Composition : Each film coated tablet contains Empagliflozin INN 5 mg & Metformin Hydrochloride USP 500 mg.

Pharmacology : Emparol-M combines two antihyperglycemic agents with complementary mechanisms of action to improve glycemic control in patients with type 2 diabetes: Empagliflozin, a Sodium-glucose co-transporter 2 (SGLT2) inhibitor, and Metformin Hydrochloride, a member of the biguanide class. Sodium-glucose co-transporter 2 (SGLT2) expressed in the proximal renal tubules, is responsible for the majority of the reabsorption or filtered glucose from the tubular lumen. By inhibiting SGLT2, Empagliflozin reduces reabsorption of filter glucose and lowers the renal threshold for glucose (RTG), and thereby increases urinary glucose excretion. The pharmacologic mechanism of action of Metformin is different from other classes of oral antihyperglycemic agents. Metformin decreases hepatic glucose production, decreases intestinal absorption of glucose, and increases peripheral glucose uptake and utilization.

Indication : Emparol-M is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes when treatment with both empagliflozin and metformin is appropriate. Empagliflozin is indicated to reduce the risk of cardiovascular death in adults with type 2 diabetes mellitus and established cardiovascular disease.

Dosage and Administration : Individualize the starting dose of **Emparol-M** based on the patient's current regimen. The maximum recommended dose is 12.5mg Empagliflozin/1000 mg Metformin twice daily. Take twice daily with meals, with gradual dose escalation to reduce the gastrointestinal side effects due to metformin. Assess renal function before initiating **Emparol-M**. Do not initiate or continue **Emparol-M** if creatinine levels > 1.5 mg/dL (males), > 1.4 mg/dL (females), or if eGFR is below 45 mL/min/1.73 m^2. Or, as directed by the registerd physician.

Contraindication : Empagliflozin is contraindicated in patients with history of serious hypersensitivity reaction to Empagliflozin or any of its ingredients, severe renal impairment, end-stage renal disease, or dialysis. It acute or chronic metabolic acidosis, including diabetic ketoacidosis, with or without coma. Renal disease or renal dysfunction e.g., as suggested by serum creatinine levels >1.5 mg/dL (males), >1.4 mg/dL (females) or abnormal creatinine clearance.

Precaution : Lactic acidosis, Hypotension, Ketoacidosis, Acute kidney injury and impairment in renal function, Hyperkalemia, Urosepsis and Pyelonephritis, Hypoglycemia, Genital mycotic infections, Hypersensitivity reactions, Bone fracture, Vitamin B1 deficiency. The risk of necrotizing fascitis of the perineum/Fournier's gangrene.

Side effects : For Empagliflozin: The most common adverse reactions are urinary tract infections and female genital mycotic infections. Others common side effects includes dehydration, hypotension, weakness, dizziness and increased thirstiness. **For**

Emparol-M 5/500
Empagliflozin INN &
Metformin Hydrochloride USP

DRUG INTERNATIONAL LTD.

Metformin: Gastrointestinal symptoms-nausea, vomiting, diarrhoea, abdominal pain and loss of appetite are very common.

Use in Pregnancy and Lactation : Pregnancy: There are no adequate and well-controlled studies of Empagliflozin & Metformin combination in pregnant women. This combination should be used duing pregnancy only if the potential benefit justifies the potential risk to the fetus. **Lactation:** It is not recommended when breastfeeding.

Use in Child : Safety and effectiveness of Empagliflozin & Metformin combination in pediatric patients under 18 years of age have not been established.

Drug Interaction : For Empagliflozin: Diuretics: Co-administration of Empagliflozin with diuretics resulted in increased urine volume. Insulin or Insulin Secretagogues: Co-administration of Empagliflozin with insulin or insulin secretagogues increases the risk for hypoglycemia. Positive Urine Glucose Test: Monitoring glycemic control with urine glucose tests is not recommended in patients taking SGLT2 Inhibitors as SGLT2 inhibitors increase urinary glucose excretion and will lead to positive urine glucose tests. Use alternative methods to monitor glycemic control. Interference with 1,5-anhydroglucitol (1,5 AG) Assay: Monitoring glycemic control with 1,5-AG assay is not recommended as measurements of 1,5-AG are unreliable in assessing glycemic control in patients taking SGLT2 inhibitors. Use alternative methods to monitor glycemic control. For Metformin: No information is available about the interaction of Metformin and furosemide when co-administered chronically. Nifedipine appears to enhance the absorption of Metformin. Metformin had minimal effects on nifedijpine. Cationic drugs (eg. amiloride, digoxin, morphine, procainamide, quinidine, quinine ranitidine, triamterene, trimethoprim, or vancomycin) that are eliminated by renal tubular secretion theoretically have the potential for interaction with Metformin by competing for common renal tubular transport systems. Metformin had no effect on cimetidine pharmacokinetics. 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.

Overdose : There were no reports of overdose during the clinical development program for empagliflozin. Removal of empagliflozin by hemodialysis has not been studied.

Storage : Store below 30^{o}C in a dry place.

Packing : Each box contains 2 x 7's tablets in bilster pack.