

This medicine is dispensed according to physician's prescription only

Glyxambi® 10 mg / 5 mg

Each coated tablet contains 5 mg linagliptin and 10 mg empagliflozin.

Glyxambi® 25 mg / 5 mg

Each coated tablet contains 5 mg linagliptin and 25 mg empagliflozin.

Film coated tablets

*Inactive ingredients and allergens in the medicine - See section 6 'Additional information'.

Read the entire leaflet carefully before using this medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness is similar to yours.

1. What is this medicine intended for?

Glyxambi is intended, in combination with diet and physical activity, to improve control of blood sugar level in adults with type 2 diabetes, in cases where combination therapy with two active ingredients linagliptin and empagliflozin is required. Glyxambi is not recommended for patients with type 1 diabetes or for treating diabetic ketoacidosis. Glyxambi has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at an increased risk of developing pancreatitis while using Glyxambi.

Therapeutic group:

Glyxambi is a combination of two active ingredients: empagliflozin and linagliptin. Empagliflozin is an SGLT2 (sodium-glucose co-transporter 2) inhibitor. Linagliptin is a DPP-4 (dipeptidyl peptidase-4) inhibitor.

2. Before using this medicine

Do not use the medicine if:

- You are sensitive (allergic) to the active ingredients empagliflozin and/or linagliptin or to any of the additional ingredients that this medicine contains (for the list of the inactive ingredients see section 6, 'Additional information'). Symptoms of a serious allergic reaction to Glyxambi may include:
 - o skin rash, itching, skin peeling
 - o raised red patches on your skin (hives)
 - o swelling of your face, lips, tongue and throat that may cause difficulty in breathing or swallowing
 - o difficulty in swallowing or breathingIf you have any of the above symptoms, stop taking the medicine and contact your doctor or go to the nearest hospital emergency room immediately.
- You have severe kidney problems, end-stage kidney disease, or if you are on dialysis.

Special warnings about using this medicine

Before treatment with Glyxambi, tell your doctor about any of your medical conditions including if you:

- Have kidney problems.
- Have liver problems.
- Have had infections in the vagina or penis.
- Have had urinary tract infections or difficulty passing urine.
- Are about to have surgery: your doctor may decide to stop Glyxambi before you have surgery. If you are about to have surgery, consult with your doctor when to stop taking Glyxambi and when to start your treatment again.
- Are eating less or there has been a change in your diet.
- Have or have had pancreas problems, including pancreatitis or pancreas surgery.
- Consume alcohol frequently, or drink large amounts of alcohol in a short period of time.
- Have type 1 diabetes. Glyxambi is not intended to be used to treat people with type 1 diabetes.
- Are pregnant or planning to become pregnant – see section 2 "Pregnancy and breastfeeding".
- Are breastfeeding or planning to breastfeed – see section 2 "Pregnancy and breastfeeding".
- Are 75 years or older.

Children and adolescents

It is not known whether the medicine is safe and effective in children. The medicine is not intended for use in children and adolescents under 18 years old.

Tests and follow-up

- The doctor may perform blood tests to check your kidney function before and during the treatment with Glyxambi.
- Sugar may appear in your urine while taking the medicine, which will show up in urine test.
- Diabetic foot: It is important to check your feet regularly according to the recommendations given by the health care professional.

Drug interactions

If you are taking or have recently taken other medicines including non-prescription medicines and food supplements, tell your doctor or pharmacist. Glyxambi may affect the way other medicines work, and other medicines may affect how Glyxambi works. In particular tell the doctor or pharmacist if you are taking one of the following medicines:

- Insulin or other medicines that can lower blood sugar level.
- Medicines used to remove fluids from the body (diuretics). Combining diuretics with empagliflozin (one of the ingredients in Glyxambi) increases urine volume and frequency of voids; this may result in loss of salts and body fluids (dehydration).
- Rifampin - an antibiotic that is used to treat tuberculosis.

