



FAXIBET PLUS® ER (DAPAGLIFLOZIN/METFORMIN HCl) EXTENDED-RELEASE F. C. TABLET

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Read this patient information carefully before you start taking Faxibet Plus® ER because it answers some common questions about Faxibet Plus® ER. 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 Novaran Daroui Kimia Co. at +982166433514 or send email to medical@kimia-pharma.co

Read this patient information carefully before you start taking Faxibet Plus® ER 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

Faxibet Plus® ER tablets are available in the following dosage/ form: Dapagliflozin (as propanediol monohydrate)/Metformin HCl extended-release: 2.5 mg/1000 mg, 10 mg/500 mg, 10 mg/1000 mg, 5 mg/500 mg, 5 mg/1000 mg

Mechanism of action

Dapagliflozin is a Sodium-glucose cotransporter 2 (SGLT2) inhibitor. Metformin is an antihyperglycemic agent.

Pharmacokinetic

Absorption

- Dapagliflozin: The maximum plasma concentration (C_{max}) is within 2 hours.
- Metformin HCl ER: C_{max} is achieved with a median value of 7 hours (4 - 8 hours).

Distribution

- Dapagliflozin: Dapagliflozin is approximately 91% protein bound.
- Metformin HCl: Distribution studies with metformin ER have not been conducted.

Metabolism

- Dapagliflozin: The metabolism is primarily mediated by UGT1A9.
- Metformin HCl: Metformin is excreted unchanged in the urine and does not undergo hepatic metabolism. Metabolism studies with extended-release metformin tablets have not been conducted.

Elimination

- Dapagliflozin and related metabolites are primarily eliminated via the renal pathway.
- Metformin HCl: Tubular secretion is the major route of elimination.

Indication

Faxibet Plus® ER is a combination of dapagliflozin, and metformin HCl, indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Dapagliflozin is indicated to reduce:

- the risk of hospitalization for heart failure in adults with type 2 diabetes mellitus and established cardiovascular disease or multiple cardiovascular risk factors.
- the risk of cardiovascular death and hospitalization for heart failure in adults with heart failure (NYHA class II-IV) with reduced ejection fraction.
- 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. It may increase the risk of diabetic ketoacidosis in these patients.
- Because of the metformin HCl component, the use of Faxibet Plus® ER is limited to adults with type 2 diabetes mellitus for all indications.
- Faxibet Plus® ER 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 Plus® ER is not expected to be effective in these populations.

It is not known if Faxibet Plus® ER is safe and effective in children younger than 18 years of age.

Dosage and administration

- Individualize the starting dose based on the patient's current treatment.
- Assess renal function before initiating and periodically thereafter.
- To improve glycemic control, for patients not already taking dapagliflozin, the recommended starting dose of dapagliflozin is 5 mg once daily.
- For indications related to heart failure and chronic kidney disease the recommended dose of dapagliflozin is 10 mg once daily.
- Do not exceed a daily dose of 10 mg dapagliflozin/2000 mg metformin HCl extended release.
- Faxibet Plus® ER may need to be discontinued at time of, or prior to, iodinated contrast imaging procedures.

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 Plus® ER. For more information, ask your healthcare provider or pharmacist.

Faxibet Plus® ER can cause serious side effects, including:

- Lactic Acidosis.** Metformin can cause a rare but serious condition called lactic acidosis (a build-up of an acid in the blood) that can be life threatening. Lactic acidosis is a medical emergency and must be treated in the hospital. Stop taking Faxibet Plus® ER and call your healthcare provider right away if you have any of the following symptoms:
 - you have stomach pains, nausea or vomiting
 - you feel dizzy or lightheaded
 - you have a slow or irregular heartbeat
 - you feel cold in your hands or feet
 - you have unusual (not normal) muscle pain
 - you have trouble breathing
 - you feel unusual sleepiness or sleep longer than usual
 - you feel very weak or tired

Most people who have had lactic acidosis with metformin have other things that, combined with the metformin use, led to the lactic acidosis. Tell your healthcare provider if you have any of the following, because you have a higher chance for getting lactic acidosis with Faxibet Plus® ER if you:

- have severe kidney problems or your kidneys are affected by certain x-ray tests that use injectable dye.
- have liver problems.
- have surgery.
- drink alcohol very often, or drink a lot of alcohol in the short-term ("binge" drinking).
- get dehydrated (lose a large amount of body fluids). This can happen if you are sick with a fever, vomiting, or diarrhea. Dehydration can also happen when you sweat a lot with activity or exercise and do not drink enough fluids.
- have new or worsening symptoms of congestive heart failure such as shortness of breath or increased fluid or swelling of the legs.
- have a heart attack, severe infection, or stroke.
- are 65 years of age or older.

