

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.

- Carcinogenicity of albiglutide could not be assessed in rodents, but other glucagon-like peptide-1 (GLP-1) receptor agonists have caused thyroid C-cell tumors in rodents at clinically relevant exposures. Human relevance of GLP-1 receptor agonist induced C-cell tumors in rodents has not been determined. It is unknown whether TANZEUM causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans (5.1, 13.1).
- 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). Counsel patients regarding the potential risk of MTC and symptoms of thyroid tumors (4.1, 5.1).

RECENT MAJOR CHANGES

Boxed Warning	03/2015
Indications and Usage, Limitations of Use (1)	03/2015
Warnings and Precautions, Risk of Thyroid C-cell Tumors (5.1)	03/2015

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

- TANZEUM is contraindicated in patients with a personal or family history of medullary thyroid carcinoma or in patients with Multiple Endocrine Neoplasia syndrome type 2. (4.1)
- TANZEUM is contraindicated in patients with a prior serious hypersensitivity reaction to albiglutide or any of the product components. (4.2, 5.4)

WARNINGS AND PRECAUTIONS

- **Thyroid C-cell Tumors:** See Boxed Warning. (5.1)
- **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 $\geq 5\%$ of patients treated with TANZEUM and more frequently than in patients on placebo, were upper respiratory tract infection, diarrhea, nausea, injection site reaction, cough, back pain, arthralgia, sinusitis, and influenza. (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.

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: 05/2015

FULL PRESCRIBING INFORMATION: CONTENTS*

WARNING: RISK OF THYROID C-CELL TUMORS

1 INDICATIONS AND USAGE

2 DOSAGE AND ADMINISTRATION

- 2.1 Dosage
- 2.2 Concomitant Use with an Insulin Secretagogue (e.g., Sulfonylurea) or with Insulin
- 2.3 Dosage in Patients with Renal Impairment
- 2.4 Reconstitution of the Lyophilized Powder
- 2.5 Important Administration Instructions

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

- 4.1 Medullary Thyroid Carcinoma
- 4.2 Hypersensitivity

5 WARNINGS AND PRECAUTIONS

- 5.1 Risk of Thyroid C-cell Tumors
- 5.2 Acute Pancreatitis
- 5.3 Hypoglycemia with Concomitant Use of Insulin Secretagogues or Insulin
- 5.4 Hypersensitivity Reactions
- 5.5 Renal Impairment
- 5.6 Macrovascular Outcomes

6 ADVERSE REACTIONS

- 6.1 Clinical Trials Experience

7 DRUG INTERACTIONS

8 USE IN SPECIFIC POPULATIONS

- 8.1 Pregnancy
- 8.3 Nursing Mothers
- 8.4 Pediatric Use
- 8.5 Geriatric Use
- 8.6 Renal Impairment

10 OVERDOSAGE

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY

- 12.1 Mechanism of Action
- 12.2 Pharmacodynamics
- 12.3 Pharmacokinetics

13 NONCLINICAL TOXICOLOGY

- 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
- 13.3 Reproductive and Developmental Toxicity

14 CLINICAL STUDIES

- 14.1 Monotherapy
- 14.2 Combination Therapy
- 14.3 Type 2 Diabetes Mellitus Patients with Renal Impairment

16 HOW SUPPLIED/STORAGE AND HANDLING

- 16.1 How Supplied
- 16.2 Storage and Handling

17 PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the full prescribing information are not listed.



1 FULL PRESCRIBING INFORMATION

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

- 3 • **Carcinogenicity of albiglutide could not be assessed in rodents, but other glucagon-like peptide-1 (GLP-1) receptor agonists have caused thyroid C-cell tumors in rodents at clinically relevant exposures. Human relevance of GLP-1 receptor agonist induced C-cell tumors in rodents has not been determined. It is unknown whether TANZEUM™ causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans [see Warnings and Precautions (5.1), Nonclinical Toxicology (13.1)].**
- 4 • **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). Counsel patients regarding the potential risk of MTC with the use of TANZEUM and inform them of the symptoms of thyroid tumors (e.g., mass in the neck, dysphagia, dyspnea, persistent hoarseness). Routine monitoring of serum calcitonin or using thyroid ultrasound monitoring is of uncertain value for early detection of MTC in patients treated with TANZEUM [see Contraindications (4.1), Warnings and Precautions (5.1)].**

16 1 INDICATIONS AND USAGE

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

19 **Limitations of Use:**

- 20 • TANZEUM is not recommended as first-line therapy for patients inadequately controlled on
21 diet and exercise because of the uncertain relevance of the rodent C-cell tumor findings to
22 humans. Prescribe TANZEUM only to patients for whom the potential benefits are
23 considered to outweigh the potential risk [see Warnings and Precautions (5.1)].
- 24 • TANZEUM has not been studied in patients with a history of pancreatitis [see Warnings and
25 Precautions (5.2)]. Consider other antidiabetic therapies in patients with a history of
26 pancreatitis.
- 27 • TANZEUM is not indicated in the treatment of patients with type 1 diabetes mellitus or for
28 the treatment of patients with diabetic ketoacidosis. TANZEUM is not a substitute for insulin
29 in these patients.
- 30 • TANZEUM has not been studied in patients with severe gastrointestinal disease, including
31 severe gastroparesis. The use of TANZEUM is not recommended in patients with pre-
32 existing severe gastrointestinal disease [see Adverse Reactions (6.1)].
- 33 • TANZEUM has not been studied in combination with prandial insulin.

34 **2 DOSAGE AND ADMINISTRATION**

35 **2.1 Dosage**

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

39 TANZEUM may be administered at any time of day without regard to meals. Instruct patients to
40 administer TANZEUM once a week on the same day each week. The day of weekly
41 administration may be changed if necessary as long as the last dose was administered 4 or more
42 days before.

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

47 **2.2 Concomitant Use with an Insulin Secretagogue (e.g., Sulfonylurea) or with** 48 **Insulin**

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

52 **2.3 Dosage in Patients with Renal Impairment**

53 No dose adjustment is needed in patients with mild, moderate, or severe renal impairment (eGFR
54 15 to 89 mL/min/1.73 m²). Use caution when initiating or escalating doses of TANZEUM in
55 patients with renal impairment. Monitor renal function in patients with renal impairment
56 reporting severe adverse gastrointestinal reactions [*see Warnings and Precautions (5.5), Use in*
57 *Specific Populations (8.6)*].

58 **2.4 Reconstitution of the Lyophilized Powder**

59 The lyophilized powder contained within the Pen must be reconstituted prior to administration.
60 See Patient Instructions for Use for complete administration instructions with illustrations. The
61 instructions may also be found at www.TANZEUM.com. Instruct patients as follows:

62 **Pen Reconstitution**

- 63 a) Hold the Pen body with the clear cartridge pointing up to see the [1] in the number window.
- 64 b) To reconstitute the lyophilized powder with the diluent in the Pen, twist the clear cartridge on
65 the Pen in the direction of the arrow until the Pen is felt/heard to “click” into place and the
66 [2] is seen in the number window. This mixes the diluent with the lyophilized powder.
- 67 c) Slowly and gently rock the Pen side-to-side 5 times to mix the reconstituted solution of
68 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 the
70 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 reconstituted
73 solution.
- 74 f) Visually inspect the reconstituted solution in the viewing window for particulate matter. The
75 reconstituted solution will be yellow in color. After reconstitution, use TANZEUM within
76 8 hours.
- 77 g) Holding the Pen upright, attach the needle to the Pen. Gently tap the clear cartridge to bring
78 large bubbles to the top.

79 See *Dosage and Administration (2.5)* for important administration instructions, including the
80 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 the 30-
83 mg Pen and 30 minutes for the 50-mg Pen after the lyophilized powder and diluent are mixed to
84 ensure reconstitution.

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

- 88 a) Follow Step A (Inspect Your Pen and Mix Your Medication) in the Instructions for
89 Use. Make sure you have:
- 90 • Inspected the Pen for [1] in the number window and expiration date.
 - 91 • Twisted the clear cartridge until [2] appears in the number window and a “click”
92 is heard. This combines the medicine powder and liquid in the clear cartridge.
- 93 b) Hold the Pen with the clear cartridge pointing up and maintain this orientation
94 throughout the reconstitution.
- 95 c) Gently swirl the Pen in small circular motions for at least one minute. Avoid
96 shaking as this can result in foaming, which may affect the dose.
- 97 d) Inspect the solution, and if needed, continue to gently swirl the Pen until all the
98 powder is dissolved and you see a clear yellow solution that is free of particles. A
99 small amount of foam, on top of the solution at the end of reconstitution, is normal.
- 100 • For 30-mg Pen: Complete dissolution usually occurs within 2 minutes but may
101 take up to 5 minutes, as confirmed by visual inspection for a clear yellow
102 solution free of particles.
 - 103 • For 50-mg Pen: Complete dissolution usually occurs within 7 minutes but may
104 take up to 10 minutes.
- 105 e) After reconstitution, continue to follow the steps in the Instructions for Use, starting
106 at Step B: Attach the Needle.

