STALIX

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

Abbreviated Prescribing information for STALIX (Sitagliptin Tablets I.P.) [Please refer the complete prescribing information available at www.torrentpharma.com]

PHARMACOLOGICAL PROPERTIES: Sitagliptin phosphate is an orally-active, potent, and highly selective inhibitor of the dipeptidyl peptidase 4 (DPP-4) enzyme for the treatment of type 2 diabetes. The DPP-4 inhibitors are a class of agents that act as incretin enhancers. By inhibiting the DPP-4 enzyme, sitagliptin increases the levels of two known active incretin hormones, 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. GLP-1 also lowers glucagon secretion from pancreatic alpha cells, leading to reduced hepatic glucose production. When blood glucose levels are low, insulin release is not enhanced and glucagon secretion is not suppressed. Sitagliptin is a potent and highly selective inhibitor of the enzyme DPP-4 and does not inhibit the closely-related enzymes DPP-8 or DPP-9 at therapeutic concentrations. Sitagliptin differs in chemical structure and pharmacological action from GLP-1 analogues, insulin, sulphonylureas or meglitinides, biguanides, peroxisome proliferator-activated receptor gamma (PPARγ) agonists, alpha-glucosidase inhibitors, and amylin analogues.

INDICATION: As adjunct to diet and exercise to improve glycaemic control in patients with type- II diabetes.

DOSAGE AND ADMINISTRATION: Film-Coated Sitagliptin Phosphate monohydrate Tablet Dose must be taken as directed by Physician**.** It can be taken with or without food.

CONTRAINDICATION: Hypersensitivity to the active substance or to any of the excipients.

WARNINGS & PRECAUTIONS: Sitagliptin should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis. *Acute 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 necrotising or haemorrhagic pancreatitis and/or death have been reported. If pancreatitis is suspected, Sitagliptin and other potentially suspect medicinal products should be discontinued; if acute pancreatitis is confirmed, Sitagliptin should not be restarted. Caution should be exercised in patients with a history of pancreatitis. *Hypoglycaemia when used in combination with other anti-hyperglycaemic medicinal products:* In clinical trials of Sitagliptin as monotherapy and as part of combination therapy with medicinal products not known to cause hypoglycaemia (i.e. metformin and/or a PPARγ agonist), rates of hypoglycaemia reported with sitagliptin were similar to rates in patients taking placebo. Hypoglycaemia has been observed when sitagliptin was used in combination with insulin or a sulphonylurea. Therefore, to reduce the risk of hypoglycaemia, a lower dose of sulphonylurea or insulin may be considered. *Renal impairment:* Sitagliptin is renally excreted. To achieve plasma concentrations of sitagliptin similar to those in patients with normal renal function, lower dosages are recommended in patients with GFR < 45 mL/min, as well as in ESRD patients requiring haemodialysis or peritoneal dialysis. 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. *Hypersensitivity reactions:* Post-marketing reports of serious hypersensitivity reactions in patients treated with sitagliptin have been reported. 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, Sitagliptin should be

discontinued, other potential causes of the event should be assessed, and alternative treatment for diabetes should be instituted. *Bullous pemphigoid:* There have been post-marketing reports of bullous pemphigoid in patients taking DPP-4 inhibitors including sitagliptin. If bullous pemphigoid is suspected, Sitagliptin should be discontinued.

DRUG INTERACTIONS: *Metformin*: Co-administration of multiple twice-daily doses of 1,000 mg metformin with 50 mg sitagliptin did not meaningfully alter the pharmacokinetics of sitagliptin in patients with type 2 diabetes. *Ciclosporin:* A study was conducted to assess the effect of ciclosporin, a potent inhibitor of p-glycoprotein, on the pharmacokinetics of sitagliptin. Co-administration of a single 100 mg oral dose of sitagliptin and a single 600 mg oral dose of ciclosporin increased the AUC and Cmax of sitagliptin by approximately 29 % and 68 %, respectively. *Digoxin:* In particular, tell your doctor if you are taking digoxin (a medicine used to treat irregular heartbeat and other heart problems). The level of digoxin in your blood may need to be checked if taking with Sitagliptin. Sitagliptin had a small effect on plasma digoxin concentrations. No dose adjustment of digoxin is recommended. However, patients at risk of digoxin toxicity should be monitored for this when sitagliptin and digoxin are administered concomitantly.

ADVERSE REACTIONS: Some patients taking metformin have experienced the following side effects after starting sitagliptin: **Common** (may affect up to 1 in 10 people): low blood sugar, nausea, flatulence, vomiting. **Uncommon** (may affect up to 1 in 100 people): stomachache, diarrhoea, constipation, drowsiness. Some patients have experienced diarrhoea, nausea, flatulence, constipation, stomachache or vomiting when starting the combination of Sitagliptin and metformin together (frequency is common). Some patients have experienced the following side effects while taking this medicine with a sulphonylurea such as glimepiride: **Very common** (may affect more than 1 in 10 people): low blood sugar. **Common**: constipation. Some patients have experienced the following side effects while taking this medicine in combination with pioglitazone: **Common**: swelling of the hands or legs. Some patients have experienced the following side effects while taking this medicine in combination with insulin: **Very common**: low blood sugar **Uncommon**: dry mouth, headache. Some patients have experienced the following side effects during clinical studies while taking sitagliptin alone (one of the medicines in Sitagliptin and metformin) or during post-approval use of Sitagliptin and metformin or sitagliptin alone or with other diabetes medicines: **Common**: low blood sugar, headache, upper respiratory infection, stuffy or runny nose and sore throat, osteoarthritis, arm or leg pain. **Uncommon**: dizziness, constipation, itching. **Rare**: reduced number of platelets. **Frequency not known**: kidney problems (sometimes requiring dialysis), vomiting, joint pain, muscle pain, back pain, interstitial lung disease, bullous pemphigoid (a type of skin blister).

MARKETED BY:

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IN/ SITAGLIPTIN 25/ 50/ 100 mg/MAR-22/01/ABPI

(Additional information is available on request)