Diajard™

(Empagliflozin)

Highnoon

COMPOSITION

Diajard 10mg Tablet: Each film-coated tablet contains:
Empagliflozin 10mg

Diajard 25mg Tablet: Each film-coated tablet contains:
Empagliflozin 25mg

DESCRIPTION

Diajard tablets contain empagliflozin, an orally-active inhibitor of the sodium-glucose co-transporter 2 (SGLT2).

MECHANISM OF ACTION

Sodium-glucose co-transporter 2 (SGLT2) is the predominant transporter responsible for reabsorption of glucose from the glomerular filtrate back into the circulation. Reversibly inhibits sodium-glucose co-transporter 2 (SGLT2) in the renal proximal convoluted tubule to reduce glucose reabsorption and increased urinary glucose excretion.

PHARMACOKINETICS

After oral administration, peak plasma concentrations of empagliflozin were reached at 1.5 hours post-dose. Plasma concentrations declined in a biphasic manner with a rapid distribution phase and a relatively slow terminal phase. Plasma protein binding was 86.2%. No major metabolites of empagliflozin were detected in human plasma and the most abundant metabolites were three glucuronide conjugates. The primary route of metabolism of empagliflozin in humans is glucuronidation by the uridine 5'-diphospho-glucuronosyltransferases UGT2B7, UGT1A3, UGT1A8, and UGT1A9. The apparent terminal elimination half-life of empagliflozin was estimated to be 12.4 hours. The majority of drug-related radioactivity recovered in feces was unchanged parent drug and approximately half of drug-related radioactivity excreted in urine was unchanged parent drug. It may be administered with or without food.

INDICATIONS AND USAGE

It is indicated:

- As an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
- Type 2 diabetes mellitus in combination with insulin or other antidiabetic drugs (if existing treatment fails to achieve adequate glycemic control.
- Reduce the risk of cardiovascular death in adult patients with type 2 diabetes mellitus and established cardiovascular disease.
- In adults for the treatment of symptomatic chronic heart failure with reduced ejection fraction.
- Reduce the risk of cardiovascular death and hospitalization for heart failure in adults with heart failure.

Limitations of Use

It is not recommended in patients with type 1 diabetes mellitus. It may increase the risk of diabetic ketoacidosis in these patients.
It is not recommended for use to improve glycemic control in adults with type 2 diabetes mellitus with an eGFR less than 45 mL/min/1.73 m^2. It is likely to be ineffective in this setting based upon its mechanism of action.

DOSAGE AND ADMINISTRATION

Before initiating the Empagliflozin assess the renal function and clinically indicated. In patients with volume depletion, correct this condition before initiating Empagliflozin.
The recommended dose of DIAJARD (Empagliflozin) is 10mg once daily in the morning, taken with or without food.

- For additional glycemic control, the dose maybe increased to 25mg in patients tolerating Empagliflozin.
- Use for glycemic control is not recommended in patients with eGFR less than 30 mL/min/1.73m^2.
- Data are insufficient to provide during recommendation in patients;
  - o who have type 2 diabetes and established cardiovascular disease with an eGFR less than 30 mL/min/1.73m^2.
  - o who have heart failure with an eGFR less than 20 mL/min/1.73m^2.

Empagliflozin is contraindicated in patients on dialysis.

CONTRAINDICATIONS

It is contraindicated:

- Diabetic ketoacidosis.
- History of serious hypersensitivity reaction to empagliflozin or any of the excipients.
- Severe renal impairment, end-stage renal disease, or dialysis.

