125 mm X 313mm

Tirzide

Tirzepatide INN

Everest

COMPOSITION

TIRZIDE 2.5 INJECTION: Each pre-filled syringe contains Tirzepatide INN 2.5 mg in 0.5 mL solution for injection.

TIRZIDE 5 INJECTION: Each pre-filled syringe contains Tirzepatide INN 5 mg in 0.5 mL solution for injection.

TIRZIDE 7.5 INJECTION: Each pre-filled syringe contains Tirzepatide INN 7.5 mg in 0.5 mL solution for injection.

TIRZIDE 10 INJECTION: Each pre-filled syringe contains Tirzepatide INN 10 mg in 0.5 mL solution for injection.

PHARMACOLOGY

Tirzepatide is a GIP (Glucose-dependent insulinotropic polypeptide) receptor and GLP-1(Glucagon-like peptide) receptor agonist. Tirzepatide selectively binds to and activates both the GIP and GLP-1 receptors to reduce gastric emptying, stimulate satiety, decrease food intake, and improve glycemic control.

INDICATION

Tirzepatide is a glucagon-like peptide 1 (GLP-1) receptor and glucose-depedent insulinotropic polypeptide (GIP) receptor agonist indicated:

–as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

–as an adjunct to diet and exercise to reduce excess body weight and maintain weight reduction long term in adults with obesity or adults with overweight in the presence of at least one weight-related comorbid condition.

–to treat moderate to severe obstructive sleep apnea (OSA) in adults with obesity.

LIMITATIONS OF USE

- Coadministration with other Tirzepatide-containing products or with any GLP-1 receptor agonist is not recommended
- It has not been studied in patients with a history of pancreatitis.
- It is not indicated for use in patients with type 1 diabetes Mellitus.

DOSAGE AND ADMINISTRATION

Obese and/or Overweight and/or Diabetes Mellitus patients

Recommended starting dosage: 2.5 mg injected subcutaneously once weekly for 4 weeks. Increase the dosage in 2.5 mg increments after at least 4 weeks until recommended maintenance dosage is achieved. Consider treatment response and tolerability when selecting the maintenance dosage.

Long-Term Maintenance Dosage: 5 mg, 10 mg, or 15 mg injected subcutaneously once weekly.

Maximum Recommended Dosage: 15 mg injected subcutaneously once weekly.

Obstructive Sleep Apnea(OSA) with Obesity: The recommended maintenance dosage is 10 mg or 15 mg injected subcutaneously once weekly.

Recommendations Regarding Missed Dose

If a dose is missed, instruct patients to administer Tirzepatide as soon as possible within 4 days (96 hours) after the missed dose. If more than 4 days have passed, skip the missed dose and administer the next dose on the regularly scheduled day. In each case, patients can then resume their regular once weekly dosing schedule. The day of weekly administration can be changed, if necessary, as long as the time between the two doses is at least 3 days (72 hours).

CLINICAL PHARMACOLOGY

Pharmacodynamics

Tirzepatide lowers fasting and postprandial glucose concentration, decreases food intake, and reduces body weight in patients with type 2 diabetes mellitus. Tirzepatide enhances the first- and second-phase insulin secretion.

Pharmacokinetics

The pharmacokinetics of Tirzepatide is similar between healthy subjects, patients with overweight or obesity, patients with OSA and obesity, and patient with Type-2 diabetes mellitus. Steady-state plasma Tirzepatide concentrations were achieved following 4 weeks of once-weekly administration. Tirzepatide exposure increases in a dose-proportional manner.

Absorption

Following subcutaneous administration, the time to maximum plasma concentration of Tirzepatide ranges from 8 to 72 hours. The mean absolute bioavailability of Tirzepatide following subcutaneous administration is 80%. Similar exposure was achieved with subcutaneous administration of Tirzepatide in the abdomen, thigh, or upper arm.