Your healthcare provider may decide to stop your Faxibet Plus® ER for a while if you have any of these things.

- Dehydration.** 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 mellitus who are taking dapagliflozin, a medicine in Faxibet Plus® ER.

You may be at a higher risk of dehydration if you:

- are 65 years of age or older
- are on a low salt diet
- have kidney problems
- take medicines to lower your blood pressure, including water pills (diuretics)

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.

- Ketoacidosis (increased ketones in your blood or urine).** Ketoacidosis has happened in people who have type 1 diabetes or type 2 diabetes, during treatment with dapagliflozin, one of the medicines in Faxibet Plus® ER. Ketoacidosis has also happened in people with diabetes who were sick or who had surgery during treatment with Faxibet Plus® ER. Ketoacidosis may be life threatening. **Ketoacidosis can happen with Faxibet Plus® ER even if your blood sugar is less than 250 mg/dL. Stop taking Faxibet Plus® ER and call your healthcare provider right away or go to the nearest hospital emergency room 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 Plus® ER, if possible, check for ketones in your urine, even if your blood sugar is less than 250 mg/dL.

- Serious urinary tract infections.** Tell your healthcare provider if you have any following signs or symptoms: 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).** If you take Faxibet Plus® ER with another medicine that can cause low blood sugar, such as sulfonylureas 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 Plus® ER. Signs and symptoms of low blood sugar may include:
 - headache
 - weakness
 - confusion
 - shaking or feeling jittery
 - sweating
 - irritability
 - dizziness
 - fast heartbeat
 - drowsiness
 - hunger

- 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 may lead to hospitalization, may require multiple surgeries and may be life threatening. **Seek medical attention immediately if you have a 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:

- o pain or tenderness
- o swelling
- o redness of skin (erythema)
- Low vitamin B₁₂ (vitamin B₁₂ deficiency).** Using metformin for long periods of time may cause a decrease in the amount of vitamin B₁₂ in your blood, especially if you have had low vitamin B₁₂ levels. Your healthcare provider may do blood tests to check your vitamin B₁₂ levels.
- Vaginal yeast infection.** Symptoms of a vaginal yeast infection include:
 - o vaginal odor
 - o vaginal itching
 - o white or yellowish vaginal discharge (discharge may be lumpy or look like cottage cheese)
- Yeast infection of the penis (balanitis or balanoposthitis).** Symptoms of a yeast infection of the penis include:
 - o redness, itching, or swelling of the penis
 - o rash of the penis
 - o foul smelling discharge from the penis
 - o 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.

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

The most common side effects of Faxibet Plus® ER include:

- o vaginal yeast infections
- o stuffy or runny nose and sore throat
- o diarrhea
- o urinary tract infection
- o nausea and vomiting
- o headache

Tell your healthcare provider or pharmacist if you have any side effect that bothers you or does not go away.

Drug interaction

- Carbonic Anhydrase Inhibitors:** Concomitant use of these drugs (Topiramate or other carbonic anhydrase inhibitors e.g., zonisamide, acetazolamide or dichlorphenamide) with Faxibet Plus® ER may increase the risk for lactic acidosis.
- Drugs that Reduce Metformin Clearance:** Concomitant use of these drugs (ranolazine, vandetanib, dolutegravir, and cimetidine) could increase systemic exposure to metformin and may increase the risk for lactic acidosis.
- Alcohol:** Alcohol is known to potentiate the effect of metformin on lactate metabolism.
- Diabetes Affecting Glycemic Control:** Certain drugs tend to produce hyperglycemia and may lead to loss of glycemic control. These medications include thiazides and other diuretics, insulin and insulin secretagogues, such as sulphonylureas, corticosteroids, phenothiazines, thyroid products, estrogens, oral contraceptives, phenytoin, nicotinic acid, sympathomimetics, calcium channel blocking drugs, and isoniazid.
- Positive Urine Glucose Test:** SGLT2 inhibitors increase urinary glucose excretion and will lead to positive urine glucose tests.
- Interference with 1,5-anhydroglucitol (1,5-AG) Assay:** Measurements of 1,5-AG are unreliable in assessing glycemic control in patients taking SGLT2 inhibitors.