ADVERSE REACTIONS

The reported adverse events are; hypotension, ketoacidosis, acute kidney injury and impairment in renal function, 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, increased low-density lipoprotein cholesterol, urinary tract infection (asymptomatic bacteriuria, cystitis), female genital mycotic infection (vulvovaginal mycotic infection, vaginal infection, vulvitis, vulvovaginal candidiasis, genital infection, genital candidiasis, genital infection fungal, genitourinary tract infection, vulvovaginitis, cervicitis, urogenital infection fungal, vaginitis bacterial), increased urination (polyuria, pollakiuria, nocturia), upper respiratory tract infection, dyslipidemia, arthralgia, male genital mycotic infections (balanoposthitis, balanitis, genital infections fungal, genitourinary tract infection, balanitis candida, scrotal abscess, penile infection), nausea, volume depletion (blood pressure systolic decreased, dehydration, hypotension, hypovolemia, orthostatic hypotension, syncope), increase urination (e.g., polyuria, pollakiuria, and nocturia), increase in serum creatinine, decreases in eGFR, phimosis, hypoglycemia, increase hematocrit, angioedema, skin reaction (rash, urticaria), thirst, constipation, increase in low density lipoprotein and pruritus generalized.

DRUG INTERACTIONS

- Coadministration of empagliflozin with diuretics resulted in increased urine volume and frequency of voids, which might enhance the potential for volume depletion. Before initiating the Empagliflozin, assess the volume status and renal function. In patients with volume depletion, correct this condition before initiating Empagliflozin. Monitor for sign and symptoms of volume depletion and renal function after initiating therapy.
- Coadministration of empagliflozin with insulin or insulin secretagogues increases the risk for hypoglycemia. Coadministration of Empagliflozin with an Insulin secretagogue (e.g., Sulfonylurea) or Insulin may require lower dose of Insulin secretagogue or Insulin to reduce the risk of hypoglycemia.
- 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.
- 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.

WARNINGS AND PRECAUTIONS

Volume Depletion

Empagliflozin causes intravascular volume depletion which may sometimes manifest as symptomatic hypotension or acute transient changes in creatinine. Patients with impaired renal function (eGFR less than 60 mL/min/1.73 m^2), elderly patients, or patients on loop diuretics may be at increased risk for volume depletion or hypotension. Symptomatic hypotension may occur after initiating particularly in patients with renal impairment, the elderly, in patients with low systolic blood pressure, and in patients on diuretics. Before initiating, assess for volume contraction and correct volume status is indicated. Monitor for signs and symptoms of hypotension after initiating therapy. Consider interrupting treatment if volume depletion occurs.

Ketoacidosis

Ketoacidosis, have been identified in patients with type 1 and type 2 diabetes mellitus receiving sodium glucose co-transporter-2 (SGLT2) inhibitors, including empagliflozin. Empagliflozin is not indicated for the treatment of patients with type 1 diabetes mellitus. Patients treated with empagliflozin 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 empagliflozin may be present even if blood glucose levels are less than 250 mg/dL. If ketoacidosis is suspected, empagliflozin should be discontinued, patient should be evaluated, and prompt treatment should be instituted. Treatment of ketoacidosis may require insulin, fluid and carbohydrate replacement.

- Before initiating Empagliflozin, consider factors in patients' history that may predispose to ketoacidosis including pancreatic insulin deficiency from any cause, caloric verification and alcoholic abuse.
- For patients who undergo surgery, consider temporarily discontinuing Empagliflozin for at least 3 days prior to surgery.
- Consider monitoring for ketoacidosis and temporarily discontinuing in other clinical situations known to predispose to ketoacidosis (e.g., prolonged fasting due to acute illness or post-surgery). Ensure risk factors for ketoacidosis are resolved prior to starting Empagliflozin.
- Educate patients on sign and symptoms of ketoacidosis and inspect patients to discontinue Empagliflozin and seek medical attention immediately, if sign and symptoms occur.

Urosepsis and Pyelonephritis

Urosepsis and pyelonephritis have been reported in patients receiving SGLT2 inhibitors, including empagliflozin. 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

Insulin and insulin secretagogues are known to cause hypoglycemia. The risk of hypoglycemia is increased when empagliflozin is used in combination with insulin secretagogues (e.g., sulfonylurea) or insulin. Therefore, a lower dose of the insulin secretagogue or insulin may be required to reduce the risk of hypoglycemia when used in combination with empagliflozin.