107 **2.5 Important Administration Instructions**

108 Instruct patients as follows:

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

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

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

123 **3 DOSAGE FORMS AND STRENGTHS**

124 TANZEUM is supplied as follows:

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

129 **4 CONTRAINDICATIONS**

130 **4.1 Medullary Thyroid Carcinoma**

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

134 **4.2 Hypersensitivity**

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

137 **5 WARNINGS AND PRECAUTIONS**

138 **5.1 Risk of Thyroid C-cell Tumors**

139 Carcinogenicity of albiglutide could not be assessed in rodents due to the rapid development of
140 drug-clearing, anti-drug antibodies [*see Nonclinical Toxicology (13.1)*]. Other GLP-1 receptor

141 agonists have caused dose-related and treatment-duration-dependent thyroid C-cell tumors
142 (adenomas or carcinomas) in rodents. Human relevance of GLP-1 receptor agonist induced C-
143 cell tumors in rodents has not been determined. It is unknown whether TANZEUM causes
144 thyroid C-cell tumors, including MTC, in humans [see *Boxed Warning, Contraindications (4.1)*].

145 Across 8 Phase III clinical trials [see *Clinical Studies (14)*], MTC was diagnosed in 1 patient
146 receiving TANZEUM and 1 patient receiving placebo. Both patients had markedly elevated
147 serum calcitonin levels at baseline. Cases of MTC in patients treated with liraglutide, another
148 GLP-1 receptor agonist, have been reported in the postmarketing period; the data in these reports
149 are insufficient to establish or exclude a causal relationship between MTC and GLP-1 receptor
150 agonist use in humans.

151 TANZEUM is contraindicated in patients with a personal or family history of MTC or in patients
152 with MEN 2. Counsel patients regarding the potential risk for MTC with the use of TANZEUM
153 and inform them of symptoms of thyroid tumors (e.g., a mass in the neck, dysphagia, dyspnea, or
154 persistent hoarseness).

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

163 **5.2 Acute Pancreatitis**

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

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

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

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

175 **5.3 Hypoglycemia with Concomitant Use of Insulin Secretagogues or Insulin**

176 The risk of hypoglycemia is increased when TANZEUM is used in combination with insulin
177 secretagogues (e.g., sulfonylureas) or insulin. Therefore, patients may require a lower dose of
178 sulfonylurea or insulin to reduce the risk of hypoglycemia in this setting [see *Dosage and*
179 *Administration (2.2), Adverse Reactions (6.1)*].

180 **5.4 Hypersensitivity Reactions**

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

185 **5.5 Renal Impairment**

186 In patients treated with GLP-1 receptor agonists, there have been postmarketing reports of acute
187 renal failure and worsening of chronic renal failure, which may sometimes require hemodialysis.
188 Some of these events were reported in patients without known underlying renal disease. A
189 majority of reported events occurred in patients who had experienced nausea, vomiting, diarrhea,
190 or dehydration. In a trial of TANZEUM in patients with renal impairment [see *Clinical Studies*
191 *(14.3)*], the frequency of such gastrointestinal reactions increased as renal function declined [see
192 *Use in Specific Populations (8.6)*]. Because these reactions may worsen renal function, use
193 caution when initiating or escalating doses of TANZEUM in patients with renal impairment [see
194 *Dosage and Administration (2.3)*, *Use in Specific Populations (8.6)*].

195 **5.6 Macrovascular Outcomes**

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

198 **6 ADVERSE REACTIONS**

199 The following serious reactions are described below or elsewhere in the prescribing information:

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

206 **6.1 Clinical Trials Experience**

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

210 Pool of Placebo-Controlled Trials

211 The data in Table 1 are derived from 4 placebo-controlled trials. TANZEUM was used as
212 monotherapy in 1 trial and as add-on therapy in 3 trials [see *Clinical Studies (14)*]. These data
213 reflect exposure of 923 patients to TANZEUM and a mean duration of exposure to TANZEUM
214 of 93 weeks. The mean age of participants was 55 years, 1% of participants were 75 years or
215 older and 53% of participants were male. The population in these studies was 48% white, 13%

216 African/African American, 7% Asian, and 29% Hispanic/Latino. At baseline, the population had
 217 type 2 diabetes for an average of 7 years and had a mean HbA1c of 8.1%. At baseline, 17% of
 218 the population in these studies reported peripheral neuropathy and 4% reported retinopathy.
 219 Baseline estimated renal function was normal or mildly impaired (eGFR >60 mL/min/1.73 m²)
 220 in 91% of the study population and moderately impaired (eGFR 30 to 60 mL/min/1.73 m²) in
 221 9%.

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

226

227 **Table 1. Adverse Reactions in Placebo-controlled Trials Reported in ≥5% of Patients**
 228 **Treated with TANZEUM^a**

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 ^b	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

229 ^a Adverse reactions reported includes adverse reactions occurring with the use of glycemic
 230 rescue medications which included metformin (17% for placebo and 10% for TANZEUM)
 231 and insulin (24% for placebo and 14% for TANZEUM).

232 ^b See below for other events of injection site reactions reported.

233

234 *Gastrointestinal Adverse Reactions*

235 In the pool of placebo-controlled trials, gastrointestinal complaints occurred more frequently
 236 among patients receiving TANZEUM (39%) than patients receiving placebo (33%). In addition
 237 to diarrhea and nausea (see Table 1), the following gastrointestinal adverse reactions also
 238 occurred more frequently in patients receiving TANZEUM: vomiting (2.6% versus 4.2% for
 239 placebo versus TANZEUM), gastroesophageal reflux disease (1.9% versus 3.5% for placebo
 240 versus TANZEUM), and dyspepsia (2.8% versus 3.4% for placebo versus TANZEUM).

241 Constipation also contributed to the frequently reported reactions. In the group treated with
 242 TANZEUM, investigators graded the severity of GI reactions as “mild” in 56% of cases,
 243 “moderate” in 37% of cases, and “severe” in 7% of cases. Discontinuation due to GI adverse
 244 reactions occurred in 2% of individuals on TANZEUM or placebo.

245 *Injection Site Reactions*

246 In the pool of placebo-controlled trials, injection site reactions occurred more frequently on
247 TANZEUM (18%) than on placebo (8%). In addition to the term injection site reaction (see
248 Table 1), the following other types of injection site reactions also occurred more frequently on
249 TANZEUM: injection site hematoma (1.9% versus 2.1% for placebo versus TANZEUM),
250 injection site erythema (0.4% versus 1.7% for placebo versus TANZEUM), injection site rash
251 (0% versus 1.4% for placebo versus TANZEUM), injection site hypersensitivity (0% versus
252 0.8% for placebo versus TANZEUM), and injection site hemorrhage (0.6% versus 0.7% for
253 placebo versus TANZEUM). Injection site pruritus also contributed to the frequently reported
254 reactions. The majority of injection site reactions were judged as “mild” by investigators in both
255 groups (73% for TANZEUM versus 94% for placebo). More patients on TANZEUM than on
256 placebo: discontinued due to an injection site reaction (2% versus 0.2%), experienced more than
257 2 reactions (38% versus 20%), had a reaction judged by investigators to be “moderate” or
258 “severe” (27% versus 6%) and required local or systemic treatment for the reactions (36% versus
259 11%).

260 Pool of Placebo- and Active-controlled Trials

261 The occurrence of adverse reactions was also evaluated in a larger pool of patients with type 2
262 diabetes participating in 7 placebo- and active-controlled trials. These trials evaluated the use of
263 TANZEUM as monotherapy, and as add-on therapy to oral antidiabetic agents, and as add-on
264 therapy to basal insulin [*see Clinical Studies (14)*]. In this pool, a total of 2,116 patients with
265 type 2 diabetes were treated with TANZEUM for a mean duration of 75 weeks. The mean age of
266 patients treated with TANZEUM was 55 years, 1.5% of the population in these studies was
267 75 years or older and 51% of participants were male. Forty-eight percent of patients were white,
268 15% African/African American, 9% Asian, and 26% were Hispanic/Latino. At baseline, the
269 population had diabetes for an average of 8 years and had a mean HbA1c of 8.2%. At baseline,
270 21% of the population reported peripheral neuropathy and 5% reported retinopathy. Baseline
271 estimated renal function was normal or mildly impaired (eGFR >60 mL/min/1.73 m²) in 92% of
272 the population and moderately impaired (eGFR 30 to 60 mL/min/1.73 m²) in 8% of the
273 population.

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

276 Other Adverse Reactions

277 *Hypoglycemia*

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

283

Table 2. Incidence (%) of Hypoglycemia in Clinical Trials of TANZEUM^a

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

285 OAD = Oral antidiabetic agents.

286 ^a Data presented are to the primary endpoint and include only events occurring on-therapy with
287 randomized medications and excludes events occurring after use of glycemic rescue
288 medications (i.e., primarily metformin or insulin).

289 ^b In this trial, no documented symptomatic or severe hypoglycemia were reported for
290 TANZEUM 50 mg and these data are omitted from the table.

291 ^c Plasma glucose concentration ≤ 70 mg/dL and presence of hypoglycemic symptoms.

