

Glazita

(Sitagliptin Phosphate U.S.P.)

گلزیٹا

(سیٹاگلیپٹن فاسفیٹ یو.ایس.پی.)

COMPOSITION

Each **Glazita** 25mg film coated tablet contains Sitagliptin Phosphate Monohydrate equivalent to Sitagliptin 25mg.

Each **Glazita** 50mg film coated tablet contains Sitagliptin Phosphate Monohydrate equivalent to Sitagliptin 50mg.

Each **Glazita** 100mg film coated tablet contains Sitagliptin Phosphate Monohydrate equivalent to Sitagliptin 100mg.

DESCRIPTION

Glazita tablets contain Sitagliptin Phosphate, an orally-active inhibitor of the dipeptidyl peptidase-4 (DPP-4) enzyme.

CLINICAL PHARMACOLOGY

Mechanism of Action

Sitagliptin is a DPP-4 inhibitor, which is believed to exert its actions in patients with type 2 diabetes by slowing the inactivation of incretin hormones. Concentrations of the active intact hormones are increased by Sitagliptin, thereby increasing and prolonging the action of these hormones. Incretin hormones, including glucagon-like peptide-1 (GLP-1) and glucose-dependent insulintropic polypeptide (GIP), are released by the intestine throughout the day, and levels are increased in response to a meal. These hormones are rapidly inactivated by the enzyme, DPP-4. The incretins are part of an endogenous system involved in the physiologic regulation of glucose homeostasis. When blood glucose concentrations are normal or elevated, GLP-1 and GIP increase insulin synthesis and release from pancreatic beta cells by intracellular signaling pathways involving cyclic AMP. GLP-1 also lowers glucagon secretion from pancreatic alpha cells, leading to reduced hepatic glucose production. By increasing and prolonging active incretin levels, Sitagliptin increases insulin release and decreases glucagon levels in the circulation in a glucose-dependent manner. Sitagliptin demonstrates selectivity for DPP-4 and does not inhibit DPP-8 or DPP-9 activity in vitro at concentrations approximating those from therapeutic doses.

PHARMACOKINETICS

The pharmacokinetics of Sitagliptin has been extensively characterized in healthy subjects and patients with type 2 diabetes. The pharmacokinetics of Sitagliptin was generally similar in healthy subjects and in patients with type 2 diabetes.

Absorption: The absolute bioavailability of Sitagliptin is approximately 87%. Because coadministration of a high-fat meal with Sitagliptin had no effect on the pharmacokinetics, Sitagliptin may be administered with or without food.

Distribution: The fraction of Sitagliptin reversibly bound to plasma proteins is low (38%).

Metabolism: Approximately 79% of Sitagliptin is excreted unchanged in the urine with metabolism being a minor pathway of elimination.

Excretion: The apparent terminal $t_{1/2}$ following a 100 mg oral dose of Sitagliptin was approximately 12.4 hours. Elimination of Sitagliptin occurs primarily via renal excretion and involves active tubular secretion.

INDICATIONS

Monotherapy and Combination Therapy: Sitagliptin is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Important Limitations of Use: Sitagliptin should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings. Sitagliptin has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for the development of pancreatitis while using Sitagliptin.

DOSAGE AND ADMINISTRATION

The dosage of Sitagliptin is depends upon the severity of disease. Sitagliptin can be taken with or without food. In patients with type 2 diabetes, administration of Sitagliptin led to inhibition of DPP-4 enzyme activity for a 24-hour period.

Recommended Dosing: The recommended dose of Sitagliptin is 100 mg once daily. Sitagliptin can be taken with or without food.

Patients with Renal Insufficiency: For patients with mild renal insufficiency no dosage adjustment for Sitagliptin is required. For patients with moderate renal insufficiency the dose of Sitagliptin is 50 mg once daily. For patients with severe renal insufficiency the dose of Sitagliptin is 25 mg once daily. Sitagliptin may be administered without regard to the timing of dialysis.