Necrotizing Fasciitis of the Perineum (Fournier's Gangrene)

Reports of necrotizing fasciitis of the perineum (Fournier's gangrene), a rare but serious and life-threatening necrotizing infection have been reported in patients with diabetes mellitus receiving SGLT2 inhibitors, including empagliflozin. Cases have been reported in both females and males.

Patients treated with empagliflozin 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 empagliflozin, closely monitor blood glucose levels, and provide appropriate alternative therapy for glycemic control.

Genital Mycotic Infections

Empagliflozin increases the risk for genital mycotic infections. Patients with a history of chtronic or recurrent genital mycotic infections were more likely to develop genital mycotic infections. Monitor and treat as appropriate.

Hypersensitivity Reactions

Hypersensitivity reactions, (e.g., angioedema) in patients treated with empagliflozin. If a hypersensitivity reaction occurs, discontinue empagliflozin; treat promptly per standard of care, and monitor until signs and symptoms resolve.

Increased Low-Density Lipoprotein Cholesterol (LDL-C)

Increases in LDL-C can occur with empagliflozin. Monitor and treat as appropriate.

USE IN SPECIFIC POPULATIONS

Pregnancy

Empagliflozin is not recommended during the second and third trimesters of pregnancy. Limited data available with empagliflozin in pregnant women are not sufficient to determine a drug associated risk for major birth defects and miscarriage. There are risks to the mother and fetus associated with poorly controlled diabetes in pregnancy. Poorly controlled diabetes in pregnancy increases the maternal risk for diabetic ketoacidosis, pre-eclampsia, spontaneous abortions, preterm delivery, stillbirth, and delivery complications. Poorly controlled diabetes increases the fetal risk for major birth defects, stillbirth, and macrosomia related morbidity.

Lactation

There is no information regarding the presence of empagliflozin in human milk, the effects of empagliflozin on the breastfed infant or the effects on milk production. Because of the potential for serious adverse reactions in a breastfed infant, including the potential for empagliflozin to affect postnatal renal development, advise women that use of empagliflozin is not recommended while breastfeeding.

Pediatric Use

The safety and effectiveness of empagliflozin in pediatric patients under 18 years of age have not been established.

Geriatric Use

No dosage change is recommended based on age. Empagliflozin is expected to have diminished glycemic efficacy in elderly patients with renal impairment. The risk of volume depletion-related adverse reactions and urinary tract infection increased in patients who were 75 years of age and older.

Renal Impairment

The efficacy and safety of empagliflozin have not been established in patients with severe renal impairment, with end stage renal disease, or receiving dialysis. Empagliflozin is not expected to be effective in these patient populations. The risks of renal impairment, volume depletion adverse reactions and urinary tract infection-related adverse reactions increased with worsening renal function.

Empagliflozin may be used in patients with an eGFR greater than or equal to 45 mL/min/1.73 m^2. Empagliflozin is not recommended in patients with an eGFR less than 45 mL/min/1.73 m^2.

Hepatic Impairment

Empagliflozin may be used in patients with hepatic impairment.

OVERDOSAGE

In the event of an overdose with empagliflozin, employ the usual supportive measures (e.g., remove unabsorbed material from the gastrointestinal tract, employ clinical monitoring, and institute supportive treatment) as dictated by the patient's clinical status. Removal of empagliflozin by hemodialysis has not been studied.

DOSAGE AND INSTRUCTIONS

To be sold and used on the prescription of a registered medical practitioner only. Keep out of reach of children. Do not store above 30°C. Keep in a dry place. Protect from light.

PRESENTATION

Diajard 10mg Tablets: Alu. Alu. Blister Pack of 2 x 7's.
Diajard 25mg Tablets: Alu. Alu. Blister Pack of 2 x 7's.

ڈائیاجارڈ™

(ایمپاگلیفلوزن)

خوراک و ہدایات:

صرف مستند ڈاکٹر کے نسخہ کے مطابق ہی دوا فروخت اور استعمال کی جائے۔
بچوں کی پہنچ سے دور رکھیں۔ 30°C سے زیادہ درجہ حرارت پر نہ رکھیں۔
خشک جگہ پر رکھیں۔ روشنی سے بچائیں۔

Manufactured by
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