**SITAXA D/ STALIX D/GLUCRETA S**

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

Abbreviated Prescribing information for SITAXA D/ STALIX D/GLUCRETA S (Dapagliflozin and Sitagliptin Tablets I.P.) [Please refer the complete prescribing information available at www.torrentpharma.com ]

**PHARMACOLOGICAL PROPERTIES:** *Sitagliptin*: 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). *Dapagliflozin:* Dapagliflozin is a highly potent (Ki: 0.55 nM), selective and reversible inhibitor of SGLT2. Inhibition of SGLT2 by dapagliflozin reduces reabsorption of glucose from the glomerular filtrate in the proximal renal tubule with a concomitant reduction in sodium reabsorption leading to urinary excretion of glucose and osmotic diuresis. Dapagliflozin therefore increases the delivery of sodium to the distal tubule which increases tubuloglomerular feedback and reduces intraglomerular pressure. This combined with osmotic diuresis leads to a reduction in volume overload, reduced blood pressure, and lower preload and afterload, which may have beneficial effects on cardiac remodelling and preserve renal function.

**INDICATION:** It is indicated for the treatment of type 2 diabetes mellitus inadequately controlled on Metformin monotherapy.

**DOSAGE AND ADMINISTRATION:** Film-Coated tablet, SITAXA D/ STALIX D/GLUCRETA S can be taken with or without food. Tablets are to be swallowed whole.

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

**WARNINGS & PRECAUTIONS:** ***Sitagliptin*-** it should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis. Acute pancreatitis, Hypoglycaemia when used in combination with other anti-hyperglycaemic medicinal products, Renal impairment, Hypersensitivity reactions, Bullous pemphigoid. ***Dapagliflozin*-** warning and precaution with renal impairment, hepatic impairment, use in patients at risk for volume depletion and/or hypotension, diabetic ketoacidosis, necrotising fasciitis of the perineum (Fournier's gangrene), urinary tract infections, cardiac failure, lower limb amputations, urine laboratory assessments. Elderly patients may be at a greater risk for volume depletion and are more likely to be treated with diuretics.

**DRUG INTERACTIONS**: *Sitagliptin interaction with other medicines*: 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: 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: Sitagliptin had a small effect on plasma digoxin concentrations. However, patients at risk of digoxin toxicity should be monitored for this when sitagliptin and digoxin are administered concomitantly. *Dapagliflozin:* Pharmacodynamic interactions- Diuretics: Dapagliflozin may add to the diuretic effect of thiazide and loop diuretics and may increase the risk of dehydration and hypotension. Insulin and insulin secretagogues: Insulin and insulin secretagogues, such as sulphonylureas, cause hypoglycaemia. Therefore, a lower dose of insulin or an insulin secretagogue may be required to reduce the risk of hypoglycaemia when used in combination with dapagliflozin in patients with type 2 diabetes mellitus. Pharmacokinetic interactions- Effect of other medicinal products on dapagliflozin: Interaction studies conducted in healthy subjects, using mainly a single-dose design, suggest that the pharmacokinetics of dapagliflozin are not altered by metformin, pioglitazone, sitagliptin, glimepiride, voglibose, hydrochlorothiazide, bumetanide, valsartan, or simvastatin. Effect of dapagliflozin on other

medicinal products: In reported interaction studies conducted in healthy subjects, using mainly a single-dose design, dapagliflozin did not alter the pharmacokinetics of metformin, pioglitazone, sitagliptin, glimepiride, hydrochlorothiazide, bumetanide, valsartan, digoxin (a P-gp substrate) or warfarin (S-warfarin, a CYP2C9 substrate), or the anticoagulatory effects of warfarin as measured by INR. Interference with 1,5-anhydroglucitol (1,5-AG) assay: Monitoring glycaemic control with 1,5-AG assay is not recommended as measurements of 1,5-AG are unreliable in assessing glycaemic control in patients taking SGLT2 inhibitors. Use of alternative methods to monitor glycaemic control is advised.

**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). ***Dapagliflozin:*** angioedema, seen *very rarely* (may affect up to 1 in 10,000 people, diabetic ketoacidosis, increased levels of "ketone bodies" in your urine or blood, feeling sick or being sick, stomach pain, excessive thirst, fast and deep breathing, confusion, unusual sleepiness or tiredness, a sweet smell to your breath, a sweet or metallic taste in your mouth or a different odour to your urine or sweat, rapid weight loss. *Common:* genital infection (thrush) of your penis or vagina (signs may include irritation, itching, unusual discharge or odour), back pain, passing more water (urine) than usual or needing to pass water more often, changes in the amount of cholesterol or fats in your blood (shown in tests), increases in the amount of red blood cells in your blood (shown in tests), decreases in creatinine renal clearance (shown in tests) in the beginning of treatment, dizziness, rash. *Uncommon (may affect up to 1 in 100 people):* loss of too much fluid from your body (dehydration, signs may include very dry or sticky mouth, passing little or no urine or fast heartbeat), thirst, constipation, awakening from sleep at night to pass urine, dry mouth, weight decreased, increases in creatinine (shown in laboratory blood tests) in the beginning of treatment, increases in urea (shown in laboratory blood tests).

**MARKETED BY:**

TORRENT PHARMACEUTICALS LTD.

**IN/ SITAXA D/ STALIX D/GLUCRETA S/ 5+50 mg and 10+100mg /JUL-22/01/ABPI**
(Additional information is available on request)