

**EMPAZIO SM 10+100+1000, EMPAZIO SM 25+100+1000, COSPIAQ SM 25+100+1000,
SITAXA EM 25+100+1000**

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

Abbreviated Prescribing information for EMPAZIO SM 10+100+1000, EMPAZIO SM 25+100+1000, COSPIAQ SM 25+100+1000, SITAXA EM 25+100+1000 [Empagliflozin, Sitagliptin and Metformin Hydrochloride Tablets]

[Please refer the complete prescribing information available at www.torrentpharma.com]

PHARMACOLOGICAL PROPERTIES:

MECHANISM OF ACTION: *Empagliflozin:* Empagliflozin is a reversible, highly potent (IC₅₀ of 1.3 nmol) and selective competitive inhibitor of sodium-glucose co-transporter 2 (SGLT2). Empagliflozin improves glycaemic control in patients with type 2 diabetes by reducing renal glucose reabsorption. The amount of glucose removed by the kidney through this glucuretic mechanism is dependent on blood glucose concentration and GFR. Inhibition of SGLT2 in patients with type 2 diabetes and hyperglycaemia leads to excess glucose excretion in the urine. *Sitagliptin:* Sitagliptin is a member of a class of oral anti-hyperglycaemic agents called dipeptidyl peptidase 4 (DPP-4) inhibitors. The improvement in glycaemic control observed with this medicinal product may be mediated by enhancing the levels of active incretin 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. *Metformin Hydrochloride:* Metformin is a biguanide that improves glycemic control in patients with type 2 diabetes mellitus, lowering both basal and postprandial plasma glucose. Metformin decreases hepatic glucose production, decreases intestinal absorption of glucose, and improves insulin sensitivity by increasing peripheral glucose uptake and utilization. With metformin therapy, insulin secretion remains unchanged while fasting insulin levels and day-long plasma insulin response may decrease.

INDICATIONS: It is indicated in patients with Type 2 Diabetes Mellitus Inadequately controlled on Metformin Monotherapy.

DOSAGE AND ADMINISTRATION: The recommended dose is one tablet daily. Each film coated tablet contains a fixed dose of Empagliflozin, Sitagliptin and Metformin ER. **Method of administration:** It should be given orally once daily.

CONTRAINDICATION: *Empagliflozin:* Empagliflozin is contraindicated in patients with a history of hypersensitivity to the active substance or to any of the excipients. *Sitagliptin:* Sitagliptin is contraindicated in patients with a history of hypersensitivity to the active substance or to any of the excipients. *Metformin Hydrochloride:* Metformin Hydrochloride is contraindicated in patients with a history of hypersensitivity to the active substance or to any of the excipients.

WARNINGS & PRECAUTIONS: *Empagliflozin:* In patients where ketoacidosis is suspected or diagnosed, treatment with Empagliflozin should be discontinued immediately. Empagliflozin and sitagliptin should not be used in patients with type 1 diabetes. Data from a clinical trial program in patients with type 1 diabetes showed increased ketoacidosis occurrence with common frequency in patients treated with empagliflozin 10 mg and 25 mg as an adjunct to insulin compared to placebo. For the indication of type 2 diabetes mellitus, in patients with an eGFR below 60 ml/min/1.73 m² or CrCl <60 ml/min the daily dose of empagliflozin is limited to 10 mg. Empagliflozin is not recommended when eGFR is below 30 ml/min/1.73 m² or CrCl below 30 ml/min. Empagliflozin should not be used in patients with ESRD or in patients on dialysis. Caution should be exercised in patients for whom an empagliflozin-induced drop in blood pressure could pose a risk. Patients aged 75 years and older may be at an increased risk of volume depletion. If Fournier's gangrene is suspected, Empagliflozin should be discontinued, and prompt treatment (including antibiotics and surgical debridement) should be instituted. *Sitagliptin:* Use of DPP-4

inhibitors has been associated with a risk of developing acute pancreatitis. Caution should be exercised in patients with a history of pancreatitis. If a hypersensitivity reaction is suspected, Sitagliptin should be discontinued. If bullous pemphigoid is suspected, Sitagliptin should be discontinued. **Metformin Hydrochloride:** If a serious hypersensitivity reaction is suspected, discontinue Linagliptin and Metformin HCl, assess for other potential causes for the event, and institute alternative treatment for diabetes. If heart failure develops, evaluate, and manage according to current standards of care and consider discontinuation of Linagliptin and Metformin HCl ER.

DRUG INTERACTIONS: **Empagliflozin:** Co-administration of empagliflozin with probenecid, an inhibitor of UGT enzymes and OAT3, resulted in a 26% increase in peak empagliflozin plasma concentrations (C_{max}) and a 53% increase in area under the concentration-time curve (AUC). Empagliflozin may increase renal lithium excretion and the blood lithium levels may be decreased. **Sitagliptin:** The potent CYP3A4 inhibitors (i.e. ketoconazole, itraconazole, ritonavir, clarithromycin) could alter the pharmacokinetics of sitagliptin in patients with severe renal impairment or ESRD. **Metformin Hydrochloride:** Topiramate or other carbonic anhydrase inhibitors (e.g., zonisamide, acetazolamide or dichlorphenamide) frequently cause a decrease in serum bicarbonate and induce non-anion gap, hyperchloremic metabolic acidosis. Concomitant use of these drugs with Linagliptin and Metformin HCl may increase the risk of lactic acidosis. Consider more frequent monitoring of these patients. Alcohol is known to potentiate the effect of metformin on lactate metabolism. Warn patients against excessive alcohol intake while receiving Empagliflozin, Sitagliptin and Metformin ER.

ADVERSE REACTIONS: **Empagliflozin:** Vaginal moniliasis, vulvovaginitis, necrotising fasciitis of the perineum (Fournier's gangrene), hypoglycaemia, thirst, diabetic ketoacidosis, constipation, pruritus, urticaria, angioedema, increased urination, dysuria, tubulo-interstitial nephritis, serum lipids increased, blood creatinine increased. **Sitagliptin:** Thrombocytopenia, headache, dizziness, interstitial lung disease, vomiting, acute pancreatitis, fatal and non-fatal haemorrhagic and necrotizing pancreatitis, cutaneous vasculitis, Stevens-Johnson syndrome, Bullous pemphigoid, arthralgia, myalgia, back pain, arthropathy, acute renal failure. **Metformin Hydrochloride:** Diarrhea, nausea, flatulence, asthenia, abdominal discomfort, decrease in Vitamin B12 absorption, cholestatic, hepatocellular, and mixed hepatocellular liver injury.

MARKETED BY:



Torrent Pharmaceuticals Limited.

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(Additional information is available on request)