FAXIBET® (DAPAGLIFLOZIN) F. C. TABLET

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DAPAGLIFLOZIN

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Read this patient information carefully before you start taking Faxibet® because it answers some common questions about Faxibet®. This medication is prescribed for your current condition, therefore do not use it in similar cases and do not recommend it to others.
To report SUSPECTED ADVERSE REACTIONS, contact Noavaran Daroui Kimia Co. at +982166433514 or send email to medical@kimia-pharma.co

Read this patient Information carefully before you start taking Faxibet® because it contains important information for you. This leaflet does not take the place of talking with your healthcare provider about your medical condition or treatment.

Composition
- Each film-coated tablet Faxibet® 5 mg contains: dapagliflozin (as propanediol monohydrate) 5 mg.
- Each film-coated tablet Faxibet® 10 mg contains: dapagliflozin (as propanediol monohydrate) 10 mg.

Mechanism of action
Dapagliflozin is a Sodium-glucose cotransporter 2 (SGLT2) inhibitor. Dapagliflozin reduces reabsorption of filtered glucose and increases urinary glucose excretion. Dapagliflozin also reduces sodium reabsorption and increases the delivery of sodium to the distal tubule. This may influence several physiological functions including, but not restricted to, lowering both pre- and afterload of the heart and downregulation of sympathetic activity.

Pharmacokinetic
- **Absorption**
  Following oral administration of Faxibet®, the maximum plasma concentration (Cmax) is usually attained within 2 hours under fasting state. The Cmax and AUC values increase dose proportionally with increase in Faxibet® dose in the therapeutic dose range. The absolute oral bioavailability of Faxibet® following the administration of a 10 mg dose is 78%. Administration of Faxibet® with a high-fat meal decreases its Cmax by up to 50% and prolongs Tmax by approximately 1 hour, but does not alter AUC as compared with the fasted state. These changes are not considered to be clinically meaningful and Faxibet® can be administered with or without food.

- **Distribution**
  Faxibet® have approximately 91% protein binding. Protein binding is not altered in patients with renal or hepatic impairment.

- **Metabolism**
  The metabolism of Faxibet® is primarily mediated by UGT1A9. CYP-mediated metabolism is a minor clearance pathway in humans. Faxibet® is extensively metabolized, primarily to yield dapagliflozin 3-O-glucuronide, which is an inactive metabolite. Dapagliflozin 3-O-glucuronide accounted for 61% of a 50 mg [^{14}C]-dapagliflozin dose and is the predominant drug-related component in human plasma.

- **Excretion**
  Faxibet® and related metabolites are primarily eliminated via the renal pathway. Following a single 50 mg dose of [^{14}C]-dapagliflozin, 75% and 21% total radioactivity is excreted in urine and feces, respectively. The mean plasma terminal half-life ($t_{½}$) for Faxibet® is approximately 12.9 hours following a single oral dose of Faxibet® 10 mg.

Indication
Faxibet® is prescribed in adults with
- as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.
- to reduce the risk of hospitalization for heart failure in adults with type 2 diabetes mellitus and either established cardiovascular disease or multiple cardiovascular risk factors.
- to reduce the risk of cardiovascular death and hospitalization for heart failure in adults with heart failure with reduced ejection fraction (NYHA class II-IV).
- to reduce the risk of sustained eGFR decline, end stage kidney disease, cardiovascular death, and hospitalization for heart failure in adults with chronic kidney disease at risk of progression.

Limitations of use
- Not for treatment of type 1 diabetes mellitus.
- Faxibet® 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 m². Faxibet® is likely to be ineffective in this setting based upon its mechanism of action.
- Faxibet® is not recommended for the treatment of chronic kidney disease in patients with polycystic kidney disease or patients requiring or with a recent history of immunosuppressive therapy for the treatment of kidney disease. Faxibet® is not expected to be effective in these populations.

Dosage and Administration
Assess volume status and correct volume depletion before initiating.
- **eGFR 45 mL/min/1.73 m² or greater**
  To improve glycemic control, the recommended starting dose is 5 mg orally once daily. Dose can be increased to 10 mg orally once daily for additional glycemic control. For all other indications, the recommended starting dose is 10 mg orally once daily.

