

Patient leaflet in accordance with the Pharmacists' Regulations (preparations)
- 1986

This medicine is to be supplied upon physician's prescription only

Jardiance Duo™ 5 mg / 500 mg

Each tablet contains 5 mg empagliflozin and 500 mg metformin hydrochloride (metformin HCl)

Jardiance Duo™ 5 mg / 850 mg

Each tablet contains 5 mg empagliflozin and 850 mg metformin hydrochloride (metformin HCl)

Jardiance Duo™ 5 mg / 1000 mg

Each tablet contains 5 mg empagliflozin and 1000 mg metformin hydrochloride (metformin HCl)

Jardiance Duo™ 12.5 mg / 500 mg

Each tablet contains 12.5 mg empagliflozin and 500 mg metformin hydrochloride (metformin HCl)

Jardiance Duo™ 12.5 mg / 850 mg

Each tablet contains 12.5 mg empagliflozin and 850 mg metformin hydrochloride (metformin HCl)

Jardiance Duo™ 12.5 mg / 1000 mg

Each tablet contains 12.5 mg empagliflozin and 1000 mg metformin hydrochloride (metformin HCl)

Film-coated tablets

*Inactive ingredients and allergens in the medicine - see section 6 - "Additional information".

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, contact your physician or pharmacist.

This medicine has been prescribed for your treatment. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar. Jardiance Duo is not intended for patients with type 1 diabetes or for patients with diabetic ketoacidosis.

Important information:

Metformin, one of the ingredients in Jardiance Duo, may cause a rare but a serious side effect called lactic acidosis, which is manifested by accumulation of lactic acid in the blood and may cause death. Lactic acidosis is a medical emergency and must be treated in a hospital. Stop taking Jardiance Duo and consult your physician right away if you get any of the signs of lactic acidosis (see also section 2 - "Special warnings related to the use of the medicine" and section 4 – "Side effects").

1. What is this medicine intended for?

Jardiance Duo is indicated, as an adjunct to diet and exercise, to improve the control of blood sugar levels in adults aged 18 and over with type 2 diabetes mellitus whose sugar levels are not adequately controlled by treatment with metformin alone or in combination with other medicines, or in patients receiving a combination of metformin and empagliflozin as separate tablets.

Therapeutic group:

Metformin: biguanide group.

Empagliflozin: SGLT2 (sodium-glucose co-transporter 2) inhibitors.

2. Before using this medicine

Do not use this medicine if:

- You are sensitive (allergic) to the active ingredients metformin and empagliflozin, or to any of the other ingredients that this medicine contains (for the list of inactive ingredients, see section 6).
- You suffer from severely reduced kidney function (your physician will establish the level of damage of your kidney function).
- You suffer from moderate to severe kidney failure, terminal kidney disease, or are on dialysis treatment.
- You suffer from metabolic acidosis or diabetic ketoacidosis (increased ketones in the blood or urine).

Before using Jardiance Duo, tell your physician if:

- You suffer from moderate to severe kidney problems.
- You suffer from liver problems.
- You have previously had urinary tract infections or problems passing urine.
- You have heart problems, including congestive heart failure.
- You are about to have surgery. If you are about to have surgery, your physician may decide to stop Jardiance Duo before you have surgery. Consult your doctor when to stop taking Jardiance Duo and when to start your treatment again.
- You are eating less or there is a change in your diet.
- You have or have had problems with your pancreas, including pancreatitis or surgery on your pancreas.
- You drink alcohol often, or drink a lot of alcohol in a short space of time ("binge" drinking).
- You are going to get an injection of dye or contrast agents for an x-ray procedure. Your medicine may need to be stopped for a short time. Talk to your physician about when you should stop the medicine and when you should start the medicine again.
- You suffer from type 1 diabetes. Jardiance Duo is not indicated for the treatment of patients with type 1 diabetes.
- You suffer from any other medical condition.
- You suffer from hypotension - Symptomatic hypotension may occur after initiating empagliflozin (one of the ingredients in Jardiance Duo), particularly in patients with renal problems, the elderly, in patients with low systolic blood pressure, and in patients on diuretics.

Special warnings regarding the use of the medicine**Lactic acidosis** - (see details in section 4 - "Side effects")

Metformin, one of the ingredients in Jardiance Duo, may cause a rare but a serious side effect called lactic acidosis, which is manifested by accumulation of lactic acid in the blood and may cause death. Lactic acidosis is a medical emergency condition and must be treated in a hospital (see also section 4 - "Side effects").

Stop taking Jardiance Duo and call your physician right away if you get any of the following symptoms of lactic acidosis:

- You feel very weak or tired.
- You have unusual (not normal) muscle pain.
- You have trouble breathing.
- You feel sleepy.
- You experience stomach pains, nausea or vomiting.

- You feel cold, especially in your hands or feet.
- You feel dizzy.
- You have a slow or irregular heartbeat.

