

Product Summary for *Tanzeum*

This information is provided in response to your request for information about Tanzeum™ (albiglutide).

SUMMARY

- Important safety information is found in the attached Prescribing Information.
- The prescribing information for this product contains a boxed warning. Please consult the WARNING section of the attached prescribing information for further details and for important safety information.

DISEASE BACKGROUND

Type 2 diabetes mellitus (T2DM) is a chronic illness characterized by insulin resistance with relative insulin deficiency, resulting in hyperglycemia.⁽¹⁾

DESCRIPTION

Tanzeum is a once weekly glucagon-like peptide-1 (GLP-1) receptor agonist delivered from a single-dose pen injection device for the treatment of T2DM in adults.⁽²⁾ It is available as 30 mg or 50 mg.

INDICATION

- *Tanzeum* is indicated as an adjunct to diet and exercise to improve glycemic control in adults with T2DM.⁽²⁾

IMPORTANT LIMITATIONS OF USE:

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

DOSING

- The recommended dosage of *Tanzeum* is 30 mg once weekly given as a subcutaneous injection in the abdomen, thigh, or upper arm region.⁽²⁾ The dosage may be increased to 50 mg once weekly if the glycemic response is inadequate.
- *Tanzeum* may be administered at any time of day without regard to meals. *Tanzeum* should be administered once a week on the same day each week. The day of weekly administration may be changed if necessary as long as the last dose was administered 4 or more days before. If a dose is missed, the patient should administer the dose as soon as possible within 3 days after the missed dose. Thereafter, the patient can resume dosing on their usual day of administration. If it is more than 3 days after the missed dose, the patient should wait until their next regularly scheduled weekly dose.

BOXED WARNING

- **WARNING: RISK OF THYROID C-CELL TUMORS:** Thyroid C-cell tumors have been observed in rodent studies with glucagon-like peptide-1 (GLP-1) receptor agonists at clinically relevant exposures.⁽²⁾ It is unknown whether *Tanzeum* causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans.
- *Tanzeum* is contraindicated in patients with a personal or family history of MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2).⁽²⁾ Routine serum calcitonin or thyroid ultrasound monitoring is of uncertain value in patients treated with *Tanzeum*. Patients should be counseled regarding the risk and symptoms of thyroid tumors.

EFFICACY DATA (PRIMARY ENDPOINT)