292 ^d Event requiring another person to administer a resuscitative action.

293 ^e Rate of documented symptomatic hypoglycemia for active controls 18% (glimepiride) and 2%
294 (sitagliptin).

295

296 *Pneumonia*

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

301 *Atrial Fibrillation/Flutter*

302 In the pool of 7 placebo- and active-controlled trials, adverse reactions of atrial fibrillation
303 (1.0%) and atrial flutter (0.2%) were reported more frequently for TANZEUM than for all
304 comparators (0.5% and 0%, respectively). In both groups, patients with events were generally
305 male, older, and had underlying renal impairment or cardiac disease (e.g., history of arrhythmia,
306 palpitations, congestive heart failure, cardiomyopathy, etc.).

307 *Appendicitis*

308 In the pool of placebo- and active-controlled trials, serious events of appendicitis occurred in
309 0.3% of patients treated with TANZEUM compared with 0% among all comparators.

310 *Immunogenicity*

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

316 Consistent with the high homology of albiglutide with human GLP-1, the majority of patients
317 (approximately 79%) with anti-albiglutide antibodies also tested positive for anti-GLP-1
318 antibodies; none were neutralizing. A minority of patients (approximately 17%) who tested
319 positive for anti-albiglutide antibodies also transiently tested positive for antibodies to human
320 albumin.

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

327 *Liver Enzyme Abnormalities*

328 In the pool of placebo- and active-controlled trials, a similar proportion of patients experienced
329 at least one event of alanine aminotransferase (ALT) increase of 3-fold or greater above the
330 upper limit of normal (0.9% and 0.9% for all comparators versus TANZEUM). Three subjects on
331 TANZEUM and one subject in the all-comparator group experienced at least one event of ALT
332 increase of 10-fold or greater above the upper limit of normal. In one of the 3 cases an alternate
333 etiology was identified to explain the rise in liver enzyme (acute viral hepatitis). In one case,

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

340 *Gamma Glutamyltransferase (GGT) Increase*

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

344 *Heart Rate Increase*

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

349 **7 DRUG INTERACTIONS**

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

355 **8 USE IN SPECIFIC POPULATIONS**

356 **8.1 Pregnancy**

357 Pregnancy Category C

358 There are no adequate and well-controlled studies of TANZEUM in pregnant women.
359 Nonclinical studies have shown reproductive toxicity, but not teratogenicity, in mice treated with
360 albiglutide at up to 39 times human exposure resulting from the maximum recommended dose of
361 50 mg/week, based on AUC [*see Nonclinical Toxicology (13.1, 13.3)*]. TANZEUM should not
362 be used during pregnancy unless the expected benefit outweighs the potential risks.

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

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

368 **8.3 Nursing Mothers**

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

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

376 **8.4 Pediatric Use**

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

379 **8.5 Geriatric Use**

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

384 **8.6 Renal Impairment**

385 Of the total number of patients (N = 2,365) in 8 Phase III clinical trials who received
386 TANZEUM, 54% (N = 1,267) had mild renal impairment (eGFR 60 to 89 mL/min/1.73 m²),
387 12% (N = 275) had moderate renal impairment (eGFR 30 to 59 mL/min/1.73 m²) and 1%
388 (N = 19) had severe renal impairment (eGFR 15 to <30 mL/min/1.73 m²).

389 No dosage adjustment is required in patients with mild (eGFR 60 to 89 mL/min/1.73 m²),
390 moderate (eGFR 30 to 59 mL/min/1.73 m²), or severe (eGFR 15 to <30 mL/min/1.73 m²) renal
391 impairment.

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

400 **10 OVERDOSAGE**

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

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

406 **11 DESCRIPTION**

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

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

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

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

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

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

426 **12 CLINICAL PHARMACOLOGY**

427 **12.1 Mechanism of Action**

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

430 **12.2 Pharmacodynamics**

431 TANZEUM lowers fasting glucose and reduces postprandial glucose excursions in patients with
432 type 2 diabetes mellitus. The majority of the observed reduction in fasting plasma glucose occurs
433 after a single dose, consistent with the pharmacokinetic profile of albiglutide. In a Phase II trial
434 in Japanese patients with type 2 diabetes mellitus who received TANZEUM 30 mg, a reduction
435 (22%) in postprandial glucose AUC_(0-3 h) was observed at steady state (Week 16) compared with
436 placebo following a mixed meal.

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

439 **Gastric Motility**

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

443 Cardiac Electrophysiology

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

446 **12.3 Pharmacokinetics**

447 Absorption

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

457 Distribution

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

461 Metabolism

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

467 Elimination

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

470 Specific Patient Populations

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

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

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

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

484 **Drug Interactions**

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

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

495

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

Co-administered Drug	Dose of Co-administered Drug ^a	Dose of TANZEUM	Geometric Mean Ratio (Ratio +/- Co-administered Drug) No Effect = 1		
			Analyte	AUC (90% CI) ^b	C_{max} (90% CI)
No dose adjustments of co-administered drug required for the following:					
Simvastatin	80 mg	50 mg QW for 5 weeks	Simvastatin	0.60 (0.52 – 0.69)	1.18 (1.02 – 1.38)
			Simvastatin acid	1.36 (1.19 – 1.55)	1.98 (1.75 – 2.25)
Digoxin	0.5 mg	50 mg QW for 5 weeks	Digoxin	1.09 (1.01 – 1.18)	1.11 (0.98 – 1.26)
Oral contraceptive ^c	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)

497 QW = Once weekly.

498 ^a Single dose unless otherwise noted.

499 ^b AUC_{inf} for drugs given as a single dose and AUC_{24h} for drugs given as multiple doses.

500 ^c Subjects received low-dose oral contraceptive for two 28-day treatment cycles (21 days
 501 active/7 days placebo).

502

503 **13 NONCLINICAL TOXICOLOGY**

504 **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

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

506 Carcinogenicity of albiglutide could not be assessed in rodents due to the rapid development of
507 drug-clearing, anti-drug antibodies. Other GLP-1 receptor agonists have caused thyroid C-cell
508 tumors in rodent carcinogenicity studies. Human relevance of GLP-1 receptor agonist induced
509 rodent thyroid C-cell tumors has not been determined.

510 In a mouse fertility study, males were treated with SC doses of 5, 15, or 50 mg/kg/day for 7 days
511 prior to cohabitation with females, and continuing through mating. In a separate fertility study,
512 females were treated with SC doses of 1, 5, or 50 mg/kg/day for 7 days prior to cohabitation with
513 males, and continuing through mating. Reductions in estrous cycles were observed at
514 50 mg/kg/day, a dose associated with maternal toxicity (body weight loss and reduced food
515 consumption). There were no effects on mating or fertility in either sex at doses up to
516 50 mg/kg/day (up to 39 times clinical exposure based on AUC).

517 **13.3 Reproductive and Developmental Toxicity**

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

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

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

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

532 Pregnant mice were given SC doses of 1, 5, or 50 mg/kg/day from gestation Day 15 to lactation
533 Day 10. Increased mortality and morbidity were seen at all doses (≥ 1 mg/kg/day) in lactating
534 females in mouse pre- and postnatal development studies. Mortalities have not been observed in
535 previous toxicology studies in non-lactating or non-pregnant mice, nor in pregnant mice. These
536 findings are consistent with lactational ileus syndrome which has been previously reported in
537 mice. Since the relative stress of lactation energy demands is lower in humans than mice and
538 humans have large energy reserves, the mortalities observed in lactating mice are of questionable
539 relevance to humans. The offspring had decreased pre-weaning body weight which reversed

540 post-weaning in males but not females at ≥ 5 mg/kg/day (2.2 times clinical exposure based on
541 AUC) with no other effects on development. Low levels of albiglutide were detected in plasma
542 of offspring.

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

547 **14 CLINICAL STUDIES**

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

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

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

559 **14.1 Monotherapy**

560 The efficacy of TANZEUM as monotherapy was evaluated in a 52-week, randomized, double-
561 blind, placebo-controlled, multicenter trial. In this trial, 296 patients with type 2 diabetes
562 inadequately controlled on diet and exercise were randomized (1:1:1) to TANZEUM 30 mg SC
563 once weekly, TANZEUM 30 mg SC once weekly uptitrated to 50 mg once weekly at Week 12,
564 or placebo. The mean age of participants was 53 years, 55% of patients were men, the mean
565 duration of diabetes was 4 years, and the mean baseline eGFR was 84 mL/min/1.73 m². Primary
566 and secondary efficacy results are presented in Table 4. Figure 1 shows the mean adjusted
567 changes in HbA1c from baseline across study visits.