- **eGFR 25 to less than 45 mL/min/1.73 m²**
  10 mg orally once daily.

- **eGFR less than 25 mL/min/1.73 m²**
  Initiation is not recommended, however patients may continue 10 mg orally once daily to reduce the risk of eGFR decline, ESKD, CV death and hHF.

- **On dialysis**
  Contraindicated.

Side effects / Adverse reactions
It should be noted that these side effects do not occur in all patients. These are not all the possible side effects of Faxibet®. For more information, ask your healthcare provider or pharmacist.

Faxibet® can cause serious side effects, including:

- **Dehydration.** Faxibet® can cause some people to become dehydrated (the loss of body water and salt). Dehydration may cause you to feel dizzy, faint, lightheaded, or weak, especially when you stand up (orthostatic hypotension). There have been reports of sudden kidney injury in people with Type 2 diabetes who are taking Faxibet®. You may be at a higher risk of dehydration if you:
  - take medicines to lower your blood pressure, including water pills (diuretics)
  - are on a low salt diet
  - are 65 years of age or older
  - have kidney problems

Talk to your healthcare provider about what you can do to prevent dehydration including how much fluid you should drink on a daily basis. Call your healthcare provider right away if you reduce the amount of food or liquid you drink, for example if you cannot eat or you start to lose liquids from your body, for example from vomiting, diarrhea, or being in the sun too long.

- **Vaginal yeast infection.** Women who take Faxibet® may get vaginal yeast infections. Symptoms of a vaginal yeast infection include:
  - vaginal odor
  - white or yellowish vaginal discharge (discharge may be lumpy or look like cottage cheese)
  - vaginal itching

- **Yeast infection of the penis (balanitis).** Men who take Faxibet® may get a yeast infection of the skin around the penis. Certain men who are not circumcised may have swelling of the penis that makes it difficult to pull back the skin around the tip of the penis. Other symptoms of yeast infection of the penis include:
  - redness, itching, or swelling of the penis
  - rash of the penis
  - foul smelling discharge from the penis
  - pain in the skin around the penis

Talk to your healthcare provider about what to do if you get symptoms of a yeast infection of the vagina or penis. Your healthcare provider may suggest you use an over-the-counter antifungal medicine. Talk to your healthcare provider right away if you use an over-the-counter antifungal medication and your symptoms do not go away.

- **Ketoacidosis in people with diabetes mellitus (increased ketones in your blood or urine).** Ketoacidosis has happened in people who have **type 1 diabetes or type 2 diabetes,** during treatment with Faxibet®. Ketoacidosis has also happened in people with diabetes who were sick or who had surgery during treatment with Faxibet®. Ketoacidosis is a serious condition, which may need to be treated in a hospital. Ketoacidosis may lead to death.

Ketoacidosis can happen with Faxibet® even if your blood sugar is less than 250 mg/dL. Stop taking Faxibet® and call your healthcare provider right away if you get any of the following symptoms:
- nausea
- tiredness
- vomiting
- trouble breathing
- stomach area (abdominal) pain

If you get any of these symptoms during treatment with Faxibet®, if possible, check for ketones in your urine, even if your blood sugar is less than 250 mg/dL.

- **Serious urinary tract infections.** Serious urinary tract infections that may lead to hospitalization have happened in people who are taking Faxibet®. Tell your healthcare provider if you have any signs or symptoms of a urinary tract infection such as a burning feeling when passing urine, a need to urinate often, the need to urinate right away, pain in the lower part of your stomach (pelvis), or blood in the urine. Sometimes people also may have a fever, back pain, nausea or vomiting.