Know the medicines you are taking, keep a list of them and present it to the doctor and pharmacist when you receive a new medicine.

Using the medicine and food

The medicine can be taken with or without food.

Pregnancy and breastfeeding

If you are pregnant, think you may be pregnant, are planning to get pregnant, breastfeeding or are planning to breastfeed, consult the doctor or pharmacist before using this medicine.

Glyxambi may harm your unborn baby. Tell the doctor as soon as possible if you become pregnant during treatment with Glyxambi. Talk to the doctor regarding the best way to control your blood sugar levels during pregnancy.

Do not breastfeed during treatment with Glyxambi. Glyxambi may pass into breast milk and may harm your baby. Consult the doctor regarding the best way to feed your baby during treatment with Glyxambi.

3. How should you use the medicine?

Always use the medicine according to your doctor's instructions. Check with the doctor or pharmacist if you are not sure about the dosage or about how to use the medicine.

The dosage and manner of treatment will be determined only by the doctor. The recommended dose is one tablet once a day in the morning, with or without food.

Your doctor can instruct you to take Glyxambi in combination with other diabetes medicines. A decrease in blood sugar level can occur more often when Glyxambi is taken with other medicines used to treat diabetes. For more information, see section 2 - "Drug interactions" and section 4 "Side effects"

Do not exceed the recommended dose.

Do not crush, split or chew the tablets.

If you have accidentally taken a higher dosage

If you have taken an overdose, or if a child has accidentally swallowed some of the medicine, go immediately to a doctor or a hospital emergency room and bring the medicine package with you.

If you forget to take this medicine at the scheduled time, take it as soon as you remember. If you do not remember until it is time for your next dose, skip the missed dose and take the next dose at the usual time. Do not take two doses at the same time.

Adhere to the treatment as recommended by your doctor.

Even if your health improves, do not stop treatment with this medicine without consulting your doctor.

If you stop taking the medicine

Do not stop taking this medicine without consulting your doctor.

Do not take medicines in the dark! Check the label and the dose each time you take the medicine. Wear glasses if you need them.

If you have any further questions about using this medicine, consult with the doctor or the pharmacist.

4. Side effects

As with any medicine, use of Glyxambi may cause side effects in some people. Do not be alarmed by the list of side effects. You may not suffer from any of them.

Glyxambi may cause the following severe side effects:

- Ketoacidosis (increased levels of ketones in your blood or urine):** ketoacidosis has occurred in people with type 2 diabetes during treatment with empagliflozin, which is one of the ingredients in Glyxambi. Ketoacidosis has also occurred in people with diabetes who were sick or who had surgery during treatment with Glyxambi. Ketoacidosis is a serious medical condition which requires treatment in a hospital. Ketoacidosis may lead to death. **Ketoacidosis may occur during treatment with Glyxambi even if your blood sugar levels are lower than 250 mg/deciliter. Stop taking Glyxambi and contact the doctor immediately or go to the nearest emergency room if you experience any of the following symptoms:** nausea, vomiting, abdominal pain (stomach area), tiredness, difficulty breathing. If you experience any of these symptoms during treatment with Glyxambi, check your urine for the presence of ketones, if possible, even if your blood sugar levels are lower than 250 mg/dL.
- Dehydration:** Glyxambi may cause dehydration in some people (loss of body fluids and salts). Dehydration may cause a dizzy feeling, fainting or weakness, especially upon transition to standing. There have been reports of sudden worsening of kidney function in people who are taking Glyxambi. You may be at higher risk of dehydration if you: are taking medicines for blood pressure lowering, including diuretics, are on low salt (sodium) diet, have kidney problems, are 65 years of age and older.

Consult with the doctor about what you can do to prevent dehydration including how much fluid you should drink on a daily basis. Contact your doctor right away if you reduce the amount of food you eat or the amount of liquid you drink, for example if you are sick and cannot eat, or start to lose liquids from your body, for example due to vomiting, diarrhea or being in the sun too long.