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

572

573 **Table 4. Results at Week 52 (LOCF^a) in a Trial of TANZEUM as Monotherapy**

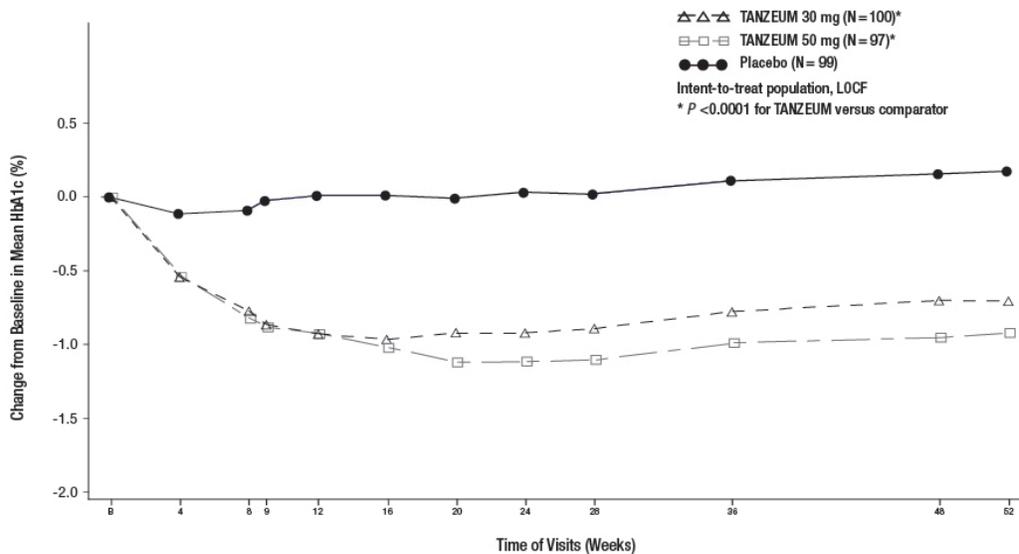
	Placebo	TANZEUM 30 mg Weekly	TANZEUM 50 mg Weekly
ITT^a (N)	99	100	97
HbA1c (%)			
Baseline (mean)	8.0	8.1	8.2
Change at Week 52 ^b	+0.2	-0.7	-0.9
Difference from placebo ^b (95% CI)		-0.8 (-1.1, -0.6) ^c	-1.0 (-1.3, -0.8) ^c
Patients (%) achieving HbA1c <7%	21	49	40
FPG (mg/dL)			
Baseline (mean)	163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

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

578 ^b Least squares mean adjusted for baseline value and stratification factors.

579 ^c *P* <0.0001 for treatment difference.

580
 581 **Figure 1. Mean HbA1c Change from Baseline (ITT Population-LOCF) in a Trial of**
 582 **TANZEUM as Monotherapy**



583
 584

585 **14.2 Combination Therapy**

586 Add-on to Metformin

587 The efficacy of TANZEUM was evaluated in a 104-week randomized, double-blind, multicenter
 588 trial in 999 patients with type 2 diabetes mellitus inadequately controlled on background

589 metformin therapy ($\geq 1,500$ mg daily). In this trial, TANZEUM 30 mg SC weekly (with optional
 590 uptitration to 50 mg weekly after a minimum of 4 weeks) was compared with placebo, sitagliptin
 591 100 mg daily, or glimepiride 2 mg daily (with optional titration to 4 mg daily). The mean age of
 592 participants was 55 years, 48% of patients were men, the mean duration of type 2 diabetes was
 593 6 years, and the mean baseline eGFR was 86 mL/min/1.73 m². Results of the primary and
 594 secondary analyses are presented in Table 5. Figure 2 shows the mean adjusted changes in
 595 HbA1c across study visits.

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

600

601 **Table 5. Results at Week 104 (LOCF^a) in a Trial Comparing TANZEUM with Placebo as**
 602 **Add-on Therapy in Patients Inadequately Controlled on Metformin**

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

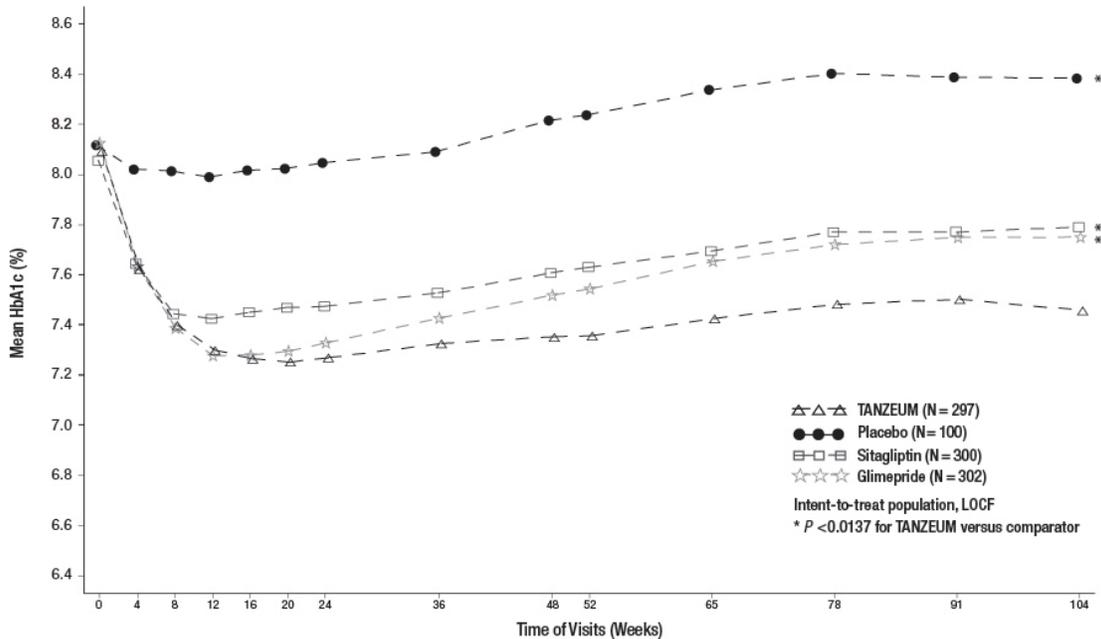
603 ^a Intent-to-treat population. Last observation carried forward (LOCF) was used to impute
 604 missing data. Data post-onset of rescue therapy are treated as missing. At Week 104, primary
 605 efficacy data was imputed for 76%, 46%, 55%, and 51% of individuals randomized to
 606 placebo, TANZEUM,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

607 ^b Least squares mean adjusted for baseline value and stratification factors.

608 ^c $P < 0.0137$ for treatment difference.

609

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



613

614

615 Add-on to Pioglitazone

616 The efficacy of TANZEUM was evaluated in a 52-week randomized, double-blind, multicenter
617 trial in 299 patients with type 2 diabetes mellitus inadequately controlled on pioglitazone ≥ 30 mg
618 daily (with or without metformin $\geq 1,500$ mg daily). Patients were randomized to receive
619 TANZEUM 30 mg SC weekly or placebo. The mean age of participants was 55 years, 60% of
620 patients were men, the mean duration of type 2 diabetes was 8 years, and the mean baseline
621 eGFR was 83 mL/min/1.73 m². Results of the primary and secondary analyses are presented in
622 Table 6.

623 Compared with placebo, treatment with TANZEUM resulted in a statistically significant
624 reduction in HbA1c from baseline at Week 52 (see Table 6). The adjusted mean change from
625 baseline in weight did not differ significantly between TANZEUM (+0.3 kg) and placebo
626 (+0.5 kg) at Week 52.

627

628 **Table 6. Results at Week 52 (LOCF^a) in a Trial Comparing TANZEUM with Placebo as**
 629 **Add-on Therapy in Patients Inadequately Controlled on Pioglitazone (with or without**
 630 **Metformin)**

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

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

635 ^b Least squares mean adjusted for baseline value and stratification factors.

636 ^c *P* <0.0001 for treatment difference.

637

638 Add-on to Metformin Plus Sulfonylurea

639 The efficacy of TANZEUM was evaluated in a 52-week randomized, double-blind, multicenter
 640 trial in 657 patients with type 2 diabetes mellitus inadequately controlled on metformin
 641 ($\geq 1,500$ mg daily) and glimepiride (4 mg daily). Patients were randomized to receive
 642 TANZEUM 30 mg SC weekly (with optional uptitration to 50 mg weekly after a minimum of
 643 4 weeks), placebo, or pioglitazone 30 mg daily (with optional titration to 45 mg/day). The mean
 644 age of participants was 55 years, 53% of patients were men, the mean duration of type 2 diabetes
 645 was 9 years, and the mean baseline eGFR was 84 mL/min/1.73 m². Results of the primary and
 646 main secondary analyses are presented in Table 7.

647 Treatment with TANZEUM resulted in statistically significant reductions in HbA1c from
 648 baseline compared with placebo (see Table 7). Treatment with TANZEUM did not meet the pre-
 649 specified, non-inferiority margin (0.3%) against pioglitazone. In this trial, TANZEUM provided
 650 less HbA1c reduction than pioglitazone and the treatment difference was statistically significant
 651 (see Table 7). The change from baseline in body weight for TANZEUM did not differ
 652 significantly from placebo but was significantly different compared with pioglitazone (see Table
 653 7).

