TAGIP (Sitagliptin)

Film Coated Tablets

COMPOSITION

TAGIP 25 mg tablets: Each film coated tablet contains: Sitagliptin (as phosphate) 25 mg.

TAGIP 50 mg tablets: Each film coated tablet contains: Sitagliptin (as phosphate) 50 mg.

TAGIP 100 mg tablets: Each film coated tablet contains: Sitagliptin (as phosphate) 100 mg.

DESCRIPTION

TAGIP tablet contains Sitagliptin Phosphate, an orally-active inhibitor of the dipeptidyl peptidase-4 (DPP-4) enzyme.

PHARMACOLOGICAL PROPERTIES

Mechanism of Action

Sitagliptin inhibits dipeptidyl peptidase-4 (DPP-4), an enzyme responsible for degradation of the incretin hormones glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP). 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 insulinotropic 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. 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, TAGIP increases insulin release and decreases glucagon levels in the circulation in a glucose-dependent manner.

Pharmacokinetics

Sitagliptin is absorbed from the gastrointestinal tract, with a peak plasma concentrations occurring about 1 to 4 hours after an oral dose, and a bioavailability of about 87%. Because co-administration of a high-fat meal with Sitagliptin had no effect on the pharmacokinetics, Sitagliptin may be administered with or without food. It undergoes minimal metabolism, mainly by the cytochrome P450 isoenzymes CYP3A4, and to a lesser extent by CYP2C8. About 79% of the dose excreted unchanged in the urine. Renal excretion of Sitagliptin involves active tubular secretions; it is a substrate for organic anion transporter-3 and P-glycoprotein. Its terminal half life is about 12 hours.

INDICATIONS

- **TAGIP** (Sitagliptin) is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus either as monotherapy or combination therapy.
- **TAGIP** (Sitagliptin) should not be used in type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis.

DOSAGE AND ADMINISTRATION

- The recommended dose of **Tagip** is 100mg once daily. Sitagliptin can be taken with or without food.
- Patients with mild renal impairment (creatinine clearance 50ml/min or more); no adjustment necessary, 100mg once daily.
- Patients with moderate renal impairment (creatinine clearance 30 to less than 50ml/min); 50mg once daily.
- Patients with severe renal impairment (creatinine clearance less than 30ml/min); or end stage renal disease requiring haemodialysis or peritoneal dialysis; 25 mg once daily. It may be given without regard to the timing of haemodialysis.

CONTRAINDICATIONS

TAGIP is contraindicated in patients with;

- Hypersensitivity to the active substance or to any of the excipients.
- Type 1 diabetes mellitus or for the treatment of ketoacidosis.

ADVERSE EFFECTS

The reported adverse effects with Sitagliptin include headache, dizziness and gastrointestinal disturbances. Peripheral oedema has occurred, particularly on patients also being treated with a thiazolidinedione. Upper Respiratory tract infections and nasopharyngitis have also occurred, but a casual relationship has not been established. Rash and other hypersensitivity reactions including anaphylaxis, angioedema, urticaria, cutaneous vasculitis and Stevens - Johnson syndrome have been reported. There have also been isolated cases of elevated liver enzyme values and pancreatitis, including haemorrhagic and necrotizing pancreatitis. Impaired renal function, including acute renal failure (some times requiring dialysis), has also been reported. Hypoglycaemia is unlike with Sitagliptin given alone, but it may contribute to hypoglycaemia caused by other oral antidiabetics such as sulfonylureas.

DRUG INTERACTION
The efficacy of Sitagliptin may be affected by other drugs that have independent effect on blood glucose. Patients receiving digoxin should be monitored appropriately. No dosage adjustment of digoxin or **TAGIP** is recommended.

WARNINGS AND PRECAUTIONS

- **Driving:** diabetes Mellitus, its complications and the medications used to treat it, may affect a patient's' ability to drive safely.
- Patients should be observed carefully for any sign and symptoms of pancreatitis. If pancreatitis is suspected, TAGIP should promptly discontinue and appropriate management should be initiated.
- Sitagliptin has been studied in patients with type 2 diabetes mellitus and renal impairment. Based on the creatinine clearance of the renal impairment patients' the dose of TAGIP is adjusted accordingly.
- Use with medications known to cause hypoglycaemia
- **Hypersensitivity reactions;** Symptoms of allergic reactions (including rash, hives, and swelling of the face, lips, tongue, and throat that may cause difficulty in breathing or swallowing) occur, patients must stop taking Sitagliptin and seek medical advice promptly. If a hypersensitivity reaction is suspected, discontinue Sitagliptin, assess for other potential causes for the event, and institute alternative treatment for diabetes.

USED IN SPECIAL POPULATION

Pregnancy Category B
There are no adequate and well controlled studies in pregnant women. This drug should be used during pregnancy only if clearly needed.

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

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

Geriatic 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.

OVERDOSAGE
Oral activated charcoal may be considered in adults and children who have ingested more than 15mg/kg of Sitagliptin and present with in one hour, provided they are conscious and the airway can be protected. Hypoglycaemia should be treated with urgency; initiate clinical monitoring (including obtaining an electrocardiogram), and institute supportive therapy as dictated by the patient's clinical status.

PRESENTATION
TAGIP 25 mg tablets: Blister pack of 2 x 7's tablet.
TAGIP 50 mg tablets: Blister pack of 2 x 7's tablet.
TAGIP 100 mg tablets: Blister pack of 2 x 7's tablet.

DOSAGE & INSTRUCTIONS
To be sold and used on the prescription of a registered medical practitioner only. Keep out of the reach of children. Store below 25°C in a dry place. Protect from light.

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(سیٹاگلپٹن)

فلم کوٹڈ گولیاں

خوراک وہدایات

صرف مستند ڈاکٹر کے نسخہ کے مطابق ہی دوا فروخت اور استعمال کی جائے۔

بچوں کی پہنچ سے دور رکھیں۔

دوا کو 25°C سے کم درجہ حرارت پر خشک جگہ پر رکھیں۔

روشنی سے بچائیں۔

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