Concomitant Use with an Insulin Secretagogue (e.g., Sulfonylurea) or with Insulin: When Sitagliptin is used in combination with an insulin secretagogue (e.g., sulfonylurea) or with insulin, a lower dose of the insulin secretagogue or insulin may be required to reduce the risk of hypoglycemia.

ADVERSE REACTIONS

Adverse reactions reported in $\geq 5\%$ of patients treated with Sitagliptin and more commonly than in patients treated with placebo are: upper respiratory tract infection, nasopharyngitis and headache. In the add-on to sulfonylurea and add-on to insulin studies, hypoglycemia was also more commonly

reported in patients treated with Sitagliptin.

DRUG INTERACTIONS

Digoxin: There was a slight increase in the area under the curve (AUC, 11%) and mean peak drug concentration (C_{max} , 18%) of digoxin with the co-administration of 100 mg Sitagliptin for 10 days. Patients receiving digoxin should be monitored appropriately. No dosage adjustment of digoxin or Sitagliptin is recommended.

WARNINGS AND PRECAUTIONS

Pancreatitis: After initiation of Sitagliptin, patients should be observed carefully for signs and symptoms of pancreatitis. If pancreatitis is suspected, Sitagliptin should promptly be discontinued and appropriate management should be initiated. It is unknown whether patients with a history of pancreatitis are at increased risk for the development of pancreatitis while using Sitagliptin.

Renal Impairment: Assessment of renal function is recommended prior to initiating Sitagliptin and periodically thereafter.

Use with Medications Known to Cause Hypoglycemia: A lower dose of sulfonylurea or insulin may be required to reduce the risk of hypoglycemia.

Hypersensitivity Reactions: There have been reports of serious hypersensitivity reactions in patients treated with Sitagliptin. These reactions include anaphylaxis, angioedema, and exfoliative skin conditions including Stevens-Johnson syndrome. Onset of these reactions occurred within the first 3 months after initiation of treatment with Sitagliptin, with some reports occurring after the first dose. If a hypersensitivity reaction is suspected, discontinue Sitagliptin, assess for other potential causes for the event, and institute alternative treatment for diabetes. Angioedema has also been reported with other dipeptidyl peptidase-4 (DPP-4) inhibitors.

Macrovascular Outcomes: There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with Sitagliptin or any other anti-diabetic drug.

USE IN SPECIFIC POPULATIONS

Pregnancy: Pregnancy Category B: There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers: It is not known whether Sitagliptin is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Sitagliptin is administered to a nursing woman.

Pediatric Use: Safety and effectiveness of Sitagliptin in pediatric patients under 18 years of age have not been established.

Geriatric Use: This drug is known to be substantially excreted by the kidney. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection in the elderly, and it may be useful to assess renal function in these patients prior to initiating dosing and periodically thereafter.

CONTRAINDICATIONS

History of a serious hypersensitivity reaction to Sitagliptin, such as anaphylaxis or angioedema.

OVERDOSAGE

In the event of an overdose, it is reasonable to employ the usual supportive measures, e.g., remove unabsorbed material from the gastrointestinal tract, employ clinical monitoring (including obtaining an electrocardiogram), and institute supportive therapy as dictated by the patient's clinical status. Sitagliptin is modestly dialyzable. In clinical studies, approximately 13.5% of the dose was removed over a 3-to 4-hour hemodialysis session. Prolonged hemodialysis may be considered if clinically appropriate. It is not known if Sitagliptin is dialyzable by peritoneal dialysis.

PRESENTATION

Glazita 25mg Tablet : 2x7's/pack.
Glazita 50mg Tablet : 2x7's/pack.
Glazita 100mg Tablet : 2x7's/pack.

خوراک:

ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

DOSAGE

As directed by the physician.

ہدایات:

دوا کو ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔

INSTRUCTIONS

Store below 30°C.
Protect from sunlight and moisture.
Keep out of reach of children.

دھوپ اور نمی سے بچائیں۔

بچوں کی پہنچ سے دور رکھیں۔

Detailed prescribing information is available on request.

Manufactured by:
AsianContinental (Pvt.) Ltd.
D-32, S.I.T.E. II, Super Highway,
Karachi-Pakistan.



An ISO Certified Company

LFT/046/00