Distribution

The mean apparent steady-state volume of distribution of Tirzepatide following subcutaneous administration in patients with type 2 diabetes mellitus is approximately 10.3 L. The mean apparent steady-state volumes of distribution of Tirzepatide following subcutaneous administration in patients with overweight or obesity and patients with OSA and obesity are approximately 9.7 L (29%) and 11.8 L (37%), respectively. Tirzepatide is highly bound to plasma albumin (99%).

Elimination

The elimination half-life of Tirzepatide is approximately 5-6 days.

Metabolism

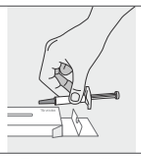
Tirzepatide is metabolized by proteolytic cleavage of the peptide backbone, beta-oxidation of the C20 fatty diacid moiety, and amide hydrolysis.

Excretion

The primary excretion routes of Tirzepatide metabolites are via urine and feces. Intact Tirzepatide is not observed in urine or feces.

Instructions for patient administration

1

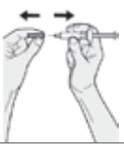


Remove Tirzide pre-filled syringe from the carton.

2

Clean the injection site with an alcohol pad. Let your skin dry before injecting.

3

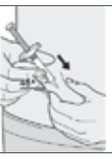


Hold the syringe in the middle and pull off the needle cap.

4

Pinch a fold of skin at the injection site. The figure above shows an example of pinching a fold of skin.

5

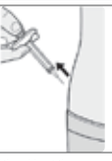


Insert the needle into the fold of the skin at about a 45° angle.

6

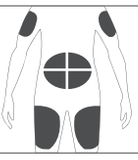
Relax the site. Push the plunger rod down slowly and steadily as far as it will go until the syringe is empty.

7



Pull the needle out of the skin at the same angle it was inserted. Throw away the syi1nge with the needle in a safe place.

8



Administer subcutaneously to the abdomen, thigh or upper arm. Choose a different site each time you inject.

125 mm X 313mm

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Mechanism of Action
Tirzepatide is a GIP receptor and GLP-1 receptor agonist. It is a 39-amino-acid modified peptide with a C20 fatty diacid moiety that enables albumin binding and prolongs the half-life. Tirzepatide selectively binds to and activates both the GIP and GLP-1 receptors, the targets for native GIP and GLP-1. Tirzepatide enhances first- and second-phase insulin secretion, and reduces glucagon levels, both in a glucose-dependent manner.

CONTRAINDICATION:
- Personal or family history of Medullary Thyroid Carcinoma (MTC) or in patients with Multiple Endocrine Neoplasia syndrome type 2.
- Known serious hypersensitivity to Tirzepatide or any of the excipients in Tirzide.

ADVERSE REACTION
The most common adverse reactions, reported in ≥5% of patients treated with Tirzepatide are:

- *Nausea.*
- *Diarrhea.*
- *Decreased Appetite.*
- *Vomiting.*
- *Constipation.*
- *Dyspepsia.*
- *Abdominal pain.*

WARNING AND PRECAUTIONS:
Severe Gastrointestinal Adverse Reactions: Use has been associated with gastrointestinal adverse reactions, sometimes severe. Tirzepatide is not recommended in patients with severe gastroparesis.

Acute Kidney Injury Due to Volume Depletion: Monitor renal function in patients reporting adverse reactions that could lead to volume depletion.

Acute Gallbladder Disease: Has been reported in clinical trials. If cholecystitis is suspected, gallbladder studies and clinical follow-up are indicated.

Acute Pancreatitis: Has been observed in patients treated with GLP-1 receptor agonists, or Tirzepatide. Discontinue if pancreatitis is suspected.

Hypersensitivity Reactions: Serious hypersensitivity reactions (e.g., anaphylaxis, angioedema) have been reported post-marketing with Tirzepatide. If suspected, advise patients to promptly seek medical attention and discontinue Tirzepatide.

Hypoglycemia: Concomitant use with insulin or an insulin secretagogue may increase the risk of hypoglycemia, including severe hypoglycemia. Reducing dose of insulin or insulin secretagogue may be necessary. Inform all patients of the risk of hypoglycemia and educate them on the signs and symptoms of hypoglycemia.

