COSPIAQ MET

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

Abbreviated Prescribing information for COSPIAQ MET (Empagliflozin and Metformin hydrochloride Film-coated Tablet 12.5 mg/500 mg, 12.5 mg/1000 mg) [Please refer the complete prescribing information for details].

PHARMACOLOGICAL PROPERTIES:

MECHANISM OF ACTION: ***Empagliflozin:*** Sodium-glucose co-transporter 2 (SGLT2) is the predominant transporter responsible for reabsorption of glucose from the glomerular filtrate back into the circulation. Empagliflozin is an inhibitor of SGLT2. By inhibiting SGLT2, empagliflozin reduces renal reabsorption of filtered glucose and lowers the renal threshold for glucose, and thereby increases urinary glucose excretion. ***Metformin:*** Metformin is an antihyperglycemic agent which improves glucose tolerance in patients with type 2 diabetes mellitus, lowering both basal and postprandial plasma glucose. It is not chemically or pharmacologically related to any other classes of oral antihyperglycemic agents. Metformin decreases hepatic glucose production, decreases intestinal absorption of glucose, and improves insulin sensitivity by increasing peripheral glucose uptake and utilization. Unlike SUs, metformin does not produce hypoglycemia in either patients with type 2 diabetes mellitus or normal subjects (except in special circumstances) and does not cause hyperinsulinemia. With metformin therapy, insulin secretion remains unchanged while fasting insulin levels and day-long plasma insulin response may actually decrease.

INDICATIONS: COSPIAQ MET is indicated as an adjunct to diet and exercise to improve glycaemic control in adult patients with type 2 diabetes mellitus.

Empagliflozin is indicated to reduce the risk of cardiovascular death in adults with type 2 diabetes mellitus and established cardiovascular disease.

DOSAGE AND ADMINISTRATION: As directed by the Physician. Tablets should be taken orally.

CONTRAINDICATION: COSPIAQ MET is contraindicated in patients with Severe renal impairment (eGFR less than 30 mL/min/1.73 m2), end stage renal disease, or dialysis, Acute or chronic metabolic acidosis, including diabetic ketoacidosis, Hypersensitivity to empagliflozin, metformin or any of the excipients in COSPIAQ MET, reactions such as angioedema have occurred.

WARNINGS & PRECAUTIONS: ***Lactic Acidosis:*** Metformin-associated lactic acidosis was characterized by elevated blood lactate concentrations (>5 mmol/Liter), anion gap acidosis (without evidence of ketonuria or ketonemia), and an increased lactate: pyruvate ratio; metformin plasma levels generally >5 mcg/mL. Metformin decreases liver uptake of lactate increasing lactate blood levels which may increase the risk of lactic acidosis, especially in patients at risk. If metformin-associated lactic acidosis is suspected, general supportive measures should be instituted promptly in a hospital setting, along with immediate discontinuation of COSPIAQ MET. In COSPIAQ MET-treated patients with a diagnosis or strong suspicion of lactic acidosis, prompt hemodialysis is recommended to correct the acidosis and remove accumulated metformin. ***Ketoacidosis:*** Reports of ketoacidosis, a serious life-threatening condition requiring urgent hospitalization have been identified in clinical trials and postmarketing surveillance in patients with type 1 and type 2 diabetes mellitus receiving sodium glucose co-transporter-2 (SGLT2) inhibitors, including empagliflozin. In placebo-controlled trials of patients with type 1 diabetes, the risk of ketoacidosis was increased in patients who received SGLT2 inhibitors compared to patients who received placebo. COSPIAQ MET is not indicated for the treatment of patients with type 1 diabetes mellitus. Patients treated with COSPIAQ MET who present with signs and symptoms consistent with severe metabolic acidosis should be assessed for ketoacidosis regardless