654
655
656

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

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

657 ^a Intent-to-treat population. Last observation carried forward (LOCF) was used to impute
658 missing data. Data post-onset of rescue therapy are treated as missing. At Week 52, primary
659 efficacy data was imputed for 70%, 35%, and 34% of individuals randomized to placebo,
660 TANZEUM, and pioglitazone.
661 ^b Least squares mean adjusted for baseline value and stratification factors.
662 ^c *P* <0.0001 for treatment difference.
663 ^d Did not meet non-inferiority margin of 0.3%.

664

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

666 The efficacy of TANZEUM was evaluated in a 32-week, randomized, open-label, liraglutide-
667 controlled, non-inferiority trial in 805 patients with type 2 diabetes mellitus inadequately
668 controlled on monotherapy or combination oral antidiabetic therapy (metformin,
669 thiazolidinedione, sulfonylurea, or a combination of these). Patients were randomized to
670 TANZEUM 30 mg SC weekly (with uptitration to 50 mg weekly at Week 6) or liraglutide
671 1.8 mg daily (titrated up from 0.6 mg at Week 1, and 1.2 mg at Week 1 to Week 2). The mean
672 age of participants was 56 years, 50% of patients were men, the mean duration of type 2 diabetes
673 was 8 years, and the mean baseline eGFR was 95 mL/min/1.73 m². Results of the primary and
674 main secondary analyses are presented in Table 8.

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

679
 680 **Table 8. Results of Controlled Trial of TANZEUM versus Liraglutide at Week 32 (LOCF^a)**

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

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

685 ^b Least squares mean adjusted for baseline value and stratification factors.

686 ^c Did not meet non-inferiority margin of 0.3%.

687 ^d $P < 0.005$ for treatment difference in favor of liraglutide.

688
 689 **Combination Therapy: Active-controlled Trial versus Basal Insulin**

690 The efficacy of TANZEUM was evaluated in a 52-week, randomized (2:1), open-label, insulin
 691 glargine-controlled, non-inferiority trial in 735 patients with type 2 diabetes mellitus
 692 inadequately controlled on metformin $\geq 1,500$ mg daily (with or without sulfonylurea). Patients
 693 were randomized to receive TANZEUM 30 mg SC weekly (with optional uptitration to 50 mg
 694 weekly) or insulin glargine (median starting of 10 units and titrated weekly per prescribing
 695 information). The primary endpoint was change in HbA1c from baseline compared with insulin
 696 glargine. The starting total daily dose of insulin glargine ranged between 2 and 40 units (median
 697 daily dose of 10 units) and ranged between 3 and 230 units (median daily dose of 30 units) at
 698 Week 52. Sixty-nine percent of patients treated with TANZEUM were uptitrated to 50 mg SC
 699 weekly. The mean age of participants was 56 years, 56% of patients were men, the mean

700 duration of type 2 diabetes was 9 years, and the mean baseline eGFR was 85 mL/min/1.73 m².

701 Results of the primary and main secondary analyses are presented in Table 9.

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

707

708 **Table 9. Results at Week 52 (LOCF^a) in a Trial Comparing TANZEUM with Insulin**
709 **Glargine as Add-on Therapy in Patients Inadequately Controlled on Metformin ±**
710 **Sulfonylurea**

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

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

715 ^b Least squares mean adjusted for baseline value and stratification factors.

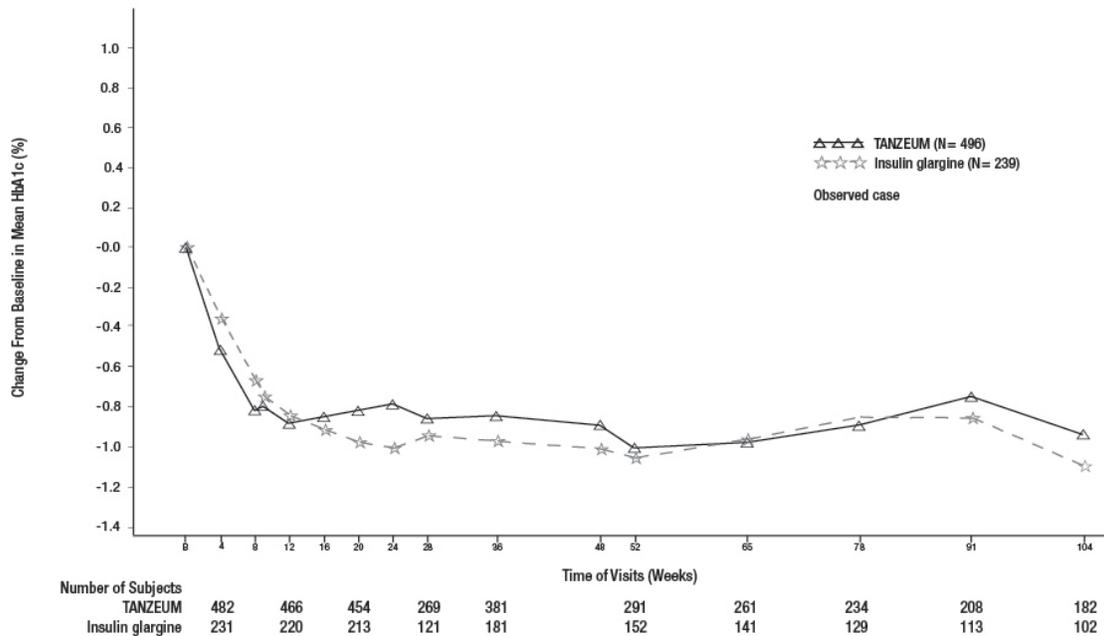
716 ^c Met non-inferiority margin of 0.3%.

717 ^d *P* <0.0001 in favor of insulin glargine.

718 ^e *P* <0.0001.

719

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



723

724

725 Combination Therapy: Active-controlled Trial versus Prandial Insulin

726 The efficacy of TANZEUM was evaluated in a 26-week, randomized, open-label, multicenter,
 727 non-inferiority trial in 563 patients with type 2 diabetes mellitus inadequately controlled on
 728 insulin glargine (≥ 20 units per day). Patients were randomized to receive TANZEUM 30 mg SC
 729 once weekly (with uptitration to 50 mg if inadequately controlled after Week 8) or insulin lispro
 730 (administered daily at meal times, started according to standard of care and titrated to effect). At
 731 Week 26, the mean daily dose of insulin glargine was 53 IU for TANZEUM and 51 IU for
 732 insulin lispro. The mean daily dose of insulin lispro at Week 26 was 31 IU, and 51% of patients
 733 treated with TANZEUM were on 50 mg weekly. The mean age of participants was 56 years,
 734 47% of patients were men, the mean duration of type 2 diabetes was 11 years, and the mean
 735 baseline eGFR was 91 mL/min/1.73 m². Results of the primary and main secondary analyses are
 736 presented in Table 10. Figure 4 shows the mean adjusted changes in HbA1c from baseline across
 737 study visits.

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

743

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

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

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

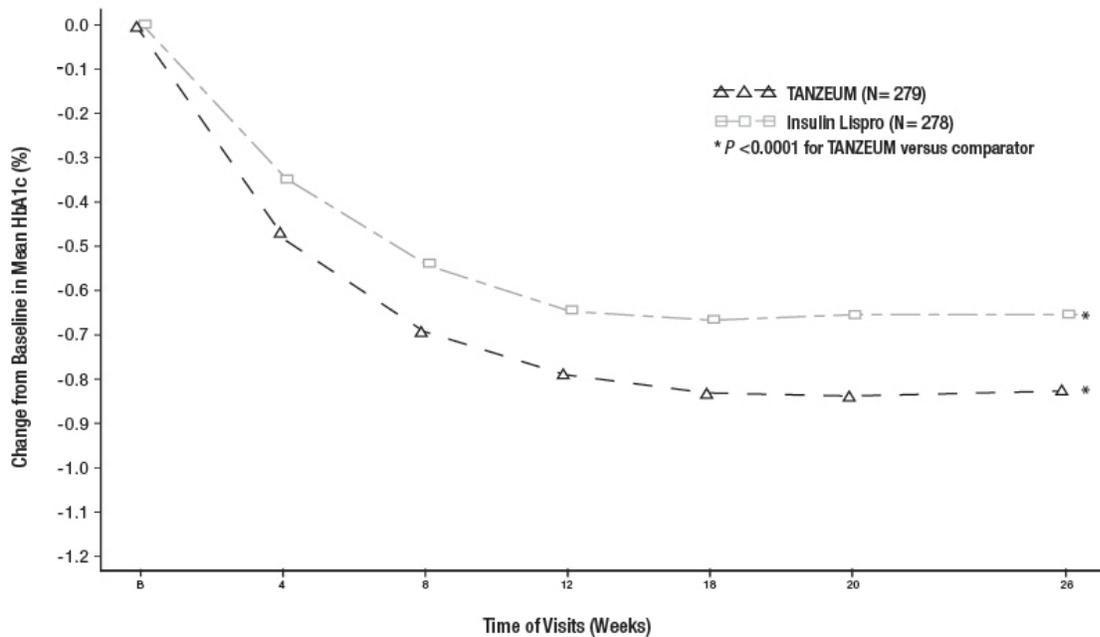
750 ^b Least squares mean adjusted for baseline value and stratification factors.