Diabetic Retinopathy Complications in Patients with Type 2 Diabetes Mellitus: Has not been studied in patients with non-proliferative diabetic retinopathy requiring acute therapy, proliferative diabetic retinopathy, or diabetic macular edema. Monitor patients with a history of diabetic retinopathy for progression.

Suicidal Behavior and Ideation: Monitor for depression or suicidal thoughts. Discontinue Tirzepatide if symptoms develop.

Pulmonary Aspiration During General Anesthesia or Deep Sedation: Has been reported in patients receiving GLP-1 receptor agonists undergoing elective surgeries or procedures. Instruct patients to inform healthcare providers of any planned surgeries or procedures.

USE IN SPECIFIC POPULATION:
Pregnancy: Weight loss offers no benefit to a pregnant patient and may cause fetal harm. Advise pregnant patients that weight loss is not recommended during pregnancy and to discontinue Tirzepatide when a pregnancy is recognized. Available data with Tirzepatide in pregnant patients are insufficient to evaluate for a drug-related risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. Based on animal reproduction studies, there may be risks to the fetus from exposure to Tirzepatide during pregnancy. Appropriate weight gain based on pre-pregnancy weight is currently recommended for all pregnant patients, including those with obesity or overweight, due to the obligatory weight gain that occurs in maternal tissues during pregnancy. There are risks to the mother and fetus associated with poorly controlled diabetes in pregnancy. Tirzepatide should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Tirzepatide and any potential adverse effects on the breastfed infant from Tirzepatide or from the underlying maternal condition.

Lactation: The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Tirzepatide and any potential adverse effects on the breastfed infant from Tirzepatide or from the underlying maternal condition.

Pediatric Patients: Safety and effectiveness of Tirzepatide have not been established in pediatric patients (younger than 18 years of age).

Geriatric Patients: No overall differences in safety or efficacy were detected between older patients and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Renal Impairment: No dosage adjustment of Tirzepatide is recommended for patients with renal impairment. In subjects with renal impairment including End-Stage Renal Disease (ESRD), no change in Tirzepatide pharmacokinetics (PK) was observed.

Hepatic Impairment: No dosage adjustment of Tirzepatide is recommended for patients with hepatic impairment. In a clinical pharmacology study in subjects with varying degrees of hepatic impairment, no change in Tirzepatide PK was observed.

DRUG INTERACTION
- Tirzepatide delays gastric emptying, and thereby has the potential to impact the absorption of concomitantly administered oral medications. Hormonal contraceptives that are not administered orally should not be affected.
- Consider reducing the dose of concomitantly administered insulin secretagogues (e.g., sulfonylurea) or insulin to reduce the risk of hypoglycemia.
- Monitor patients on oral medications with low therapeutic index (e.g., warfarin) when concomitantly administered.

PHARMACEUTICAL INFORMATION:

Storage
Keep out of the reach and sight of children. Store in a refrigerator at 2°C to 8°C. Do not freeze and protect from light. Do not use it if it has been frozen. To be taken and sold only on the prescription of a registered physician.

How Supplied
TIRZIDE 2.5 INJECTION: Each box contains 1 pre-filled syringe containing Tirzepatide INN 2.5 mg/0.5 mL, an alcohol pad, and first aid bandage.
TIRZIDE 5 INJECTION: Each box contains 1 pre-filled syringe containing Tirzepatide INN 5 mg/0.5 mL, an alcohol pad, and first aid bandage.
TIRZIDE 7.5 INJECTION: Each box contains 1 pre-filled syringe containing Tirzepatide INN 7.5 mg/0.5 mL, an alcohol pad, and first aid bandage.
TIRZIDE 10 INJECTION: Each box contains 1 pre-filled syringe containing Tirzepatide INN 10 mg/0.5 mL, an alcohol pad, and first aid bandage.

Manufactured by
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