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JARDY™
[EMPAGLIFLOZIN]

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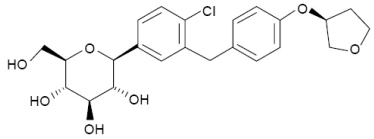
COMPOSITION:
JARDY Tablet 10 mg:
Each film coated tablet contains:
Empagliflozin ..... 10 mg.

Product Specs.: Innovator

JARDY Tablet 25 mg:
Each film coated tablet contains:
Empagliflozin ..... 25 mg.

Product Specs.: Innovator

DESCRIPTION:
JARDY tablets contain empagliflozin, an orally-active inhibitor of the sodium-glucose co-transporter 2 (SGLT2).
The chemical name of empagliflozin is D-Glucitol,1,5-anhydro-1-C-[4-chloro-3-[[4-[[(3S)-tetrahydro-3 furanyl]oxy]phenyl]methyl]phenyl]-, (1S). Its molecular formula is $C_{23}H_{27}ClO_7$ and the molecular weight is 450.91. The structural formula is:



CLINICAL PHARMACOLOGY:
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. 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.
Pharmacokinetics:
Absorption:
After oral administration, peak plasma concentrations of empagliflozin reached at 1.5 hours. The steady state mean plasma AUC and C_{max} were 1870 nmol·h/L and 259 nmol/L, respectively, with 10 mg empagliflozin once daily treatment, and 4740 nmol·h/L and 687 nmol/L, respectively, with 25 mg empagliflozin once daily treatment. Empagliflozin may be administered with or without food.
Distribution:
The apparent steady-state volume of distribution is estimated to be 73.8 L and plasma protein binding is 86.2%.
Metabolism:
Primary route of metabolism of empagliflozin in humans is glucuronidation by the uridine 5'-diphospho-glucuronosyltransferases UGT2B7, UGT1A3, UGT1A8, and UGT1A9.
Elimination:
The apparent terminal elimination half-life of empagliflozin is estimated to be 12.4 h and apparent oral clearance is 10.6 L/h. Following administration of an oral [14C]-empagliflozin solution to healthy subjects, approximately 95.6% of the drug-related radioactivity is eliminated in feces (41.2%) or urine (54.4%). 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.
Pharmacokinetics in Special Populations:
Renal Impairment:
In patients with mild (eGFR: 60 to less than 90 mL/min/1.73 m^2), moderate (eGFR: 30 to less than 60 mL/min/1.73 m^2), and severe (eGFR: less than 30 mL/min/1.73 m^2) renal impairment and subjects with kidney failure/end stage renal disease (ESRD) patients, AUC of empagliflozin increased by approximately 18%, 20%, 66%, and 48%, respectively.
Hepatic Impairment:
In subjects with mild, moderate, and severe hepatic impairment according to the Child-Pugh classification, AUC of empagliflozin increased by approximately 23%, 47%, and 75%, and C_{max} increased by approximately 4%, 23%, and 48%, respectively.
Effects of Age, Body Mass Index, Gender, and Race:
Based on the population PK analysis, age, body mass index (BMI), gender and race (Asians versus primarily Whites) do not have a clinically meaningful effect on pharmacokinetics of empagliflozin.
Pediatric:
Studies characterizing the pharmacokinetics of empagliflozin in pediatric patients have not been performed.

INDICATIONS AND USAGE:
JARDY is indicated:
- As an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus,
- To reduce the risk of cardiovascular death in adult patients with type 2 diabetes mellitus and established cardiovascular disease.

Limitations of Use:
Not recommended for patients with type 1 diabetes or for the treatment of diabetic ketoacidosis.

DOSAGE AND ADMINISTRATION:
Administration:
The recommended dose of JARDY is 10 mg once daily in the morning, taken with or without food. In patients tolerating JARDY, the dose may be increased to 25 mg. In patients with volume depletion, correcting this condition prior to initiation of JARDY is recommended

Dose Modification Recommendations:
Patients with Renal Impairment:
- Assessment of renal function is recommended prior to initiation of JARDY and periodically thereafter.
- JARDY should not be initiated in patients with an eGFR less than 45 mL/min/1.73 m^2.
- No dose adjustment is needed in patients with an eGFR greater than or equal to 45 mL/min/1.73 m^2.
- JARDY should be discontinued if eGFR is less than 45 mL/min/1.73 m^2.
- JARDY is not indicated for the treatment of patients with type 1 diabetes mellitus.

CONTRAINDICATIONS:
- History of serious hypersensitivity reaction
- Severe renal impairment, end-stage renal disease, or dialysis.