- *Tanzeum* has been studied as monotherapy and in combination with metformin, metformin and a sulfonylurea, a thiazolidinedione (with and without metformin), and insulin glargine (with or without oral anti-diabetic drugs). The efficacy of *Tanzeum* was compared with placebo, glimepiride, pioglitazone, liraglutide, sitagliptin, insulin lispro, and insulin glargine. Trials evaluated the use of *Tanzeum* 30 mg and 50 mg. Five of the 8 trials allowed optional uptitration of *Tanzeum* from 30 mg to 50 mg if glycemic response with 30 mg was inadequate.
- The efficacy of *Tanzeum* was evaluated in a 52-week, randomized, double-blind, placebo-controlled, multicenter trial (HARMONY 2).⁽²⁾ In this trial, 296 patients with T2DM inadequately controlled on diet and exercise were randomized (1:1:1) to *Tanzeum* 30 mg once weekly, *Tanzeum* 30 mg once weekly uptitrated to 50 mg once weekly at Week 12, or placebo. A decrease in HbA_{1c} from baseline to week 52 was observed in group treated with *Tanzeum* 30 mg (-0.7%, N = 100) and the group treated with *Tanzeum* 50 mg (-0.9%, N = 97), and increased in the group treated with placebo (+0.2%, N = 99). The treatment differences (*Tanzeum* - placebo) of -0.8% (95% CI: 1.1, 0.6; *P* < 0.0001) for patients on *Tanzeum* 30 mg and -1.0% (95% CI: 1.3, 0.8; *P* < 0.0001) for patients on *Tanzeum* 50 mg were both statistically significant.
- The efficacy of *Tanzeum* was evaluated in a 104-week randomized, double-blind, multicenter trial in 999 patients with T2DM inadequately controlled metformin therapy (≥1,500 mg daily) (HARMONY 3).⁽³⁾ In this trial, *Tanzeum* 30 mg weekly (with optional uptitration to 50 mg weekly after a minimum of 4 weeks) was compared with placebo, sitagliptin 100 mg daily, or glimepiride 2 mg daily (with optional titration to 4 mg daily). A decrease in HbA_{1c} from baseline to week 104 was observed in groups treated with *Tanzeum* (-0.6%, N = 297), sitagliptin (-0.3%, N = 300), and glimepiride (-0.4%, N = 302), while an increase was observed in the group treated with placebo (0.3 %, N = 100). The treatment difference was statistically significant between *Tanzeum* and placebo (-0.9%; 95% CI: -1.16%, -0.65%, *P* < 0.0137), sitagliptin (-0.4%; 95% CI: -0.53%, -0.1%, *P* < 0.0137) and glimepiride (-0.3%; 95% CI: -0.45%, -0.09%, *P* < 0.0137).
- The efficacy of *Tanzeum* was evaluated in a 52-week randomized, double-blind, multicenter trial in 299 patients with T2DM inadequately controlled on pioglitazone ≥30 mg daily (with or without metformin ≥1,500 mg daily) (HARMONY 1).⁽⁴⁾ Patients were randomized to receive *Tanzeum* 30 mg weekly or placebo. A decrease in mean HbA_{1c} from baseline to week 52 was observed in both the group treated

with *Tanzeum* (-0.8%, N = 150) and the group treated with placebo (-0.1%, N = 149), resulting in a significant treatment difference of -0.8% (95% CI: -0.95%, -0.56%; $P < 0.0001$).