- Pancreatitis** may be severe and even life-threatening, may occur in patients taking Glyxambi. Certain medical conditions may increase the risk of developing pancreatitis. Before treatment with Glyxambi, tell your doctor if you have or have had any of the following conditions: pancreatitis, gallstones, history of alcoholism, high levels of triglycerides in the blood. Stop taking Glyxambi and call the doctor right away if you feel severe abdominal pain that does not go away. This pain may be felt moving from your abdomen to your back. This pain may occur with or without vomiting. These may be symptoms of pancreatitis.
- Severe urinary tract infections:** Severe urinary tract infections that may result in hospitalization have occurred in patients taking empagliflozin, which is one of the ingredients of Glyxambi. Tell the doctor if you experience any signs or symptoms of urinary tract infection such as burning sensation while passing urine, passing urine frequently and urgently, pelvic pain, or blood in the urine. Sometimes people may also suffer from fever, back pain, nausea, or vomiting.
- Low blood sugar levels (hypoglycemia):** If you take Glyxambi with an additional medicine that can cause low blood sugar levels, such as medicines from the sulfonylurea class or insulin, your risk of having low blood sugar levels is higher. The dosage of sulfonylurea or insulin may need to be lowered while you are taking Glyxambi. Signs and symptoms of low blood sugar levels can include: headache, drowsiness, weakness, irritability,

hunger, heart-beat-beat, confusion, shaking or feeling jittery, dizziness, sweating.

- See a doctor as soon as possible if you notice any of the following side effects:**

Redness, pain, tenderness, or swelling in the area of the genitals till the anus with a fever higher than 38°C or feeling generally unwell and weak (malaise). These side effects could be signs of Fournier's gangrene which is a rare but life-threatening bacterial infection in the tissue under the skin in the area of the genitals (all the way to the anus). There are a number of reports of this side effect happening in women and men taking a diabetes medicine from the same group as Glyxambi. This side effect may lead to hospitalization, may require surgery, and may even lead to death. The symptoms of Fournier's gangrene can get worse quickly so it is important to get medical help quickly if you notice any of these symptoms.

- Vaginal yeast infection** - Symptoms of a vaginal yeast infection include: vaginal odor, white or yellowish vaginal discharge (the discharge may be lumpy or look like cottage cheese), vaginal itching.
- Yeast infection of the penis** - Swelling of an uncircumcised penis may develop, which may make it difficult to pull back the skin around the tip of the penis. Additional symptoms of yeast infection of the penis include: redness, itching or swelling of the penis, rash on the penis, foul smelling discharge from the penis, pain of the skin around penis.

Consult your doctor if you develop symptoms of a yeast infection in the vagina or penis. The doctor may recommend using non-prescription antifungal medicines. Consult your doctor immediately if you use a non-prescription antifungal medicine and your symptoms do not go away.

- Allergic reactions (hypersensitivity):** Serious allergic reactions have occurred in patients who were taking Glyxambi. Symptoms may include: swelling of the face, lips, tongue, throat, and other skin areas, difficulty with breathing or swallowing, hives (raised red areas on the skin), rash, itchy or peeling skin. If you have any of these symptoms, stop taking Glyxambi and contact your doctor immediately or go to the nearest hospital emergency room immediately.
- Joint pain:** Some patients taking DPP-4 inhibitors (linagliptin), which is one of the ingredients in Glyxambi, may develop joint pain which could be severe. Contact your doctor if you experience severe joint pain.
- Skin reactions:** Certain patients taking DPP-4 inhibitors, which is one of the ingredients in Glyxambi, may develop a skin reaction called bullous pemphigoid (an autoimmune skin disease that causes blisters and bubbles on the skin surface) which can require treatment in hospital. Contact your doctor immediately if blisters or wounds develop in the outer layer of the skin. The doctor may tell you to stop taking Glyxambi.
- Heart failure** is a condition in which your heart does not pump enough blood. **Before you start taking Glyxambi,** tell your doctor if you have or have had heart failure or kidney problems. Consult the doctor immediately if you experience any of the following symptoms:
 - increasing shortness of breath or difficulty breathing, particularly when lying down;
 - swelling or fluid retention particularly in the feet, ankles, or legs;
 - a fast and unusual weight gain;
 - unusual tiredness.These could all be symptoms of heart failure.