751 ^c Rules out a non-inferiority margin of 0.4%.

752 ^d *P* <0.0001 for treatment difference.

753

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



757
758

759 **14.3 Type 2 Diabetes Mellitus Patients with Renal Impairment**

760 The efficacy of TANZEUM was evaluated in a 26-week, randomized, double-blind, active-
 761 controlled trial in 486 patients with mild (n = 250), moderate (n = 200), and severe renal
 762 impairment (n = 36) inadequately controlled on a current regimen of diet and exercise or other
 763 antidiabetic therapy. Patients were randomized to receive TANZEUM 30 mg SC weekly (with
 764 uptitration to 50 mg weekly if needed as early as Week 4) or sitagliptin. Sitagliptin was dosed
 765 according to renal function (100 mg, 50 mg, and 25 mg daily in mild, moderate, and severe renal
 766 impairment, respectively). The mean age of participants was 63 years, 54% of patients were men,
 767 the mean duration of type 2 diabetes was 11 years, and the mean baseline eGFR was
 768 60 mL/min/1.73 m².

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

772

773 **Table 11. Results at Week 26 (LOCF^a) in a Trial Comparing TANZEUM with Sitagliptin**
 774 **in Patients with Renal Impairment**

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

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

779 ^b Least squares mean adjusted for baseline value and stratification factors.

780 ^c *P* <0.0003 for treatment difference.

781 ^d *P* = 0.0281 for treatment difference.

782

783 **16 HOW SUPPLIED/STORAGE AND HANDLING**

784 **16.1 How Supplied**

785 TANZEUM is available in the following strengths and package size:

786 30 mg single-dose Pen (NDC 0173-0866-01):

- 787 • carton of 4 (containing four 29-gauge, 5-mm, thinwall needles): NDC 0173-0866-35

788 50 mg single-dose Pen (NDC 0173-0867-01):

- 789 • carton of 4 (containing four 29-gauge, 5-mm, thinwall needles): NDC 0173-0867-35

790 **16.2 Storage and Handling**

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

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

799 **17 PATIENT COUNSELING INFORMATION**

800 Advise the patient to read the FDA-approved patient labeling (Medication Guide and Instructions
801 for Use). The Medication Guide is contained in a separate leaflet that accompanies the product.

- 802 • Inform patients about self-management practices, including the importance of proper storage
803 of TANZEUM, injection technique, timing of dosage of TANZEUM and concomitant oral
804 drugs, and recognition and management of hypoglycemia.
- 805 • Inform patients that thyroid C-cell tumors have been observed in rodents treated with some
806 GLP-1 receptor agonists, and the human relevance of this finding has not been determined.
807 Counsel patients to report symptoms of thyroid tumors (e.g., a lump in the neck, dysphagia,
808 dyspnea, or persistent hoarseness) to their physician [*see Boxed Warning, Warnings and*
809 *Precautions (5.1)*].
- 810 • Advise patients that persistent, severe abdominal pain that may radiate to the back and which
811 may (or may not) be accompanied by vomiting is the hallmark symptom of acute
812 pancreatitis. Instruct patients to discontinue TANZEUM promptly and to contact their
813 physician if persistent, severe abdominal pain occurs [*see Warnings and Precautions (5.2)*].
- 814 • The risk of hypoglycemia is increased when TANZEUM is used in combination with an
815 agent that induces hypoglycemia, such as sulfonylurea or insulin. Instructions for
816 hypoglycemia should be reviewed with patients and reinforced when initiating therapy with
817 TANZEUM, particularly when concomitantly administered with a sulfonylurea or insulin
818 [*see Warnings and Precautions (5.3)*].
- 819 • Advise patients on the symptoms of hypersensitivity reactions and instruct them to stop
820 taking TANZEUM and seek medical advice promptly if such symptoms occur [*see Warnings*
821 *and Precautions (5.4)*].
- 822 • Instruct patients to read the Instructions for Use before starting therapy. Instruct patients on
823 proper use, storage, and disposal of the pen [*see How Supplied/Storage and Handling (16.2),*
824 *Patient Instructions for Use*].
- 825 • Instruct patients to read the Medication Guide before starting TANZEUM and to read again
826 each time the prescription is renewed. Instruct patients to inform their doctor or pharmacist if
827 they develop any unusual symptom, or if any known symptom persists or worsens.
- 828 • Inform patients not to take an extra dose of TANZEUM to make up for a missed dose. If a
829 dose is missed, instruct patients to take a dose as soon as possible within 3 days after the

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

833

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



835

836 Manufactured by **GlaxoSmithKline LLC**

837 Wilmington, DE 19808

838 U.S. Lic. No. 1727

839 Marketed by **GlaxoSmithKline**

840 Research Triangle Park, NC 27709

841 ©2015, the GSK group of companies. All rights reserved.

842 TNZ:XPI

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

Read this Medication Guide before you start using 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?

TANZEUM may cause serious side effects, 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 (MTC) in people.
- **Do not use TANZEUM if you** or any of your family have ever had a type of thyroid cancer called medullary thyroid carcinoma (MTC) or if you have an endocrine system condition 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 have 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 for use in people with severe stomach or intestinal problems.
- It is not known if TANZEUM can be used with mealtime insulin.
- It is not known if TANZEUM is safe and effective for use in children under 18 years of age.

Who should not use TANZEUM?

Do not use TANZEUM if:

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

What should I tell my healthcare provider before using TANZEUM?

Before using TANZEUM, tell your healthcare provider 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
- have any other medical conditions
- 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 should not use TANZEUM while breastfeeding without first talking with your healthcare provider.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. TANZEUM may affect the way some medicines work and some medicines may affect the way TANZEUM works.

Before using TANZEUM, talk to your healthcare provider about low blood sugar and how to manage it. Tell your healthcare provider if you are taking other medicines to treat diabetes including insulin or sulfonylureas.

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when

you get a new medicine.

How should I use TANZEUM?

- Read the **Instructions for Use** that comes with TANZEUM.
- Use TANZEUM exactly as your healthcare provider tells you to.
- **Your healthcare provider should show you how to use TANZEUM before you use it for the first time.**
- TANZEUM is injected under the skin (subcutaneously) of your stomach (abdomen), thigh, or upper arm. **Do not** inject TANZEUM into a muscle (intramuscularly) or vein (intravenously).
- **Use TANZEUM 1 time each week on the same day each week at any time of the day.**
- You may change the 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. **Do not** take 2 doses of TANZEUM within 3 days of each other.
- TANZEUM may be taken with or without food.
- TANZEUM should be injected within 8 hours after mixing your medicine.
- TANZEUM should be injected right after you attach the needle.
- **Do not** mix insulin and TANZEUM together in the same injection.
- Change (rotate) your injection site with each weekly injection. **Do not** use the same site for each injection.

Do not share your TANZEUM pen or needles with another person. You may give another person an infection or get an infection from them.

Your dose of TANZEUM and other diabetes medicines may need to change because of:

change in level of physical activity or exercise, weight gain or loss, increased stress, illness, change in diet, or because of other medicines you take.

What are the possible side effects of TANZEUM?

TANZEUM may cause serious side effects, including:

- **See “What is the most important information I should know about TANZEUM?”**
- **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 from your abdomen to your back.
- **low blood sugar (hypoglycemia).** Your risk for getting low blood sugar may be higher if you use TANZEUM with another medicine that can cause low blood sugar, such as a sulfonylurea or insulin. 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 or drowsiness
 - shakiness
 - feeling jittery
 - headache
 - fast heart beat
 - weakness
- **serious allergic reactions.** Stop using TANZEUM and get medical help right away if you have any symptoms of a serious allergic reaction including itching, rash, or difficulty breathing.
- **kidney problems (kidney failure).** In people who have kidney problems, diarrhea, nausea, and vomiting may cause a loss of fluids (dehydration) which may cause kidney problems to get worse.

The most common side effects of TANZEUM may include diarrhea, nausea, reactions at your injection site, cough, back pain, cold or flu symptoms.

Talk to your healthcare provider about any side effect that bothers you or does not go away. 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. 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.

This Medication Guide summarizes the most important information about TANZEUM. If you would like more information, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about TANZEUM that is written for health professionals.
For more information, go to www.TANZEUM.com or call 1-888-825-5249.

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.

