Glusit Tablets

گلوسٹ گولیاں

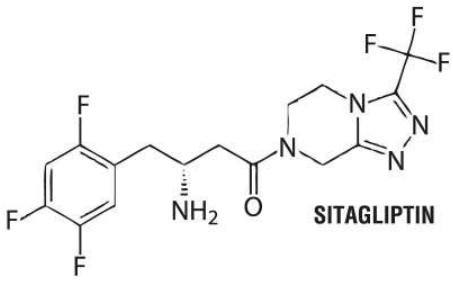
(Sitagliptin)

QUALITATIVE & QUANTITATIVE COMPOSITION:
Glusit (Sitagliptin) is available for oral administration as:

1. Glusit Tablets 50mg
Each film coated tablet contains:
Sitagliptin phosphate monohydrate equivalent to Sitagliptin.....50mg

2. Glusit Tablets 100mg
Each film coated tablet contains:
Sitagliptin phosphate monohydrate equivalent to Sitagliptin.....100mg

DESCRIPTION
GLUSIT (Sitagliptin) is an orally-active, potent and highly selective inhibitor of the dipeptidyl peptidase-4 (DPP-4) enzyme used for the treatment of type 2 diabetes. Chemically, it is 7-[(3R)-3- amino -1-oxo -4- (2,4,5- trifluorophenyl) butyl] -5,6,7,8 -tetrahydro -3- (trifluoromethyl)-1,2,4-triazolo[4,3-a]pyrazine phosphate (1:1) monohydrate. Its molecular formula is $C_{16}H_{15}F_6N_5O \cdot H_3PO_4 \cdot H_2O$ and the structural formula is:



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, including glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP). The incretin 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.

Pharmacokinetics
Absorption
Following oral administration of a 100mg dose, Sitagliptin absorbs rapidly with peak plasma concentration (median Tmax) occurring 1 to 4 hours post-dose, mean plasma AUC of Sitagliptin is 8.52 µm•hr, with Cmax 950nM. The absolute bioavailability of Sitagliptin is approximately 87%. Plasma AUC of Sitagliptin increased in a dose-proportional manner. Distribution. The mean volume of distribution at steady state following a single 100mg intravenous dose of Sitagliptin is approximately 198 liters. The fraction of Sitagliptin reversibly bound to plasma proteins is low (38%). Metabolism & Excretion. Sitagliptin is primarily eliminated unchanged in urine (approximately 79%), and metabolism is a minor pathway. Following administration of an oral [14C] Sitagliptin dose, approximately 100% of the administered radioactivity eliminate in feaces (13%) or urine (87%) within one week of dosing. The apparent terminal t1/2 following a 100mg oral dose of Sitagliptin is approximately 12.4 hours and renal clearance is approximately 350mL/min.

Special Populations
Renal Insufficiency
Patients with mild renal insufficiency did not have a clinically meaningful increase in the plasma concentration of Sitagliptin. The plasma AUC of Sitagliptin increases approximately 2-fold in patients with moderate renal insufficiency, and an approximately 4-fold in patients with severe renal insufficiency and in patients with ESRD on hemodialysis. Hepatic Insufficiency. There is no clinical experience in patients with severe hepatic insufficiency (Child-Pugh score> 9). However, because Sitagliptin is primarily renally eliminated, severe hepatic insufficiency is not expected to affect the pharmacokinetics of Sitagliptin.
Elderly
Elderly subjects (65 to 80 years) had approximately 19% higher plasma concentrations of Sitagliptin as compared to younger subjects.

THERAPEUTIC INDICATIONS
Sitagliptin is indicated in patients with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemic control as:
- Monotherapy
- Dual Therapy
In combination with Metformin HCl or with a sulfonylurea or with a PPARß agonist (i.e., thiazolidinediones) when the treatment with the single agent alone, with diet and exercise, does not provide adequate glycemic control.
- Triple Therapy
In combination with Metformin HCl and a sulfonylurea or with Metformin HCl and a PPARß (i.e., thiazolidinediones) when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.
- Combination with Insulin.

