix Your Medicine

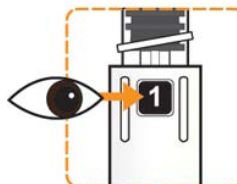
#### Inspect Your Pen

- 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.

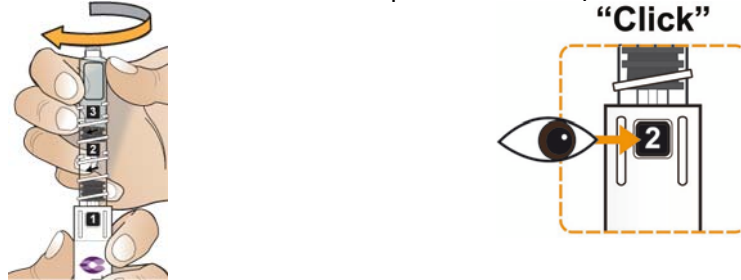


- Check that the pen has a **[1]** in the number window. **Do not** use if the **[1]** is not showing.



### 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.



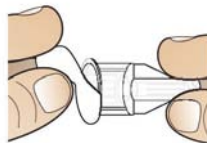
- Look through the viewing window to check that the liquid in the cartridge is clear and free of solid particles.



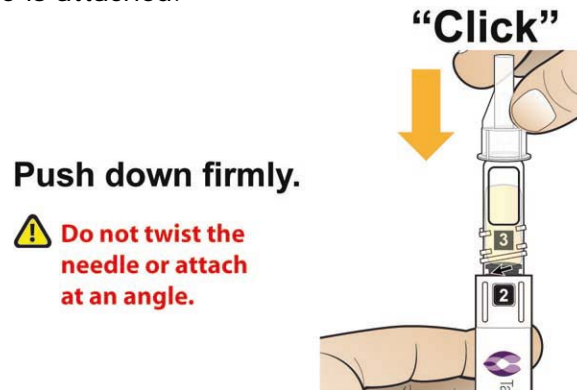
- The liquid will have a yellow color and there will be **large air bubbles** on top of the liquid.

#### 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

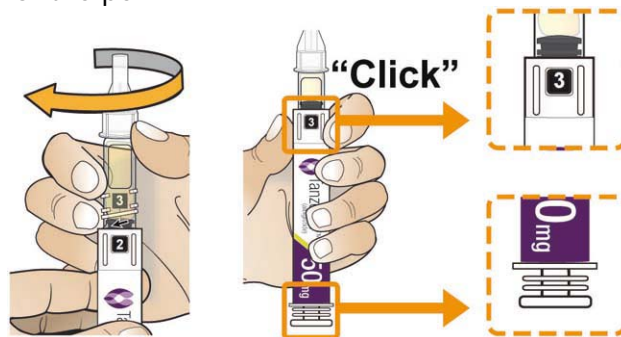
- With the needle point up, gently tap the clear cartridge **2 to 3** times to bring large air bubbles to the top.



**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.

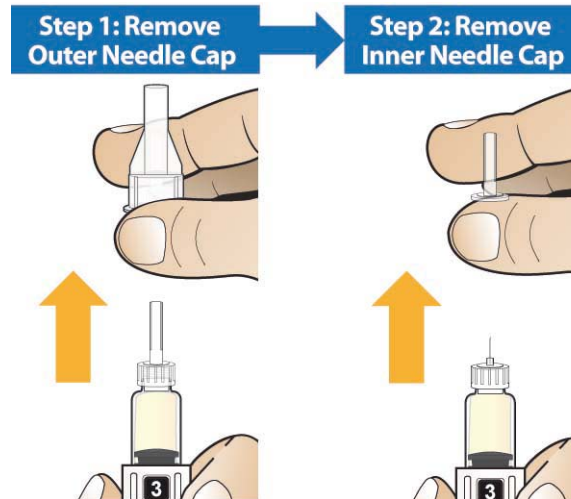


## STEP C

### Remove Both Needle Caps and Inject Your Medicine

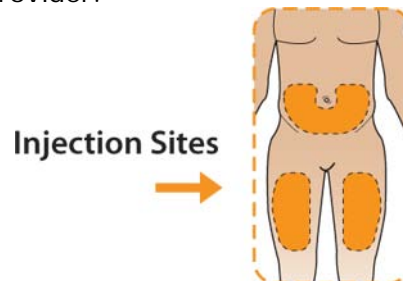
#### Remove Needle Caps

- 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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