This Medication Guide has been approved by the U.S. Food and Drug Administration. Revised: March 2015



Manufactured by **GlaxoSmithKline LLC**
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.
©YEAR, the GSK group of companies. All rights reserved.
TNZ: XMG

INSTRUCTIONS FOR USE

TANZEUM™ (TAN-zee-um)

(albiglutide)

for injection, for subcutaneous use

TANZEUM (albiglutide) Pen 30 mg

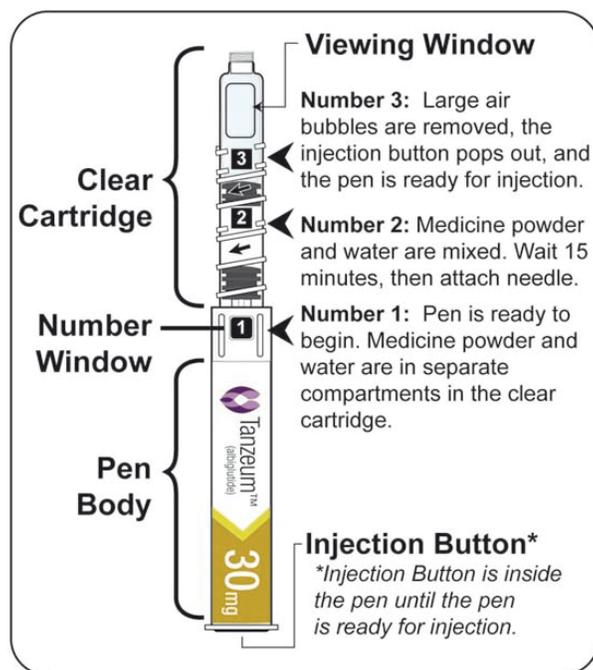
Use 1 Time Each Week

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

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

Information About This Pen

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



CAUTION:

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

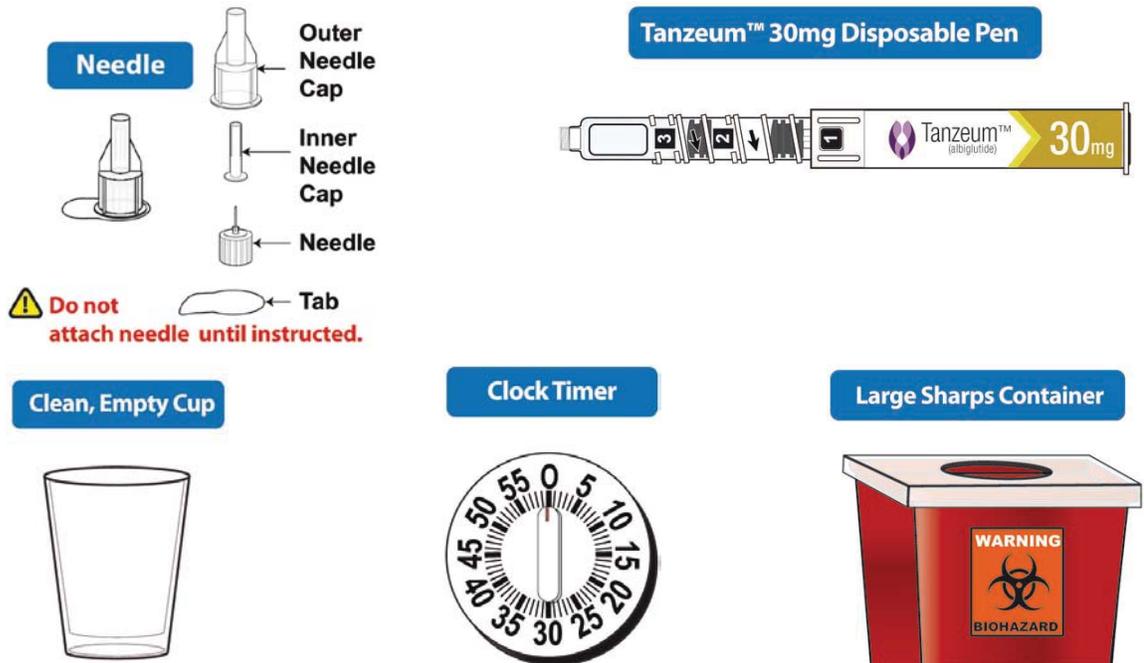
If stored in refrigerator, allow to sit at room temperature for 15 minutes before starting Step A.

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

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

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

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



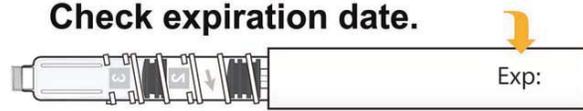
STEP A

Inspect Your Pen and Mix Your Medicine

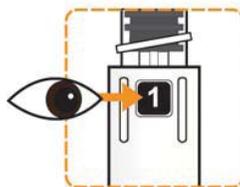
Inspect Your Pen

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

Check expiration date.

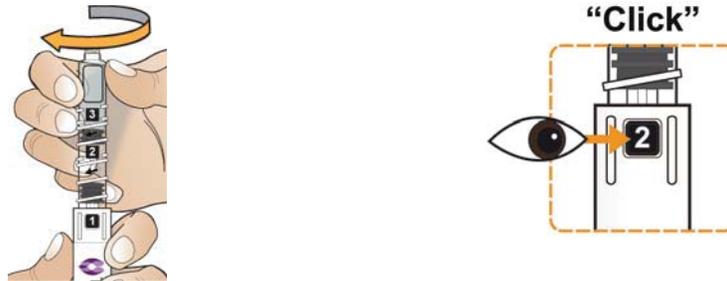


- Check that the pen has a **[1]** in the number window. **Do not** use if the **[1]** is not showing.



Twist Pen to Mix Your Medicine

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



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



Wait for Medicine to Dissolve

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



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

STEP B

Attach the Needle and Prepare the Pen for Injection

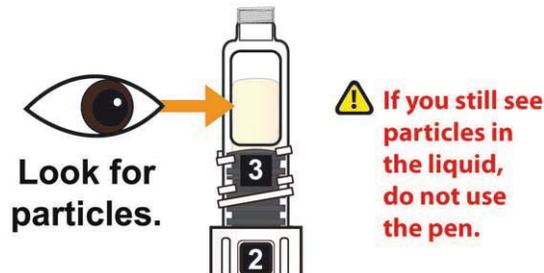
After the 15 minute wait, wash your hands and finish the rest of the steps right away.

Inspect Your Dissolved Medicine

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



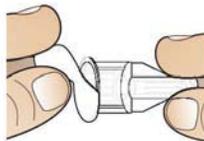
- Look through the viewing window to check that the liquid in the cartridge is clear and free of solid particles.



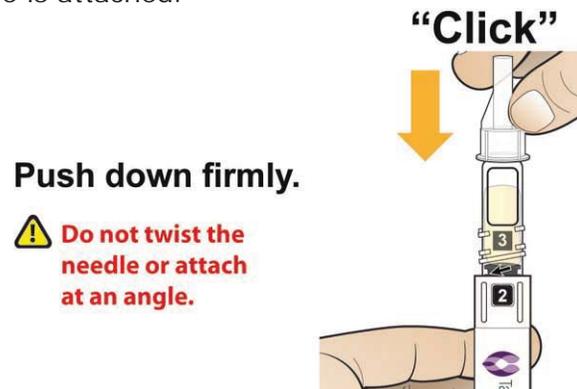
- The liquid will have a yellow color and there will be **large air bubbles** on top of the liquid.

Attach the Needle

- Peel the tab from the outer needle cap.



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



Tap for Air Bubbles

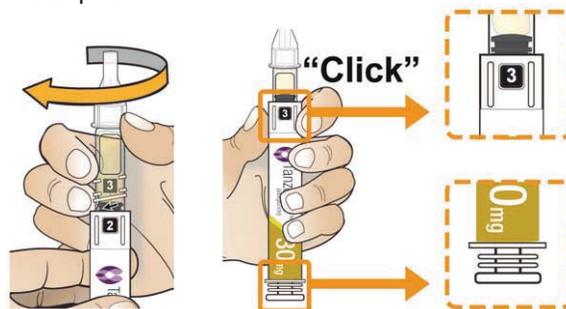
- With the needle point up, gently tap the clear cartridge **2 to 3** times to bring large air bubbles to the top.



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

Twist Pen to Prime the Needle

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

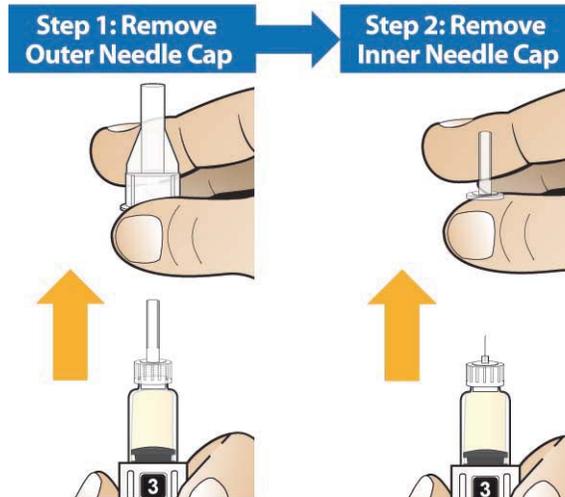


STEP C

Remove Both Needle Caps and Inject Your Medicine

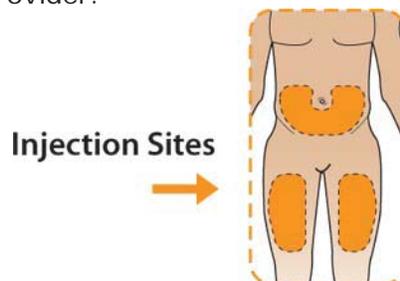
Remove Needle Caps

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

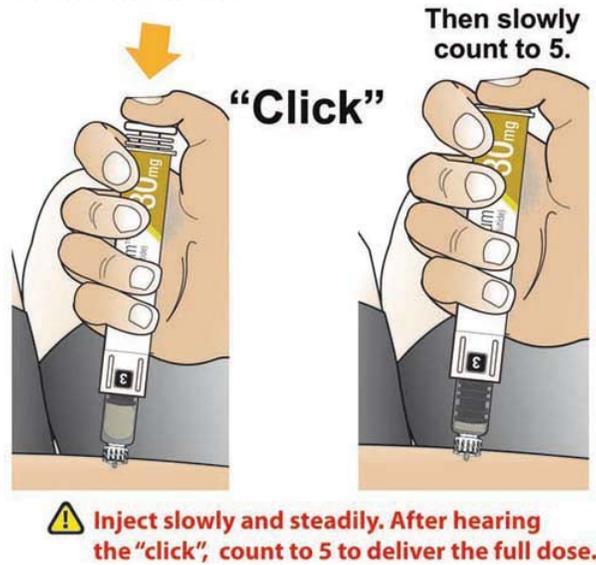


Inject the Medicine

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



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



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

Disposing of Your Used Pens and Needles

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



General Information About the Safe and Effective Use of TANZEUM

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

Frequently Asked Questions

Medicine Dosing

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

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

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

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

Storage

How should I store my medicine?