There is a higher chance of getting lactic acidosis with Jardiance Duo if you:

- Suffer from moderate to severe kidney problems or your kidneys are affected by injectable dyes used for certain x-ray tests.
- Suffer from liver problems.
- Drink alcohol often, or drink a lot of alcohol in a short space of time (“binge” drinking, see section ‘Using the medicine and alcohol consumption’).
- Suffer from dehydration (lose a large amount of body fluids). This can happen when you are sick with a fever, vomiting, or diarrhea, and also when you sweat a lot during activity or exercise and do not drink enough fluids.
- Are going to have a surgery.
- Suffer from a heart attack, severe infection, or stroke.
- Are 65 years old or older, because at this age you may have problems with your kidney, liver, or heart function. You must be sure to have your kidney function tested frequently.

Children and adolescents

This medicine is not intended for children and adolescents under the age of 18.

Dehydration

Jardiance Duo may cause dehydration (loss of body fluids and salts) in some patients. Dehydration may cause dizziness, fainting or weakness, especially when you stand up from a sitting / lying down position.

Dehydration may increase the risk of hypotension. Ensure adequate intake of fluids during the day. If you experience hypotension, inform the physician. The risk of dehydration is higher if you:

- Suffer from low blood pressure.
- Take medicines to reduce your blood pressure, including diuretics.
- Are on a low sodium or salt diet.
- Suffer from kidney problems.
- Are 65 years old or older.

Tests and follow-up

- During treatment, check your blood sugar levels as your physician tells you to.
- Taking the medicine could cause a presence of sugar in your urine, which will show up on a urine test.
- Stay on your prescribed diet and exercise program while taking Jardiance Duo.
- Consult your physician about how to prevent, recognize and treat low blood sugar (hypoglycemia), high blood sugar (hyperglycemia), and complications of diabetes.
- Your physician will monitor your diabetes with regular blood tests, including blood sugar levels and glycated hemoglobin (HbA_{1C}).
- Your physician will do blood tests to check how well your kidneys are working before and during your treatment with the medicine.
- Your physician may do certain blood tests before you start using the medicine and during treatment.
- Your physician may do blood tests to check your vitamin B₁₂ and LDL (cholesterol) levels.
- Diabetic foot: It is important to check your feet regularly according to the recommendations given by your health care professional.

Other medicines and Jardiance Duo

If you are taking or have recently taken other medicines, including non-prescription medicines and food supplements, tell the physician or the pharmacist. Jardiance Duo may affect the way other medicines work, and other medicines may affect how Jardiance Duo works. Particularly tell your physician or pharmacist if you are taking:

- **Medicines that are used to get rid of fluids from the body (diuretics)** - Co-administration with empagliflozin (one of Jardiance Duo ingredients) may result in increased urine volume and frequency of voids, which may increase the risk of dehydration.
- **Insulin or medicines increasing insulin secretion** (such as sulfonylurea) - Concomitant treatment with empagliflozin (one of Jardiance Duo ingredients) increase the risk of low blood sugar levels (hypoglycemia) – The physician may consider reducing the doses of these medicines (See section 4 - “Side effects” for possible signs of low blood sugar).
- **Medicines that reduce metformin clearance** (such as ranolazine, vandetanib, dolutegravir) may raise the levels of metformin in your blood and increase your risk of lactic acidosis – your physician may consider a suitable treatment.
- **Carbonic Anhydrase Inhibitors medicines** (e.g., topiramate, zonisamide, acetazolamide or dichlorphenamide) - concomitant use of these medicines may increase the risk of lactic acidosis.
- **Medicines that tend to produce hyperglycemia:** thiazides and other diuretics, corticosteroids, phenothiazines, thyroid medicines, estrogens, oral contraceptives, phenytoin, nicotinic acid, sympathomimetics, calcium channel blocking medicines, and isoniazid.

Using the medicine and food

Take the medicine with a meal. Taking with food may lower the incidence of digestive problems.

Using the medicine and alcohol consumption

Avoid drinking large quantities of alcohol while taking this medicine. Alcohol consumption increases the risk of getting lactic acidosis (See also section 2 under "Special warnings regarding the use of the medicine").

Pregnancy and breastfeeding

Consult a physician prior to beginning treatment, if you are pregnant, plan to become pregnant, are breastfeeding or plan to breastfeed. Do not use Jardiance Duo when pregnant, because it may harm your unborn baby.

If you are pregnant, consult your physician regarding the best way to control your blood sugar levels during pregnancy.

Do not use Jardiance Duo if you are breastfeeding. Jardiance Duo may pass into your breast milk and harm your baby. Consult your physician about the best way to feed your baby if you are taking Jardiance Duo.

Fertility in women

If you are a premenopausal woman (before the menopause) who does not have periods regularly or at all, and you do not want to become pregnant, talk to your physician about birth control choices while taking Jardiance Duo, because Jardiance Duo may increase your chance of becoming pregnant.

3. How should you use the medicine?

Always use according to the physician's instructions. Check with the physician or the pharmacist if you are not sure about your dose or about how you should take this medicine.