Very common side effects (affect more than 1 user out of 10) include:

Urinary tract infections, elevated levels of lipases (enzymes that break down fats), upper respiratory tract infections, stuffy or runny nose and sore throat.

Common side effects (affect 1-10 users out of 100) include:

Low blood sugar (hypoglycemia), infections of the female and male genitals, upper respiratory tract infections, increased urination, dyslipidemia, nausea, changes in blood test results (rise in cholesterol levels and hematocrit), common cold (runny nose and throat ache), diarrhea, cough, increase in uric acid level, increased level of amylase, thirst, dehydration-related incidents (low blood pressure and dizziness), joint pain (data from clinical studies of empagliflozin).

Side effects reported post-marketing whose frequency cannot be established include:

Acute pancreatitis that has also resulted in death, ketoacidosis, inflammation of the kidney and renal pelvis (Pyelonephritis) and sepsis as a result of a urinary tract infection (Urosepsis), allergic reactions including anaphylaxis, swelling of the face, the lips, the tongue, the throat (angioedema) and skin peeling, severe and debilitating joint pain, rash, hives, mouth ulcers, stomatitis (inflammation of the gums), necrotizing fasciitis (Fournier's gangrene), breakdown of muscle (rhabdomyolysis), acute renal injury.

If you experience a side effect, if any side effect gets worse, or if you experience a side effect not indicated in this leaflet, consult your doctor.

Reporting side effects

You can report side effects to the Ministry of Health (MoH) by following the link 'Reporting Side Effects of Medication' on the MoH home page (www.health.gov.il) which links to an online form for reporting side effects. You can also use this link: <https://sideeffects.health.gov.il>

5. How to store the medicine?

Avoid poisoning! To prevent poisoning, keep this, and all other medicines, in a closed place out of reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor.

Do not use the medicine after the expiry date (exp. date) appearing on the carton and blister tray. The expiry date refers to the last day of that month.

Storage conditions:

Do not store above 25°C.

6. Additional information

- In addition to the active ingredients the medicine also contains:
 - Tablet core:
 - Mannitol, maize starch, pregelatinized starch, talc, copovidone, croscopvidone, magnesium stearate.
 - Tablet coating (Glyxambi 10 mg / 5 mg) contains: Opadry® Yellow, hypromellose 2910, mannitol, talc, titanium dioxide, Macroglol 400, Iron oxide yellow.
 - Tablet coating (Glyxambi 25 mg / 5 mg) contains: Opadry® Pink, hypromellose 2910, mannitol, talc, titanium dioxide, Macroglol 400, Iron oxide red.
- What the medicine looks like and what are the contents of the package:
 - Glyxambi 10 mg / 5 mg film-coated tablets
 - pale yellow, arc triangular, flat-faced, bevel-edged tablets. One side is debossed with the Boehringer Ingelheim company symbol; the other side is debossed with "10/5".
 - Glyxambi 25 mg / 5 mg film-coated tablets
 - pale pink, arc triangular, flat-faced, bevel-edged tablets. One side is debossed with the Boehringer Ingelheim company symbol; the other side is debossed with "25/5".

The tablets are packed in blister trays. Each package containing 7 or 30 film-coated tablets. Not all pack sizes may be marketed.

Manufacturer's name and address: Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim am Rhein, Germany.

Registration holder's name and address: Boehringer Ingelheim Israel Ltd., 89 Medinat Ha-Yehudim St., P.O.B. 4124, Hertzliya-Pituach 4676672.

This leaflet was revised in December 2021 according to MOH guidelines.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: Glyxambi 10 mg / 5 mg: 155-76-34531-00
Glyxambi 25 mg / 5 mg: 155-75-34509-00