EMPAGLIBET® F. C. TABLET

EMPAGLIBET®
EMPAGLIFLOZIN

EMPAGLIBET® (EMPAGLIFLOZIN) F. C. TABLET FOR ORAL USE
Read this patient information carefully before you start taking Empaglibet® because it answers some common questions about Empaglibet®. 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 Empaglibet® 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 Empaglibet® 10 mg contains: 10 mg of Empagliflozin.
Each film-coated tablet Empaglibet® 25 mg contains: 25 mg of Empagliflozin.

Mechanism of action
Empagliflozin is an inhibitor of Sodium-glucose co-transporter 2 (SGLT2). By inhibiting SGLT2, Empagliflozin reduces renal reabsorption of filtered glucose and thereby increases urinary glucose excretion.

Pharmacokinetic
Absorption
After oral administration, peak plasma concentrations of Empaglibet® were reached at 1.5 hours post-dose. Empaglibet® may be administered with or without food.
Distribution
The apparent steady-state volume of distribution was estimated to be 73.8 L. Following administration of an oral [^{14}C]-empagliflozin solution to healthy subjects, the plasma protein binding was 86.2%.
Elimination
The apparent terminal elimination half-life of Empaglibet® was estimated to be 12.4 h and apparent oral clearance was 10.6 L/h.
Metabolism
No major metabolites of Empaglibet® were detected in human plasma.
Excretion
Following administration of an oral [^{14}C]-empagliflozin solution to healthy subjects, approximately 95.6% of the drug-related radioactivity was eliminated in feces (41.2%) or urine (54.4%).

Indication
Empaglibet® is indicated:
- To reduce the risk of cardiovascular death and hospitalization for heart failure in adults with heart failure.
- To reduce the risk of cardiovascular death in adults with type 2 diabetes mellitus and established cardiovascular disease.
- As an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of Use:
- Not recommended in patients with type 1 diabetes mellitus. It may increase the risk of diabetic ketoacidosis in these patients.
- Not recommended for use to improve glycemic control in adults with type 2 diabetes mellitus with an eGFR less than 30 mL/min/1.73 m^2.

It is not known if Empaglibet® is safe and effective in children.

Dosage and Administration
- Assess volume status and correct volume depletion before initiating.
- Recommended dose is 10 mg once daily in the morning, taken with or without food.
- For additional glycemic control, dose may be increased to 25 mg in patients tolerating Empaglibet®.

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

Empaglibet® may cause serious side effects including:

- **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 Empaglibet®. Ketoacidosis has also happened in people with diabetes who were sick or who had surgery during treatment with Empaglibet®. Ketoacidosis is a serious condition, which needs to be treated in a hospital. Ketoacidosis may be life-threatening. **Ketoacidosis can happen with Empaglibet® even if your blood sugar is less than 250 mg/dL. Stop taking Empaglibet® and call your healthcare provider right away or go to the nearest hospital emergency room if you get any of the following symptoms:**
  - o nausea
  - o tiredness
  - o vomiting
  - o trouble breathing
  - o stomach-area (abdominal) pain

  If you get any of these symptoms during treatment with Empaglibet®, if possible, check for ketones in your urine, even if your blood sugar is less than 250 mg/dL.
- **Dehydration.** Empaglibet® can cause some people to become dehydrated (the loss of body water and salt). Dehydration may cause you to feel dizzy, faint, light-headed, or weak, especially when you stand up (orthostatic hypotension). There have been reports of sudden worsening of kidney function in people who are taking Empaglibet®. You may be at higher risk of dehydration if you:
  - o take medicines to lower your blood pressure, including diuretics (water pills)
  - o are on low sodium (salt) diet
  - o have kidney problems
  - o are 65 years of age or older

  Talk to your healthcare provider about what you can do to prevent dehydration including how much fluid you should drink on a daily basis. Talk to your healthcare provider right away if you reduce the amount of food or liquid you drink, for example if you are sick or cannot eat, or start to lose liquids from your body, for example from vomiting, diarrhea or being in the sun too long.
- **Serious urinary tract infections.** Serious urinary tract infections that may lead to hospitalization have happened in people who are taking Empaglibet®. 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).** If you take Empaglibet® 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 Empaglibet®. Signs and symptoms of low blood sugar may include:
  - o headache
  - o irritability
  - o confusion
  - o dizziness
  - o drowsiness
  - o hunger
  - o fast heartbeat
  - o sweating
  - o weakness
  - o shaking or feeling jittery
- **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 who take Empaglibet®. 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 your anus and genitals:**
  - o pain or tenderness
  - o swelling
  - o redness of skin (erythema)
- **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).** Swelling of an uncircumcised penis may develop that makes it difficult to pull back the skin around the tip of the penis. Other symptoms of 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 penis

