Ajardy M

Empagliflozin INN & Metformin Hydrochloride BP

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

Pharmacology
Empagliflozin is an inhibitor of Sodium-glucose co-transporter 2 (SGLT2). SGLT2 is the predominant transporter responsible for reabsorption of glucose from kidney back into the circulation. By inhibiting SGLT2, Empagliflozin reduces renal reabsorption of filtered glucose and lowers the renal threshold for glucose, and thereby increases urinary glucose excretion.
Metformin Hydrochloride is a biguanide type oral antihyperglycemic drug, used in the management of type 2 diabetes. It lowers both basal and postprandial plasma glucose. It does not produce hypoglycemia. Metformin Hydrochloride decreases hepatic glucose production, decreases intestinal absorption of glucose and improves insulin sensitivity by an increase in peripheral glucose uptake and utilization.

Indication
Ajardy M is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both Empagliflozin and Metformin Hydrochloride is appropriate. Empagliflozin is indicated to reduce the risk of cardiovascular death in adult patients with type 2 diabetes mellitus and established cardiovascular disease.

Dosage and Administration
The dosage of **Ajardy M** should be individualized based on effectiveness and tolerability. **Ajardy M** should be taken twice daily with meals. Dose escalation should be gradual to reduce the gastrointestinal side effects due to Metformin Hydrochloride. Maximum recommended daily dose of Metformin Hydrochloride is 2000 mg and Empagliflozin is 25 mg.

Recommended individualized starting dose: In patients on Metformin Hydrochloride, switch to **Ajardy M** containing Empagliflozin 5 mg with a similar total daily dose of Metformin Hydrochloride.
In patients on Empagliflozin, switch to **Ajardy M** containing Metformin Hydrochloride 500 mg with a similar total daily dose of Empagliflozin.
In patients already treated with Empagliflozin and Metformin Hydrochloride separately, switch to **Ajardy M** containing the same total daily doses of each component. In patients with volume depletion not previously treated with Empagliflozin, correcting this condition prior to initiation of **Ajardy M** is recommended.
Renal impaired patient: Assess renal function before initiating **Ajardy M**. In patients with an eGFR below 45 mL/min/1.73 m^2 **Ajardy M** is contraindicated.

Contraindication
Ajardy M is contraindicated in patients with moderate to severe renal impairment and End Stage Renal Disease (ESRD). It is also contraindicated in patients with metabolic acidosis, including diabetic ketoacidosis and patients with history of serious hypersensitivity reaction to Empagliflozin, Metformin Hydrochloride or any of the excipients of **Ajardy M**.

Warning and Precaution
Lactic Acidosis: Postmarketing cases showed Metformin Hydrochloride-associated lactic acidosis. If lactic acidosis is suspected, general supportive measures should be instituted properly in a hospital setting, along with immediate discontinuation of **Ajardy M**. Hypotension: Before initiating **Ajardy M**, assess and correct volume status in patients with renal impairment, the elderly, in patients with low systolic blood pressure and in patients on diuretics. Monitor for signs and symptoms of hypotension after initiating therapy and increase monitoring clinical situations where volume contraction is expected. Ketoacidosis: Before initiating **Ajardy M** assess patients who present with signs and symptoms of metabolic acidosis for ketoacidosis, regardless of blood glucose level. If suspected, discontinue **Ajardy M**, evaluate and treat promptly. Acute kidney injury & impairment in renal function: Consider temporarily discontinuing **Ajardy M** in settings of reduced oral intake or fluid losses. If acute kidney injury occurs, discontinue **Ajardy M** promptly and institute treatment. Urosepis, Pyelonephritis, Fourniers's gangrene and Genital mycotic infections: Treatment with SGLT-2 inhibitors increases the risk for urinary tract infections. Evaluate patients for signs and symptoms of urinary tract infections and treat promptly, if indicated. Hypoglycemia: Consider lowering the dose of insulin secretagogue or insulin to reduce the risk of hypoglycemia when initiating **Ajardy M**. Vitamin B12 Deficiency: Metformin Hydrochloride may lower vitamin B12 levels. Monitor hematologic parameters annually. Increased LDL-C: Monitor and treat as appropriate. Macrovascular Outcomes: There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with **Ajardy M**.

Side Effects:
The most common adverse reactions associated with Empagliflozin (5% or greater incidence) are urinary tract infections and female genital mycotic infections. Most common adverse reactions associated with Metformin Hydrochloride (>5%) are diarrhea, nausea, vomiting, flatulence, abdominal discomfort, indigestion, asthenia and headache.

Drug Interaction:
Carbonic Anhydrase inhibitors may increase risk of lactic acidosis. Consider more frequent monitoring. Drugs that reduce Metformin Hydrochloride clearance (such as Ranolazine, Vandetanib, Dolutegravir and Cimetidine) may increase the accumulation of Metformin Hydrochloride. Consider the benefits and risks of concomitant use. Alcohol can potentiate the effect of Metformin Hydrochloride on lactate metabolism. Warn patients against excessive alcohol intake.

Use in pregnancy and Lactation:
Advise pregnant women of the potential risk to a fetus during the second and third trimesters. **Ajardy M** is not recommended when breastfeeding.

Overdosage:
In the event of an overdose with **Ajardy M**, employ the usual supportive measures as dictated by the patient's clinical status (e.g., remove unabsorbed material from the gastrointestinal tract, employ clinical monitoring, and institute supportive treatment). Removal of empagliflozin by hemodialysis has not been studied. Metformin Hydrochloride is dialyzable with a clearance of up to 170 mL/min under good hemodynamic conditions. Therefore, hemodialysis may be useful partly for removal of accumulated Metformin hydrochloride from patients in whom **Ajardy M** overdosage is suspected.

Storage
Do not store above 25°C. Protect from light. Keep out of the reach of children.

Packaging
Ajardy M: Each box contains 4X8's tablets in blister pack.

Manufactured by
ZISKA PHARMA
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