- The efficacy of *Tanzeum* was evaluated in a 52-week randomized, double-blind, multicenter trial in 657 patients with T2DM inadequately controlled on metformin ($\geq 1,500$ mg daily) and glimepiride (4 mg daily) (HARMONY 5).⁽²⁾ Patients were randomized to receive *Tanzeum* 30 mg weekly (with optional uptitration to 50 mg weekly after a minimum of 4 weeks), placebo, or pioglitazone 30 mg daily (with optional titration to 45 mg/day). A decrease in HbA_{1c} from baseline to week 52 was observed in both the group treated with *Tanzeum* (-0.6%, N = 269) and the group treated with pioglitazone (-0.8%, N = 273), while an increase was observed in the group treated with placebo (+0.3%, N = 115). The treatment difference for *Tanzeum* compared with placebo was statistically significant (-0.9%; 95% CI: 1.07, 0.68, $P < 0.0001$). The treatment difference for *Tanzeum* compared with pioglitazone was 0.25% (95% CI: 0.10%, 0.40%), which exceeded the pre-specified non-inferiority margin of 0.3% for the upper bounds of the CI. *Tanzeum* provided less HbA_{1c} reduction than pioglitazone and the treatment was statistically significant.
- The efficacy of *Tanzeum* was evaluated in a 32-week, randomized, open-label, non-inferiority trial in 805 patients with T2DM inadequately controlled on monotherapy or combination oral antidiabetic therapy (metformin, thiazolidinedione, sulfonylurea, or a combination of these) (HARMONY 7).⁽⁵⁾ Patients were randomized to *Tanzeum* 30 mg weekly (with uptitration to 50 mg weekly at Week 6) or liraglutide 1.8 mg daily (titrated up from 0.6 mg at Week 1, and 1.2 mg at Week 1 to Week 2). A decrease in HbA_{1c} from baseline at week 32 was observed in both the group treated with *Tanzeum* (-0.8%, N = 402) and the group treated with liraglutide (-1.0%, N = 403), resulting in a treatment difference of 0.2% (95% CI: 0.08%, 0.34%). Since the upper bound of the 95% CI exceeded the pre-specified non-inferiority margin of 0.3%, non-inferiority was not established. *Tanzeum* provided less HbA_{1c} reduction than liraglutide and the treatment difference was statistically significant.
- The efficacy of *Tanzeum* was evaluated in a 52-week, randomized (2:1), open-label, non-inferiority trial in 735 patients with T2DM who were inadequately controlled on metformin $\geq 1,500$ mg daily (with or without sulfonylurea) (HARMONY 4).⁽⁶⁾ Patients were randomized to receive *Tanzeum* 30 mg weekly (with optional uptitration to 50 mg weekly) or insulin glargine (started at 10 units and titrated weekly per prescribing information). A decrease in HbA_{1c} from baseline at week 52 was observed in both the group treated with *Tanzeum* (-0.7%, N = 496) and the group treated with insulin glargine (-0.8%, N = 239). The treatment difference of 0.1% (95% CI: -0.04%, 0.27%) met the pre-specified non-inferiority margin of 0.3%.
- The efficacy of *Tanzeum* was evaluated in a 26-week, randomized, open-label, multicenter, non-inferiority trial in 563 patients with T2DM inadequately controlled on insulin glargine (started at 10 units and titrated to ≥ 20 units per day) (HARMONY 6).⁽⁷⁾ Patients were randomized to receive *Tanzeum* 30 mg once weekly (with uptitration to 50 mg if inadequately controlled after Week 8) or insulin lispro (administered daily at meal times, started according to standard of care and titrated to effect). A decrease in mean HbA_{1c} from baseline at week 26 was observed in both the group treated with *Tanzeum* (-0.8%, N = 282) and the group treated with insulin lispro (-0.7%, N = 281). The treatment difference of -0.2% (95% CI: -0.32%, 0.00%) met the pre-specified non-inferiority margin of 0.4%.
- The efficacy of *Tanzeum* was evaluated in a 26-week, randomized, double-blind, active-controlled trial in 486 patients with mild (n = 250), moderate (n = 200), and severe renal impairment (n = 36) inadequately controlled on a current regimen of diet and exercise or other antidiabetic therapy (HARMONY 8).⁽⁸⁾ Patients were randomized to receive *Tanzeum* 30 mg weekly (with uptitration to 50 mg weekly if needed as early as Week 4) or sitagliptin. Sitagliptin was dosed according to renal function (100 mg, 50 mg, and 25 mg daily in mild, moderate, and severe renal impairment, respectively). A decrease in mean HbA_{1c} from baseline at week 26 was observed in both the group treated with *Tanzeum* (-0.8%, N = 246) and the group treated with sitagliptin (-0.5%, N = 240). The treatment difference of -0.3% (95% CI: -0.49%, -0.15%) met the pre-specified non-inferiority margin of 0.4%, and also met criteria for superiority to sitagliptin ($P < 0.0003$).

CONTRAINDICATIONS

- *Tanzeum* is contraindicated in patients with a personal or family history of MTC or in patients with MEN 2.⁽²⁾
- *Tanzeum* is contraindicated in patients with a prior serious hypersensitivity reaction to albiglutide or to any of the product components.