DOSAGE AND ADMINISTRATION
The recommended dose of GLUSIT (Sitagliptin) is 100mg once daily as monotherapy or as combination therapy with Metformin HCl, a sulfonylurea, insulin (with or without Metformin HCl), a PPARß agonist (i.e., thiazolidinediones), Metformin HCl plus a sulfonylurea, or Metformin HCl plus a PPARß agonist (i.e., thiazolidinediones).
When GLUSIT (Sitagliptin) is used in combination with a sulfonylurea or with insulin, a lower dose of sulfonylurea or insulin may be considered to reduce the risk of sulfonylurea or insulin-induced hypoglycemia.
Co-administration of a high-fat meal with GLUSIT (Sitagliptin) had no effect on the pharmacokinetics, GLUSIT (Sitagliptin) may be administered with or without food. If a dose of GLUSIT (Sitagliptin) is missed, it should be taken as soon as the patient remembers. A double dose should not be taken on the same day.

Special Populations
Renal Insufficiency
For patients with mild renal insufficiency (creatinine clearance [Clcr 50mL/min, approximately corresponding to serum creatinine levels of ≤1.7mg/dL in men and ≤1.5mg/dL in women), no dosage adjustment for Sitagliptin is required.
For patients with moderate renal insufficiency (Clcr ≥30 to <50 mL/min, approximately corresponding to serum creatinine levels of ≤1.7 to ≤3.0mg/dL in men and >1.5 to ≤2.5 mg/dL in women), the dose of Sitagliptin is 50 mg once daily.
For patients with severe renal insufficiency (Clcr<30 mL/min, approximately corresponding to serum creatinine levels of >3.0 mg/dL in men and >2.5 mg/dL in women) or with end-stage renal disease (ESRD) requiring hemodialysis or peritoneal dialysis, the dose of Sitagliptin is 25mg once daily. Sitagliptin may be administered without regard to the timing of hemodialysis.
Elderly
No dose adjustment is required based on age

ADVERSE REACTIONS
Monotherapy
Upper respiratory-tract infections, headache and nasopharyngitis.

Sitagliptin with Metformin HCl
Common: Nausea.
Uncommon: Somnolence, diarrhea, upper abdominal pain and blood glucose decreased.

Sitagliptin with Sulfonylurea
Common: Hypoglycemia.

Sitagliptin with Pioglitazone
Common: Hypoglycemia, flatulence and peripheral edema.

Sitagliptin with Sulfonylurea and Metformin HCl
Very common: Hypoglycemia.
Common: Constipation.

Sitagliptin with a Rosigiltazone and Metformin HCl
Common: Hypoglycemia, headache, diarrhea, vomiting and peripheral edema.

Sitagliptin with Insulin
Common: Influenza, hypoglycemia and headache.
Uncommon: Dry mouth and constipation.

CONTRAINDICATIONS
Sitagliptin is contraindicated in:
- Patients with known hypersensitivity to Sitagliptin or any of the components of the product.
- Patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.
- Children below 18 years of age.
Pregnancy
The safety of Sitagliptin in pregnant women is not known. Sitagliptin, like other oral antihyperglycemic agents, is not recommended for use in pregnancy.
Nursing Mother
It is not known whether Sitagliptin is excreted in human milk. Because many drugs are excreted in human milk, Sitagliptin should not be administered during nursing.

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.
- Hypoglycemia
When Sitagliptin is used in combination with a sulfonylurea or with insulin, medications known to cause hypoglycemia, the incidence of hypoglycemia increases when used in combination with a sulfonylurea or with insulin. Therefore, a lower dose of sulfonylurea or insulin may be required to reduce the risk of hypoglycemia.
Drug Interactions
Digoxin
Sitagliptin has a small effect on plasma digoxin concentrations. No dosage adjustment of digoxin is recommended. However, patients at risk of digoxin toxicity should be monitored for this when Sitagliptin and digoxin are administered concomitantly.

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. Prolonged hemodialysis may be considered if clinically appropriate. It is not known if Sitagliptin is dialyzable by peritoneal dialysis.

STORAGE
Store below 25°C (Excursions permitted between 15°C to 30°C).
Protect from sunlight & moisture.
The expiration date refers to the product correctly stored at the required conditions.

HOW SUPPLIED
GLUSIT (Sitagliptin) Tablets 50mg are available in alu alu blister packs of 14's.
GLUSIT (Sitagliptin) Tablets 100mg are available in alu alu blister packs of 14's.

Keep out of reach of children.
To be sold on prescription of a registered medical practitioner only.

Glusit Tablets 50mg:
Product Specs:Manufacturer's
Mfg. Lic. No.: 000046
Reg. No.: 076369

Glusit Tablets 100mg:
Product Specs:Manufacturer's
Mfg. Lic. No.: 000046
Reg. No.: 076370

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