  Talk to your doctor 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.
- **Allergic (hypersensitivity) reactions.** Serious allergic reactions have happened in people who are taking Empaglibet®. Symptoms may include:
  - o swelling of your face, lips, throat and other areas of your skin
  - o difficulty with swallowing or breathing.
  - o raised, red areas on your skin (hives)

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

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

The most common side effects of Empaglibet® include:
- urinary tract infections
- yeast infections in females

Drug interaction
- **Diuretics**
  Coadministration of Empaglibet® with diuretics resulted in increased urine volume and frequency of voids, which might enhance the potential for volume depletion. Before initiating Empaglibet®, assess volume status and renal function. In patients with volume depletion, correct this condition before initiating Empaglibet®. Monitor for signs and symptoms of volume depletion, and renal function after initiating therapy.
- **Insulin or Insulin Secretagogues**
  The risk of hypoglycemia is increased when Empaglibet® is used in combination with insulin secretagogues (e.g., sulfonylurea) or insulin. Coadministration of Empaglibet® with an insulin secretagogue (e.g., sulfonylurea) or insulin may require lower doses of the insulin secretagogue or insulin to reduce the risk of hypoglycemia.
- **Lithium**
  Concomitant use of an SGLT2 inhibitor with lithium may decrease serum lithium concentrations. Monitor serum lithium concentration more frequently during Empaglibet® initiation and dosage changes.
- **Positive Urine Glucose Test**
  SGLT2 inhibitors increase urinary glucose excretion and will lead to positive urine glucose tests. Monitoring glycemic control with urine glucose tests is not recommended in patients taking SGLT2 inhibitors. Use alternative methods to monitor glycemic control.
- **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. Monitoring glycemic control with 1,5-AG assay is not recommended. Use alternative methods to monitor glycemic control.
- **Inducers of UGT enzymes**
  Co-treatment with known inducers of UGT enzymes is not recommended due to a potential risk of decreased efficacy. If an inducer of these UGT enzymes (e.g. Rifampicin, phenobarbital, phenytoin, and carbamazepine, ...) must be co-administered, monitoring of glycemic control to assess response to Empaglibet® is appropriate.

Warnings
Before taking Empaglibet®, tell your healthcare provider about all of your medical conditions, including if you:
- have kidney problems.
- have liver problems.
- have a history of infection of the vagina or penis.
- have a history of urinary tract infections or problems with urination.
- are going to have surgery. Your healthcare provider may stop your Empaglibet® before you have surgery. Empaglibet® should be interrupted in patients who are hospitalized for major surgery or acute serious illnesses. Talk to your healthcare provider if you are having surgery about when to stop taking Empaglibet® 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).
- have type 1 diabetes. Empaglibet® should not be used to treat people with type 1 diabetes.
- are pregnant or plan to become pregnant. Empaglibet® 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. Empaglibet® may affect the way other medicines work, and other medicines may affect how Empaglibet® works.

Do not take Empaglibet® if you are on dialysis.

Missed dose
If you miss a dose, take it as soon as you remember. If you do not remember until it is time for your next dose, or less than 12 hours to the next dose, skip the missed dose and go back to your regular schedule. Do not take two doses of Empaglibet® at the same time. Talk with your healthcare provider if you have questions about a missed dose.

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

Pregnancy and lactation
Empaglibet® may harm your unborn baby. Do not use Empaglibet® if you are pregnant. If you become pregnant while taking Empaglibet®, tell your healthcare provider as soon as possible. Talk with your healthcare provider about the best way to control your blood sugar while you are pregnant.
Empaglibet® may pass into your breast milk and may harm your baby. Talk with your healthcare provider about the best way to feed your baby if you are taking Empaglibet®. Do not breastfeed while taking Empaglibet®.

Patient information
- Take Empaglibet® exactly as your healthcare provider tells you to take it.
- Take Empaglibet® by mouth 1 time in the morning each day, with or without food.
- Your healthcare provider may change your dose if needed.
- Your healthcare provider may tell you to take Empaglibet® along with other diabetes medicines. Low blood sugar can happen more often when Empaglibet® is taken with certain other diabetes medicines.
- When taking Empaglibet®, you may have sugar in your urine, which will show up on a urine test.
- Your healthcare provider may do blood tests to check how well your kidneys are working before and during your treatment with Empaglibet®.
- Empaglibet® contains lactose (milk sugar). If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

Storage
- Keep away from light and moisture. Store below 30°C.
- Keep out of the reach of children.
- Keep the desiccant in the bottle. Do not eat or throw away desiccant pack.
- Keep in the original container.
- Safely throw away medicine that is out of date or that you no longer need.

Packaging
Bottle of 30 F. C. Tablets.

License Holder:
Noavaran Daroui Kimia Co., Tehran, Iran.
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www.kimia-pharma.co

References
https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/204629s039lbl.pdf
https://www.ema.europa.eu/en/documents/product-information/jardiance-epar-product-information_en.pdf
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