WARNINGS AND PRECAUTIONS

- Nonclinical studies in rodents of clinically relevant doses of GLP-1 receptor agonists showed dose-related and treatment-duration-dependent increases in the incidence of thyroid C-cell tumors (adenomas and carcinomas).⁽²⁾ Carcinogenicity studies could not be conducted with *Tanzeum* because drug-clearing, anti-drug antibodies develop in animals used for these types of studies. It is unknown whether GLP-1 receptor agonists are associated with thyroid C-cell tumors, including MTC in humans. Across 8 Phase III clinical trials, MTC was diagnosed in 1 patient receiving *Tanzeum* and 1 patient receiving placebo. Both patients had markedly elevated serum calcitonin levels at baseline. *Tanzeum* is contraindicated in patients with a personal or family history of MTC or in patients with MEN 2. Counsel patients regarding the risk for MTC with the use of *Tanzeum* and inform them of symptoms of thyroid tumors (e.g., a mass in the neck, dysphagia, dyspnea, persistent hoarseness). The clinical value of routine monitoring of serum calcitonin to diagnose MTC in patients at risk for MTC has not been established. Elevated serum calcitonin is a biological marker of MTC. Patients with MTC usually have calcitonin values >50 ng/L. Patients with thyroid nodules noted on physical examination or neck imaging should be referred to an endocrinologist for further evaluation. Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with *Tanzeum*. Such monitoring may increase the risk of unnecessary procedures, due to the low specificity of serum calcitonin testing for MTC and a high background incidence of thyroid disease. If serum calcitonin is measured and found to be elevated, the patient should be referred to an endocrinologist for further evaluation.
- In clinical trials, acute pancreatitis has been reported in association with *Tanzeum*. Across 8 Phase III clinical trials, pancreatitis adjudicated as likely related to therapy occurred more frequently in patients receiving *Tanzeum* (6 of 2,365 [0.3%]) than in patients receiving placebo (0 of 468 [0%]) or active comparators (2 of 2,065 [0.1%]). After initiation of *Tanzeum*, observe patients carefully for signs and symptoms of pancreatitis (including persistent severe abdominal pain, sometimes radiating to the back and which may or may not be accompanied by vomiting). If pancreatitis is suspected, promptly discontinue *Tanzeum*. If pancreatitis is confirmed, *Tanzeum* should not be restarted. *Tanzeum* has not been studied in patients with a history of pancreatitis to determine whether these patients are at increased risk for pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.

- The risk of hypoglycemia is increased when *Tanzeum* is used in combination with insulin secretagogues (e.g., sulfonylureas) or insulin. Therefore, patients may require a lower dose of sulfonylurea or insulin to reduce the risk of hypoglycemia in this setting.
- Across 8 Phase III clinical trials, a serious hypersensitivity reaction with pruritus, rash, and dyspnea occurred in a patient treated with *Tanzeum*. If hypersensitivity reactions occur, discontinue use of *Tanzeum*; treat promptly per standard of care and monitor until signs and symptoms resolve.
- In patients treated with GLP-1 receptor agonists, there have been post-marketing reports of acute renal failure and worsening of chronic renal failure, which may sometimes require hemodialysis. Some of these events were reported in patients without known underlying renal disease. A majority of reported events occurred in patients who had experienced nausea, vomiting, diarrhea, or dehydration. In a trial of *Tanzeum* in patients with renal impairment, the frequency of such gastrointestinal reactions increased as renal function declined. Because these reactions may worsen renal function, use caution when initiating or escalating doses of *Tanzeum* in patients with renal impairment.
- There have been no clinical trials establishing conclusive evidence of macrovascular risk reduction with *Tanzeum* or any other antidiabetic drug.
- Adverse reactions, reported in $\geq 5\%$ of patients treated with *Tanzeum* and more frequently than in patients on placebo, were upper respiratory tract infection (14.2%), diarrhea (13.1%), nausea (11.1%), injection site reaction (10.5%), cough (6.9%), back pain (6.7%), arthralgia (6.6%), sinusitis (6.2%), and influenza (5.2%).

Some information contained in this response may not be included in the approved Prescribing Information for this product. The comparator data cited in this response does not necessarily establish superior or comparable safety or efficacy. This response is not intended to offer recommendations for administering our product in a manner inconsistent with its approved labeling.

In order for GlaxoSmithKline to monitor the safety of our products, we encourage healthcare professionals to report adverse events or suspected overdoses to the company at 888-825-5249. Please consult the attached Prescribing Information.

This response was developed according to the principles of evidence-based medicine and, therefore, references may not be all-inclusive.

REFERENCE(S)

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