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

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

Number Window

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

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

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

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

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

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

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

Step A: Inspect Your Pen and Mix Your Medicine

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

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

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

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

Step B: Attach the Needle and Prepare Pen for Injection

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

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

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

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

Step C: Remove Both Needle Caps and Inject Your Medicine

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

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

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

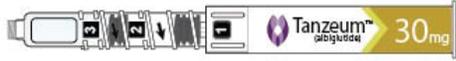
- This is normal. If you have heard or felt the injection button “click” and slowly counted to **5** before pulling the needle out of your skin, you should have received the full dose of your medicine.

How should I dispose of the pen?

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

about sharps disposal in the state that you live in, go to the FDA's website at:
<http://www.fda.gov/safesharpsdisposal>.

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



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

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

Approved: April 2014

 GlaxoSmithKline	Manufactured by GlaxoSmithKline LLC 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
--	--	--

INSTRUCTIONS FOR USE

TANZEUM™ (TAN-zee-um) (albiglutide)

for injection, for subcutaneous use

TANZEUM (albiglutide) Pen 50 mg

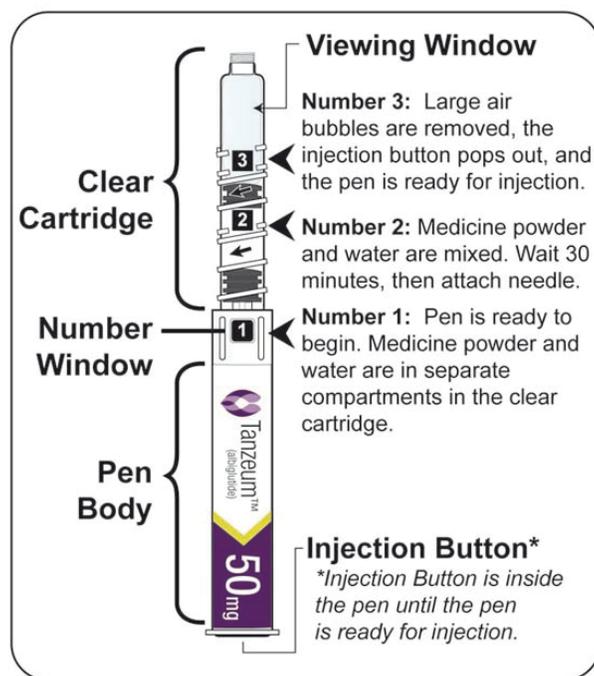
Use 1 Time Each Week

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.

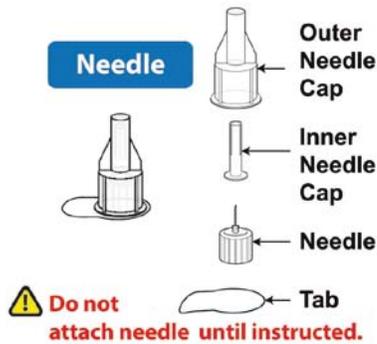
If stored in refrigerator, allow to sit at room temperature for 15 minutes before starting Step A.

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

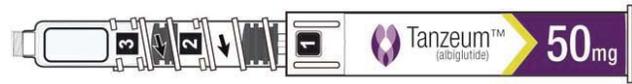
Before you Begin: Wash Your Hands, Gather and Inspect Your Supplies

- 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



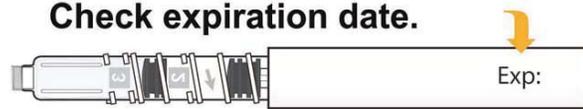
STEP A

Inspect Your Pen and Mix Your Medicine

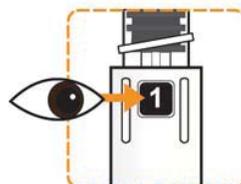
Inspect Your Pen

- 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

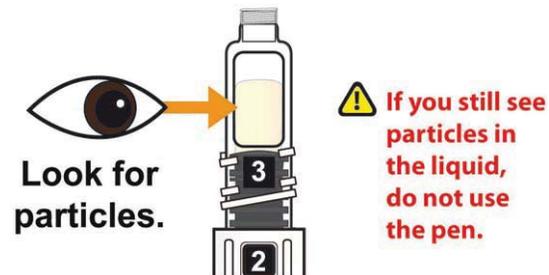
After the 30 minute wait, wash your hands and finish the rest of the steps right away.

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.



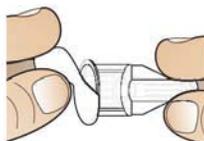
- Look through the viewing window to check that the liquid in the cartridge is clear and free of solid particles.



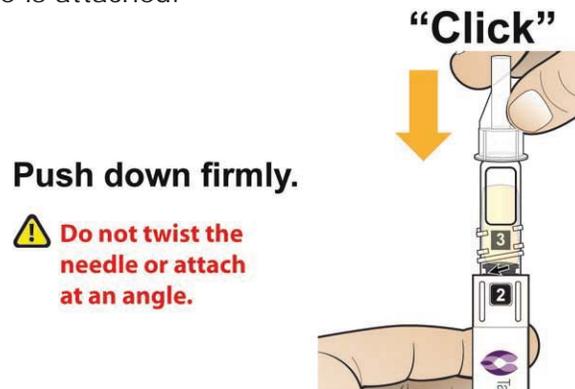
- The liquid will have a yellow color and there will be **large air bubbles** on top of the liquid.

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

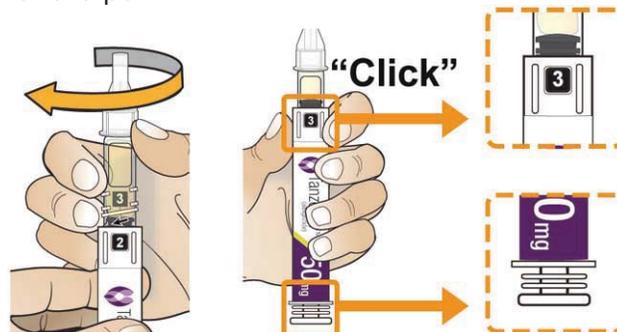
- With the needle point up, gently tap the clear cartridge **2 to 3** times to bring large air bubbles to the top.



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.

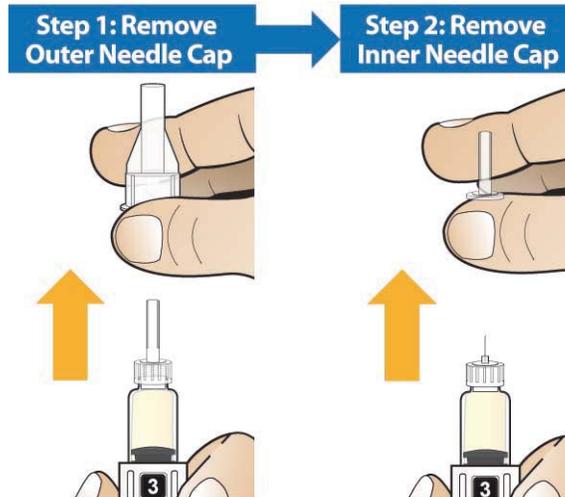


STEP C

Remove Both Needle Caps and Inject Your Medicine

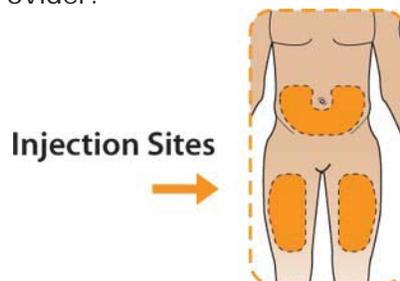
Remove Needle Caps

- 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

 GlaxoSmithKline	Manufactured by GlaxoSmithKline LLC 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-50
--	--	--