

Zein Plus

Film Coated Tablets & Extended Release Film Coated Tablets



Composition: Each Zein Plus (5/500+5/1000+12.5/500+12.5/1000) Film Coated Tablet contains:

- Empagliflozin 5 mg and Metformin HCl 500 mg.
 - Empagliflozin 5 mg and Metformin HCl 1000 mg.
 - Empagliflozin 12.5 mg and Metformin HCl 500 mg.
 - Empagliflozin 12.5 mg and Metformin HCl 1000 mg.
- Each Zein Plus (25/1000) Extended Release Film Coated Tablet contains Empagliflozin 25 mg and Metformin HCl Extended Release 1000 mg.

Mechanism of Action:

Zein Plus combines two antihyperglycaemic medicinal products with complementary mechanisms of action to improve glycaemic control in patients with type 2 diabetes: Empagliflozin is an inhibitor of the sodium-glucose co-transporter 2 (SGLT2). Empagliflozin reduces renal reabsorption of filtered glucose and lowers the renal threshold for glucose, and thereby increases urinary glucose excretion. Metformin is a biguanide with antihyperglycaemic effects, lowering plasma glucose.

Pharmacokinetics:

After oral administration, peak plasma concentrations of Empagliflozin reach after 1.5 hours. The apparent steady-state volume of distribution is about 73.8 liters. The terminal elimination half-life is 12.4 hours. No major metabolites of Empagliflozin have been detected in plasma. The most abundant metabolites are the three glucuronide conjugates. In healthy subjects, 95.6% of the drug is eliminated, in feces (41.2%) or urine (54.4%). After oral administration, absorption of Metformin is incomplete. Peak concentration is reached within 2.5 hours. When Metformin is administered at recommended doses, steady-state plasma concentrations are reached within 24 to 48 hours. Its binding to plasma proteins is negligible. Metformin is excreted in the urine unchanged.

Indications:

- Zein Plus is indicated for the treatment of adults with type 2 diabetes mellitus as an adjunct to diet and exercise:
- In patients insufficiently controlled on their maximally tolerated dose of Metformin alone.
- In combination with other medicinal products for the treatment of diabetes, in patients insufficiently controlled with Metformin and these medicinal products.
- Empagliflozin is indicated to reduce the risk of cardiovascular death in adults with type 2 diabetes mellitus and established cardiovascular disease.

Contraindications:

- Hypersensitivity to the active substance or to any of the excipients.
- 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.

Warnings & Precautions:

- Rare cases of ketoacidosis have been reported in patients with diabetes mellitus treated with SGLT2 inhibitors, including Empagliflozin.
- Caution should be exercised in patients for whom an Empagliflozin-induced drop in blood pressure could pose a risk.
- Cases of necrotising fasciitis of the perineum, (also known as Fournier's gangrene), have been reported in female and male patients with diabetes mellitus taking SGLT2 inhibitors.
- Hematocrit increase was observed with Empagliflozin treatment.
- Patients who take Zein Plus show positive results for glucose in the urine.
- Zein Plus is not recommended in hepatic impairment or hypoxic states and is contraindicated in renal impairment.
- Metformin may lower vitamin B12 levels.

Pregnancy & Lactation:

Pregnancy: Pregnancy Category C. There are no data from the use of Zein Plus in pregnant women. Zein Plus should be used during pregnancy only if the potential benefit justifies the

potential risk to the fetus.

Lactation: It is not recommended to use Zein Plus during lactation.

Driving & Using Machines: Zein Plus has minor influence on the ability to drive and use machines.

Drug Interactions:

- Insulin and insulin secretagogues, such as sulphonylureas, may increase the risk of hypoglycaemia.
- Empagliflozin may add to the diuretic effect of thiazide and loop diuretics and may increase the risk of dehydration and hypotension.
- Alcohol intoxication is associated with an increased risk of lactic acidosis, particularly in cases of fasting, malnutrition or hepatic impairment.
- Careful patient monitoring and dose adjustment of Zein Plus and/or the interfering drug is recommended in patients who are taking cationic medications (e.g., amiloride, digoxin, morphine, trimethoprim, or vancomycin) that are excreted via the proximal renal tubule.
- Concomitant use with Topiramate or other carbonic anhydrase inhibitors may induce metabolic acidosis.

Side Effects:

Common adverse reactions associated with Zein Plus include: Hypoglycaemia (when used with sulphonylurea or insulin), taste disturbance, vitamin B12 deficiency, thirst, constipation, diarrhea, nausea/vomiting, flatulence, pruritus, rash, increased urination, urinary tract infections and female genital mycotic infections.

Dosage & Administration:

- The doctor may resort to prescribing Zein Plus in patients whose blood sugar levels are not controlled by monotherapy, and the starting dose must be adjusted on an individual basis and based on the current treatment regimen of the patient.
- Monitor effectiveness and tolerability, and adjust dosing as appropriate, not to exceed the maximum recommended daily dose of Empagliflozin 25 mg and Metformin 2000 mg.
- The dose of Metformin should be gradually escalated to reduce the gastrointestinal side effects due to Metformin.
- Take Zein Plus orally once daily with a meal in the morning.
- Zein Plus 25/1000 Extended Release Tablets should be taken as a single tablet once daily.

Renal Impairment:

- Initiation of Zein Plus is not recommended in patients with an eGFR less than 45 mL/min/1.73 m², due to the Metformin component.
- Zein Plus is contraindicated in patients with an eGFR less than 30 mL/min/1.73 m² or in patients on dialysis

Hepatic impairment:

This medicinal product must not be used in patients with hepatic impairment.

Overdose:

Symptoms: In controlled clinical studies single doses of up to 800 mg Empagliflozin in healthy volunteers and multiple daily doses of up to 100 mg Empagliflozin in patients with type 2 diabetes did not show any toxicity. Empagliflozin increased urine glucose excretion leading to an increase in urine volume. Lactic acidosis has been reported in approximately 32% of Metformin overdose cases.

Treatment: In the event of an overdose, treatment should be initiated as appropriate to the patient's clinical status. The removal of Empagliflozin by haemodialysis has not been studied. However, Metformin is dialyzable. Therefore, hemodialysis may be useful partly for removal of accumulated Metformin from patients in whom Zein Plus overdose is suspected.

Storage:

Store at a temperature below 30°C. Keep out of reach of children.

Packaging:

Each Zein Plus carton box contains 20 or 30 film coated tablets in two or three blister strips

- A medication is a product which affects your health, and it's consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medication.
- The doctor and the pharmacist experts in medicine, it's benefits and risks.
- Do not repeat the same prescription without consulting your doctor.
KEPITH MEDIAN AS A PART OF KEPITH OF CHILDREN
Council of Arab Health Ministers- Union of Arab Pharmacies

Reva Pharma for Pharmaceutical Industries - Idlib - Syria

POD030 / R02

