SPMC
SITAGLIPTIN TABLETS BP 50 mg

PRESENTATION:
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Pack size- Bulk pack -500'S /1000'S tablets**,**
Blister- 200 Tablets (20X10)

Light brown colour, circular, double convex tablets of 6.30 mm diameter.Each coated tablet contains Sitagliptin phosphate monohydrate, equivalent to 50 mg Sitagliptin.

MECHANISM OF ACTION:
Sitagliptin, a dipeptidyl peptidase-4 (DPP-4) inhibitor, improves glycaemic control by enhancing the levels and prolonging the effects of active incretin hormones such as glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP). These hormones regulate glucose homeostasis and are rapidly inactivated by the DPP-4 enzyme. Both GLP-1 and GIP increase insulin synthesis and release from pancreatic β cells by intracellular signalling pathways involving cyclic AMP, while GLP-1 lowers glucagon secretion from pancreatic α cells resulting in lower hepatic glucose production. Sitagliptin prevents the hydrolysis of incretin hormones caused by DPP-4 enzyme, thereby increasing and prolonging active incretin levels that elevate insulin release and decrease glucagon concentrations in the circulation (glucose-dependent manner).

INDICATIONS AND DOSE:
Type 2 diabetes mellitus as monotherapy (if metformin inappropriate), or in combination with other antidiabetic drugs (including insulin) if existing treatment fails to achieve adequate glycaemic control
Adult: 100 mg once daily, for further information on use with other antidiabetic drugs—consult product literature

DOSE ADJUSTMENTS DUE TO INTERACTIONS:
Dose of concomitant sulfonylurea or insulin may need to be reduced.

SIDE EFFECTS:
Significant: Hypoglycaemia (particularly in combination with sulfonylureas or insulins); worsening renal function, including acute renal failure (may require dialysis); severe and disabling arthralgia, bullous pemphigoid.
Gastrointestinal disorders: Constipation, vomiting, mouth ulceration, stomatitis.
Musculoskeletal and connective tissue disorders: Myalgia, back pain.
Nervous system disorders: Headache, dizziness.
Respiratory, thoracic and mediastinal disorders: Nasopharyngitis, upper respiratory tract infection, interstitial lung disease.
Skin and subcutaneous tissue disorders: Rash, urticaria, pruritus.
Potentially Fatal: Acute pancreatitis including haemorrhagic or necrotising pancreatitis, serious hypersensitivity reactions (e.g. anaphylaxis, angioedema, cutaneous vasculitis, exfoliative skin conditions including Stevens-Johnson syndrome).

SIDE-EFFECTS, FURTHER INFORMATION:
Discontinue if symptoms of acute pancreatitis occur such as persistent, severe abdominal pain.
Potentially Fatal: Acute pancreatitis including haemorrhagic or necrotising pancreatitis, serious hypersensitivity reactions (e.g. anaphylaxis, angioedema, cutaneous vasculitis, exfoliative skin conditions including Stevens-Johnson syndrome).

PATIENT COUNSELING INFORMATION:
This drug, particularly when taken in combination with other certain antidiabetics, may impair the patient's ability to concentrate and react due to hypoglycaemia; if affected, do not drive or operate machinery.

MONITORING REQUIREMENTS:
Obtain renal function before treatment initiation and periodically thereafter. Monitor HbA_{1c} (at least twice yearly in patients with stable glycaemic control; quarterly in patients not meeting therapy goals or with changes in treatment); serum glucose. Assess for signs and symptoms of pancreatitis, heart failure, and hypersensitivity reactions; development of erosions or blisters.

ADMINISTRATION:
May be taken with or without food.

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 < 90 mL/min), no dose adjustment is required. For patients with moderate renal impairment (GFR ≥ 45 to < 60 mL/min), no dosage adjustment is required. For patients with moderate renal impairment (GFR ≥ 30 to < 45 mL/min), the dose of Sitagliptin is 50 mg once daily. For patients with severe renal impairment (GFR ≥ 15 to <30 mL/min) or with end-stage renal disease (ESRD) (GFR < 15 mL/min), including those requiring haemodialysis or peritoneal dialysis, the dose of Sitagliptin is 25 mg 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.

HEPATIC IMPAIRMENT:
No dose adjustment is necessary for patients with mild to moderate hepatic impairment. Januvia has not been studied in patients with severe hepatic impairment and care should be exercised. However, because sitagliptin is primarily renally eliminated, severe hepatic impairment is not expected to affect the pharmacokinetics of sitagliptin.

SPECIAL PRECAUTIONS:
Patient with history of pancreatitis, heart failure, or history of serious hypersensitivity reaction (e.g. angioedema) with other DPP-4 inhibitors. Patient undergoing periods of stress (e.g. trauma, infection, fever, surgery). Not indicated for use in patients with type 1 diabetes mellitus or diabetic ketoacidosis. Moderate to severe (eGFR <45 mL/min/1.73 m^2) renal impairment, including ESRD requiring haemodialysis or peritoneal dialysis. Pregnancy and lactation.

CONTRAINDICATION:
Hypersensitivity to the active substance, Ketoacidosis

PREGNANCY:
There are no adequate data from the use of sitagliptin in pregnant women. Studies in animals have shown reproductive toxicity at high doses. The potential risk for humans is unknown. Due to lack of human data, Sitagliptin should not be used during pregnancy.

BREAST FEEDING:
It is unknown whether sitagliptin is excreted in human breast milk. Animal studies have shown excretion of sitagliptin in breast milk. sitagliptin should not be used during breast-feeding.

DRUG INTERACTIONS:
Increased risk of hypoglycaemia when co-administered with sulfonylureas (e.g. glipizide, glimepiride) and insulins; consider lowering the dose of insulins or sulfonylureas. May slightly increase the serum concentration of digoxin.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:
Sitagliptin. has no or negligible influence on the ability to drive and use machines. However, when driving or using machines, it should be taken into account that dizziness and somnolence have been reported. In addition, patients should be alerted to the risk of hypoglycaemia when Januvia is used in combination with a sulphonylurea or with insulin.

OVERDOSAGE:
During controlled clinical trials in healthy subjects, single doses of up to 800 mg sitagliptin were administered. Minimal increases in QTc, not considered to be clinically relevant, were observed in one study at a dose of 800 mg sitagliptin. There is no experience with doses above 800 mg in clinical studies. In Phase I multiple-dose studies, there were no dose-related clinical adverse reactions observed with sitagliptin with doses of up to 600 mg per day for periods of up to 10 days and 400 mg per day for periods of up to 28 days.
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 if required.
Sitagliptin is modestly dialysable. In clinical studies, approximately 13.5 % of the dose was removed over a 3- to 4-hour haemodialysis session. Prolonged haemodialysis may be considered if clinically appropriate. It is not known if sitagliptin is dialysable by peritoneal dialysis.

STORAGE:
Keep tightly closed in a cool & dry place in a original container at a temperature not exceeding 30 ^{0}C.

Keep all the medicines away from the reach of children

Manufactured by:
State Pharmaceuticals Manufacturing Corporation
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