- **Low blood sugar (hypoglycemia) in patients with diabetes mellitus.** If you take Faxibet® with another medicine that can cause low blood sugar, such as a sulfonylurea or insulin, your risk of getting low blood sugar is higher. The dose of your sulfonylurea medicine or insulin may need to be lowered while you take Faxibet®. Signs and symptoms of low blood sugar may include:
  - headache
  - weakness
  - confusion
  - shaking or feeling jittery
  - drowsiness
  - dizziness
  - irritability
  - sweating
  - hunger
  - fast heartbeat

- **A rare but serious bacterial infection that causes damage to the tissue under the skin (necrotizing fasciitis) in the area between and around the anus and genitals (perineum).** Necrotizing fasciitis of the perineum has happened in women and men with diabetes mellitus who take Faxibet®. Necrotizing fasciitis of the perineum may lead to hospitalization, may require multiple surgeries, and may lead to death. **Seek medical attention immediately if you have fever or you are feeling very weak, tired, or uncomfortable (malaise) and you develop any of the following symptoms in the area between and around the anus and genitals:**
  - pain or tenderness
  - swelling
  - redness of skin (erythema)

Call your healthcare provider right away if you have aforementioned symptoms.

- **The most common side effects of Faxibet® include:**
  - vaginal yeast infections and yeast infections of the penis
  - stuffy or runny nose and sore throat
  - changes in urination, including urgent need to urinate more often, in larger amounts, or at night

Drug interaction
- **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.

Warnings
Before you take Faxibet®, tell your healthcare provider if you:
- have type 1 diabetes or have had diabetic ketoacidosis.
- have liver problems.
- have a history of urinary tract infections or problems urinating.
- are going to have surgery. Faxibet® should be interrupted in patients who are hospitalised for major surgery or acute serious illnesses .Talk to your doctor if you are having surgery about when to stop taking Faxibet® and when to start it again.
- are eating less or there is a change in your diet.
- have or have had problems with your pancreas, including pancreatitis or surgery on your pancreas.
- drink alcohol very often or drink a lot of alcohol in the short term (“binge” drinking).
- are pregnant or plan to become pregnant. Faxibet® may harm your unborn baby.
- are breastfeeding or plan to breastfeed.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Faxibet® and other medicines may affect each other causing side effects.

Missed dose
If you miss a dose, take it as soon as you remember. If it is almost time for your next dose, skip the missed dose and take the medicine at the next regularly scheduled time. Do not take 2 doses of Faxibet® at the same time.

Overdose
If you take too much Faxibet®, call your healthcare provider or go to the nearest emergency room right away.

Pregnancy and lactation
Faxibet® may harm your unborn baby. If you become pregnant while taking Faxibet®, your healthcare provider may switch you to a different medicine to control your blood sugar. Talk to your healthcare provider about the best way to control your blood sugar if you plan to become pregnant or while you are pregnant.
It is not known if Faxibet® passes into your breast milk. You should not breastfeed if you take Faxibet®.

Patient information
- Take Faxibet® exactly as your healthcare provider tells you to take it.
- Do not change your dose of Faxibet® without talking to your healthcare provider.
- Take Faxibet® by mouth at the same time each day, with or without food.
- Stay on your prescribed diet and exercise program while taking Faxibet®.
- Faxibet® will cause your urine to test positive for glucose.
- Your healthcare provider may do certain blood tests before you start Faxibet® and during your treatment.
- If you have diabetes
  - When your body is under some types of stress, such as fever, trauma (such as a car accident), infection, or surgery, the amount of diabetes medicine you need may change. Tell your healthcare provider right away if you have any of these conditions and follow your healthcare provider's instructions.
  - Your healthcare provider will check your diabetes with regular blood tests, including your blood sugar levels and your HbA1c.
  - Follow your healthcare provider's instructions for treating low blood sugar (hypoglycemia). Talk to your healthcare provider if low blood sugar is a problem for you.

Storage
- Keep away from light and moisture. Store below 30°C.
- Safely throw away medicine that is out of date or that you no longer need. Ask your pharmacist how to safely throw away Faxibet® tablets.
- Keep out of the reach of children.

Packaging
- Bottle of 30 F. C. tablets

References

- https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/202293s024lbl.pdf
- https://www.ema.europa.eu/en/documents/product-information/forxiga-epar-product-information_en.pdf
- BNF 80: September 2020 - March 2021

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