

Sitapin

(Sitagliptin) Tablets USP

50mg & 100mg Tablets

سیٹاپین
(سیتاگلیپٹین) ٹیبلیٹس یو ایس پی
50 ملی گرام اور 100 ملی گرام ٹیبلیٹس

COMPOSITION

Sitapin Tablets 50mg.
Each film coated tablet contains:
Sitagliptin 50mg.
(As Sitagliptin phosphate monohydrate USP)
Finished Product Specification: USP

Sitapin Tablets 100mg.
Each film coated tablet contains:
Sitagliptin 100mg.
(As Sitagliptin phosphate monohydrate USP)
Finished Product Specification: USP

DESCRIPTION

Sitapin (Sitagliptin) is an orally-active, potent and highly selective inhibitor of the dipeptidyl peptidase-4 (DPP-4) enzyme used for the management of type 2 diabetes.

CLINICAL PHARMACOLOGY

Pharmacodynamics:

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 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.

Pharmacokinetics:

Absorption: Following oral administration of a 100mg dose, sitagliptin absorbs rapidly with peak plasma concentration (median T_{max}) occurring 1 to 4 hours post dose. 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%).

Elimination: Sitagliptin is primarily eliminated in urine (87%) & in feces (13%). Renal clearance is approximately 350 ml/min.

Special Population:

Renal Impairment: Patients with mild renal impairment 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 impairment, and an approximately 4-fold in patients with severe renal impairment and in patients with ESRD on hemodialysis.

Hepatic Impairment: There is no clinical experience in patients with severe hepatic impairment (Child-Pugh score > 9). However, because sitagliptin is primarily renally eliminated, severe hepatic impairment is not expected to affect the pharmacokinetics of sitagliptin.

Elderly: Elderly subjects (65 to 80 years) had approximately 19% higher plasma concentrations of sitagliptin compared to younger subjects.

THERAPEUTIC INDICATIONS

Sitapin (Sitagliptin) is indicated in patients with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycemic control as:

- **Monotherapy:** In patients inadequately controlled by diet and exercise alone and for whom metformin is inappropriate due to contraindications or tolerance.

- **Dual Therapy:** In combination with metformin HCl or with a sulphonylurea or with a PPAR γ 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 sulphonylurea or with metformin HCl and a PPAR γ (i.e., thiazolidinediones) when dual therapy with these agents, with diet and exercise, does not provide adequate glycemic control.

- **Combination with Insulin:** Sitapin is also indicated as add-on to insulin (with or without metformin) when diet and exercise plus stable dose of insulin do not provide adequate glycaemic control.

DOSAGE AND ADMINISTRATION

The dose is 100mg sitagliptin once daily. When used in combination with metformin and/or a PPAR γ agonist, the dose of metformin and/or PPAR γ agonist should be maintained and Sitapin administered concomitantly.

When SITAPIN (Sitagliptin) is used in combination with a sulphonylurea or with insulin, a lower dose of sulphonylurea or insulin may be considered to reduce the risk of sulphonylurea or insulin-induced hypoglycemia.

SITAPIN (Sitagliptin) may be administered with or without food. If a dose of SITAPIN (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 Population:

Renal Impairment: When considering the use of sitagliptin in combination with another anti-diabetic medicinal Product, its conditions for use in patients with renal impairment should be checked. For patients with mild renal impairment (glomerular filtration rate [GFR] > 60 to < 90ml/min), no dose adjustment is required.

For patients with moderate renal impairment (GFR > 45 to < 60mL/min), no dosage adjustment is required.

For patients with moderate renal impairment (GFR > 30 to < 45mL/min), the dose of Sitagliptin

is 50 mg once daily.

For patients with severe renal impairment (GFR > 15 to <30mL/min) or with end-stage renal disease (ESRD) (GFR < 15mL/min), including those requiring haemodialysis or peritoneal dialysis, the dose of Sitagliptin is 25mg once daily. Treatment may be administered without regard to the timing of dialysis. Because there is a dosage adjustment based upon renal function, assessment of renal function is recommended prior to initiation of Sitagliptin and periodically thereafter.

Elderly: No dose adjustment is required based on age.

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.

ADVERSE REACTIONS

Monotherapy: Upper respiratory-tract infections, headache and nasopharyngitis.

Sitagliptin with Metformin:

Common: Nausea.

Uncommon: Somnolence, diarrhea, upper abdominal pain and blood glucose decreased.

Sitagliptin with Sulphonylurea:

Common: Hypoglycemia.

Sitagliptin with Pioglitazone:

Common: Hypoglycemia, flatulence and peripheral edema.

Sitagliptin with Sulphonylurea and Metformin:

Very common: Hypoglycemia.

Common: Constipation.

Sitagliptin with Insulin:

Common: Influenza and hypoglycemia.

Uncommon: Dry mouth and headache.

WARNINGS AND PRECAUTIONS

Pancreatitis: Use of DPP-4 inhibitors has been associated with a risk of developing acute pancreatitis. Patients should be informed of the characteristic symptom of acute pancreatitis: persistent, severe abdominal pain. Resolution of pancreatitis has been observed after discontinuation of sitagliptin (with or without supportive treatment), but very rare cases of necrotizing or haemorrhagic pancreatitis and/or death have been reported.

Hypoglycemia: When sitagliptin is used in combination with a sulphonylurea or with insulin (medications known to cause hypoglycemia), the incidence of hypoglycemia increases. Therefore, a lower dose of sulphonylurea or insulin may be required to reduce the risk of hypoglycemia.

Pregnancy & Lactation: Due to lack of human data, Sitagliptin should not be used during pregnancy & breast-feeding.

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 30°C.

Protect from heat, light and moisture.

PRESENTATION

Sitapin (Sitagliptin) Tablets 50mg are available in Alu-Alu blister pack of 14's.

Sitapin (Sitagliptin) Tablets 100mg are available in Alu-Alu blister pack of 14's.

Keep all medicines out of the reach of children.

To be sold on prescription of a registered medical practitioner only.



Manufactured by :

Indus Pharma (Pvt.) Ltd.
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