Warnings

Before taking Faxibet Plus® ER tell your healthcare provider about all of your medical conditions, including if you:

- have type 1 diabetes or have had diabetic ketoacidosis.
- have a history of urinary tract infections or problems urinating.
- have kidney or liver problems.
- are 65 years of age or older.
- have a history of infection of the vagina or penis.
- have heart problems, including congestive heart failure.
- are eating less, or there is a change in your diet.
- are breastfeeding or plan to breastfeed.
- have low levels of vitamin B₁₂ in your blood.
- are going to have surgery and will not be able to eat or drink much. Your healthcare provider may stop Faxibet Plus® ER before you have surgery. Talk to your healthcare provider if you are having surgery about when to stop taking Faxibet Plus® ER and when to start it again.
- are 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 going to get an injection of dye or contrast agents for an x-ray procedure. Faxibet Plus® ER may need to be stopped for a short time. Talk to your healthcare provider about when you should stop Faxibet Plus® ER and when you should start Faxibet Plus® ER again.
- are pregnant or plan to become pregnant. Faxibet Plus® ER may harm your unborn baby.
- are a person who has not gone through menopause (premenopausal) who does not have periods regularly or at all. Faxibet Plus® ER can cause the release of an egg from an ovary in a person (ovulation). This can increase your chance of getting pregnant.

Do not take Faxibet Plus® ER if you:

- have severe kidney problems or are on dialysis.
- have a history of a serious hypersensitivity reaction to dapagliflozin, such as anaphylactic reactions or angioedema, or hypersensitivity to metformin HCl.
- are allergic to dapagliflozin, metformin HCl, or any of the ingredients in Faxibet Plus® ER. Symptoms of a serious allergic reaction to Faxibet Plus® ER may include:
 - o skin rash
 - o raised red patches on your skin (hives)
 - o swelling of the face, lips, tongue, and throat that may cause difficulty in breathing or swallowing

If you have any of these symptoms, stop taking Faxibet Plus® ER and contact your healthcare provider or go to the nearest hospital emergency room right away.

- have a condition called metabolic acidosis or diabetic ketoacidosis (increased ketones in your blood or urine).

Tell your healthcare provider about all the medicines you take, including prescription medicines and over-the-counter medicines, vitamins, and herbal supplements.

Especially tell your healthcare provider if you take:

- water pills (diuretics)
- rifampin (used to treat or prevent tuberculosis)
- phenytoin (used to control seizures)
- digoxin (used to treat heart problems)

Missed dose

If you miss a dose of Faxibet Plus® ER, 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.

Overdose

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

Pregnancy and lactation

Faxibet Plus® ER may cause harm to your unborn baby, especially during the second and third trimesters. Do not take Faxibet Plus® ER if you are pregnant. Tell your healthcare provider right away if you are pregnant, or planning to become pregnant. Talk to your healthcare provider about the best way to control your blood sugar while you are pregnant. There is a potential for an unintended pregnancy in premenopausal females as therapy with metformin may result in ovulation in some an ovulatory women.

Faxibet Plus® ER is not recommended while breastfeeding. Talk to your healthcare provider if you would like to or are breast-feeding before taking this medicine. Metformin passes into human milk in small amounts. It is not known if dapagliflozin passes into human breast milk.

Patient information

- Take Faxibet Plus® ER exactly as your healthcare provider tells you to take it.
- Do not change your dose of Faxibet Plus® ER without talking to your healthcare provider.
- Take Faxibet Plus® ER by mouth 1 time each day with meals to lower your chance of an upset stomach. Talk to your healthcare provider about the best time of day for you.
- Swallow Faxibet Plus® ER whole. Do not crush, cut, or chew Faxibet Plus® ER.
- You may sometimes pass a soft mass in your stools (bowel movement) that looks like Faxibet Plus® ER tablets.
- 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.
- Stay on your prescribed diet and exercise program while taking Faxibet Plus® ER.
- Faxibet Plus® ER will cause your urine to test positive for glucose.
- Your healthcare provider will check your diabetes with regular blood tests, including your blood sugar levels and your A1c.
- 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.
- Avoid drinking alcohol very often, or drinking a lot of alcohol in a short period of time ("binge" drinking). It can increase your chances of getting serious side effects.

Storage

- Keep away from light and moisture. Store below 30 °C.
- Keep Faxibet Plus® ER and all medicines out of the reach of children.
- Keep the desiccant in the bottle. Do not eat or throw away desiccant pack.

Packaging

Bottle of 30 F. C. Tablets.

License Holder:

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www.kimia-pharma.co

References

https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/205649s017tbl.pdf
https://www.ema.europa.eu/en/documents/product-information/xigduo-epar-product-information_en.pdf
BNF B3: March-September 2022