WARNINGS AND PRECAUTIONS:
Hypotension:
JARDY causes intravascular volume contraction. Symptomatic hypotension may occur after initiating JARDY, particularly in patients with renal impairment, the elderly, in patients with low systolic blood pressure, and in patients on diuretics. Before initiating JARDY, assess for volume contraction and correct volume status if indicated. Monitor for signs and symptoms of hypotension after initiating therapy and increase monitoring in clinical situations where volume contraction is expected
Ketoacidosis:
Patients treated with JARDY 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 JARDY may be present even if blood glucose levels are less than 250 mg/dL. If ketoacidosis is suspected, JARDY should be discontinued, patient should be evaluated, and prompt treatment should be instituted. Treatment of ketoacidosis may require insulin, fluid and carbohydrate replacement.
Acute Kidney Injury and Impairment in Renal Function:
Empagliflozin causes intravascular volume contraction and can cause renal impairment. Before initiating consider factors that may predispose patients to acute kidney injury including hypovolemia, chronic renal insufficiency, congestive heart failure and concomitant medications (diuretics, ACE inhibitors, ARBs, NSAIDs). Consider temporarily discontinuing in any setting of reduced oral intake (such as acute illness or fasting) or fluid losses (such as gastrointestinal illness or excessive heat exposure); monitor patients for signs and symptoms of acute kidney injury.
More frequent renal function monitoring is recommended in patients with an eGFR below 60 mL/min/1.73 m^2. Use of JARDY is not recommended when eGFR is persistently less than 45 mL/min/1.73 m^2 and is contraindicated in patients with an eGFR less than 30 mL/min/1.73 m^2.
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

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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 JARDY 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 JARDY.
Genital Mycotic Infections:
JARDY increases the risk for genital mycotic infections. Patients with a history of chronic or recurrent genital mycotic infections were more likely to develop mycotic genital infections. Monitor and treat as appropriate.
Increased Low-Density Lipoprotein Cholesterol (LDL-C):
Increases in LDL-C can occur Monitor and treat as appropriate.

DRUG INTERACTIONS:
Diuretics:
Co-administration 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:
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.

USE IN SPECIFIC POPULATION:
Pregnancy:
Empagliflozin is not recommended during the second and third trimesters of pregnancy. 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.
Nursing Mothers:
Because of the potential for serious adverse reactions in a breastfed infant, advise women that use of JARDY 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 JARDY dosage change is recommended based on age. JARDY is expected to have diminished glycemic efficacy in elderly patients with renal impairment. The risk of volume depletion-related adverse reactions and urinary tract infections increased in patients who were 75 years of age and older to 2.3%, 4.4% and to 15.7%, and 15.1% for empagliflozin 10 mg and 25 mg.
Renal Impairment:
The glucose lowering benefit decreased in patients with worsening renal function. The risks of renal impairment, volume depletion, adverse reactions and urinary tract infection-related adverse reactions increased with worsening renal function.
The efficacy and safety have not been established in patients with severe renal impairment, with ESRD, or receiving dialysis. Empagliflozin is not expected to be effective in these patient populations.
Hepatic Impairment:
JARDY may be used in patients with hepatic impairment.

ADVERSE REACTIONS:
The following important adverse reactions are:
- Hypotension
- Ketoacidosis
- Acute Kidney Injury and Impairment in Renal Function
- Urosepsis and Pyelonephritis
- Hypoglycemia with Concomitant Use with Insulin and Insulin Secretagogues
- Genital Mycotic Infections
- Increased Low-Density Lipoprotein Cholesterol (LDL-C)

Postmarketing experience:
Additional adverse reactions have been identified during post approval use of empagliflozin.
- Ketoacidosis
- Urosepsis and pyelonephritis

OVERDOSAGE:
In the event of an overdose, employ supportive measures, as dictated by the patient's clinical status.

INSTRUCTIONS:
- Store below 30°C.
- Protect from heat, sunlight & moisture.
- Keep out of the reach of children.
- To be sold on the prescription of a registered medical practitioner only.

PRESENTATION:

JARDY Tablet 10 mg	:	Pack of 2 x 7 tablets.
JARDY Tablet 25 mg	:	Pack of 2 x 7 tablets.

ہدایات:
۳۰ درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
گرمی، دھوپ اور نمی سے بچائیں۔
بچوں کی پہنچ سے دور رکھیں۔
صرف ڈاکٹر کے نسخہ پر فروخت کریں۔

FOR FURTHER INFORMATIONS PLEASE CONTACT:

CCL
Manufactured by:
CCL Pharmaceuticals (Pvt.) Ltd.
62 Industrial Estate, Kot Lakhpat, Lahore, Pakistan.

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