of presenting blood glucose levels, as ketoacidosis associated with COSPIAQ MET may be present even if blood glucose levels are less than 250 mg/dL. If ketoacidosis is suspected, COSPIAQ MET should be discontinued, patient should be evaluated, and prompt treatment should be instituted. Treatment of ketoacidosis may require insulin, fluid and carbohydrate replacement. ***Volume Depletion*** Empagliflozin can cause intravascular volume depletion which may sometimes manifest as symptomatic hypotension or acute transient changes in creatinine. There have been post-marketing reports of acute kidney injury, some requiring hospitalization and dialysis, in patients with type 2 diabetes mellitus receiving SGLT2 inhibitors, including empagliflozin. Patients with impaired renal function (eGFR less than 60 mL/min/1.73 m2), elderly patients, or patients on loop diuretics may be at increased risk for volume depletion or hypotension. Before initiating COSPIAQ MET in patients with one or more of these characteristics, assess volume status and renal function. In patients with volume depletion, correct this condition before initiating COSPIAQ MET. Monitor for signs and symptoms of volume depletion, and renal function after initiating therapy ***Urosepsis and Pyelonephritis*** Treatment with SGLT2 inhibitors increases the risk for urinary tract infections. Evaluate patients for signs and symptoms of urinary tract infections and treat promptly if indicated. ***Hypoglycemia with Concomitant Use with Insulin and Insulin Secretagogues*** The risk of hypoglycemia is increased when empagliflozin is used in combination with insulin secretagogues (e.g., sulfonylurea) or insulin. ***Necrotizing Fasciitis of the Perineum (Fournier's Gangrene):*** Patients treated with COSPIAQ MET presenting with pain or tenderness, erythema, or swelling in the genital or perineal area, along with fever or malaise, should be assessed for necrotizing fasciitis. If suspected, start treatment immediately with broad-spectrum antibiotics and, if necessary, surgical debridement. Discontinue COSPIAQ MET closely monitor blood glucose levels, and provide appropriate alternative therapy for glycemic control. ***Vitamin B12 Deficiency:*** A decrease to subnormal levels of previously normal serum vitamin B12 levels was observed in approximately 7% of metformin-treated patients. ***Hypersensitivity Reactions:*** COSPIAQ MET is contraindicated in patients with hypersensitivity to empagliflozin or any of the excipients in COSPIAQ MET. ***Genital Mycotic Infections:*** Empagliflozin increases the risk for genital mycotic infections Patients with a history of chronic or recurrent genital mycotic infections were more likely to develop genital mycotic infections.

DRUG INTERACTIONS: ***Carbonic Anhydrase Inhibitors:*** Topiramate or other carbonic anhydrase inhibitors (e.g., zonisamide, acetazolamide or dichlorphenamide) frequently causes a decrease in serum bicarbonate and induce non-anion gap, hyperchloremic metabolic acidosis. ***Drugs that Reduce Metformin Clearance:*** Concomitant use of drugs that interfere with common renal tubular transport systems involved in the renal elimination of metformin (e.g., organic cationic transporter-2 [OCT2] multidrug and toxin extrusion [MATE] inhibitors such as ranolazine, vandetanib, dolutegravir, and cimetidine) could increase systemic exposure to metformin and may increase the risk for lactic acidosis, ***Alcohol:*** is known to potentiate the effect of metformin on lactate metabolism ***Diuretics:*** Coadministration of empagliflozin with diuretics resulted in increased urine volume and frequency of voids, which might enhance the potential for volume depletion. ***Insulin or Insulin Secretagogues:*** The risk of hypoglycemia is increased when empagliflozin is used in combination with insulin secretagogues (e.g., sulfonylurea) or insulin. Metformin may increase the risk of hypoglycemia when combined with insulin and/or an insulin secretagogue. ***Drugs Affecting Glycemic Control:*** Certain drugs tend to produce hyperglycemia and may lead to loss of glycemic control. These drugs include the thiazides and other diuretics, corticosteroids, phenothiazines, thyroid products, estrogens, oral contraceptives, phenytoin, nicotinic acid, sympathomimetics, calcium channel blocking drugs, and isoniazid. ***Positive Urine Glucose Test:*** SGLT2 inhibitors increase urinary glucose excretion and will lead to positive urine glucose tests. ***Interference with 1,5-anhydroglucitol (1,5-AG) Assay:*** Measurements of 1,5-AG are unreliable in assessing glycemic control in patients taking SGLT2 inhibitors.

ADVERSE REACTIONS: Lactic Acidosis, Ketoacidosis,Volume Depletion, Urosepsis and Pyelonephritis, Hypoglycemia with Concomitant Use with Insulin and Insulin Secretagogues, Necrotizing Fasciitis of the Perineum (Fournier's Gangrene), Genital Mycotic Infections Hypersensitivity Reactions, Vitamin B12 Deficiency.

Please email at pv@torrentpharma.com for reporting of any adverse event.

MARKETED BY:

TORRENT PHARMACEUTICALS LTD.

Torrent House, Off Ashram Road,

Ahmedabad-380 009, INDIA

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(Additional information is available on request)