The dosage and treatment will be determined only by the physician. The recommended dose is one tablet twice daily with a meal. Taking with food may lower your risk of digestive problems.

Do not exceed the recommended dose.

The tablets must not be crushed, split or chewed.

The physician may instruct you to take Jardiance Duo with other anti-diabetic medicines. Low blood sugar levels (hypoglycemia) may occur more often if certain anti-diabetic medicines are taken concomitantly (See section 2 - "Other medicines and Jardiance Duo". See also section 4, "Side effects").

If you have reduced kidney function, your physician may prescribe a lower dose.

When your body is under some types of stress, such as fever, trauma (such as a car accident), infection or surgery, the dose of diabetes medicine that you need may change. Tell your physician right away if you have any of these conditions and follow your physician's instructions.

If you have accidentally taken a higher dosage or a child has accidentally swallowed this medicine, refer immediately to a physician or to a hospital emergency room and bring the medicine package with you.

If you have forgotten to take the medicine at the scheduled time, take the dose immediately as you have remembered. If it is time to take the next dose, skip the forgotten dose and take the next dose at the usual time. Do not take a double dose. Persist with the treatment as recommended by the physician.

Even if your condition has improved, do not discontinue treatment with the medicine without consulting the physician or the pharmacist.

If you stop taking the medicine, your blood sugar levels may increase.

Do not take medicines in the dark! Check the label and the dose each time you take a medicine. Wear glasses if you need them. If you have any further questions regarding the use of this medicine, contact your physician or the pharmacist.

4. Side Effects

As with any medicine, use of Jardiance Duo may cause side effects in some users. Do not be alarmed by reading the list of side effects. You may not experience any of them.

Serious side effects

- **Stop taking Jardiance Duo and consult your physician right away if you get one or more of the following symptoms of lactic acidosis** (see also section 2 under "Special warnings regarding the use of the medicine"): You feel very weak or tired, you have unusual (not normal) muscle pain, you have trouble breathing, you feel sleepy, you experience stomach pains, nausea or vomiting, you feel

cold, especially in your hands and feet, you feel dizzy and/or you have a slow or irregular heartbeat.

- **Severe fluid loss (dehydration):**

Jardiance Duo can cause dehydration (the loss of body water and salt) in some people. Dehydration may cause you to feel dizzy, faint, or weak, especially when you stand up (orthostatic hypotension).

You may be at higher risk of dehydration if you suffer from low blood pressure, suffer from kidney problems, are 65 years old or older, are on low sodium (salt) diet and/or take medicines to lower your blood pressure, including diuretics (water pill).

Ketoacidosis (increased ketones in the blood or urine):

Ketoacidosis has happened in patients who have **type 1 diabetes or type 2 diabetes**, during treatment with empagliflozin, one of the ingredients in Jardiance Duo. Ketoacidosis has happened in people with diabetes who were sick or who had surgery during treatment with empagliflozin, one of the ingredients of Jardiance Duo. **Ketoacidosis can be life-threatening and may need to be treated in a hospital. Ketoacidosis can happen with Jardiance Duo even if your blood sugar is less than 250 mg/dL. Stop taking Jardiance Duo and consult your physician right away if you get any of the following symptoms:** nausea, vomiting, stomach-area (abdominal) pain, tiredness and trouble breathing.

If you get any of these symptoms during treatment with Jardiance Duo, 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 patients who are taking empagliflozin, one of the ingredients in Jardiance Duo. Tell your physician 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 patients also may have a fever, back pain, nausea or vomiting.

- **Hypoglycemia (low blood sugar levels):**

If you take Jardiance Duo with other medicines that can cause low blood sugar levels, such as sulfonylurea or insulin, your risk of getting low blood sugar levels is higher.

Signs and symptoms of low blood sugar may include headache, drowsiness, weakness, irritability, hunger, fast heartbeat, confusion, shaking and feeling jittery, dizziness and sweating.

- **Consult your physician 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, together with a fever higher than 38°C or feeling generally unwell and weak. These side effects could be signs of Fournier's gangrene. This is a rare but life-threatening bacterial infection of tissue under the skin in the genitals area (all the way to the anus). There are a number of reports of this side effect in both men and women taking medicines for diabetes from the same group to which Jardiance Duo belongs. This side effect may result in hospitalization, surgery, and even death. Symptoms of Fournier's gangrene may get worse quickly, so it

is important to get medical treatment quickly if you notice any of these symptoms.

- **Kidney problems:**

Sudden kidney injury has happened to people taking Jardiance Duo. Talk to your physician right away if you:

- reduce the amount of food or liquid you drink for example, if you are sick or 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 Jardiance Duo 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) or vaginal itching.

- **Yeast infection of the penis:**

Men who take Jardiance Duo 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 and pain in the skin around penis.

Talk to your physician if you get symptoms of a yeast infection of the vagina or penis. Your physician may suggest you use an antifungal medicine. Talk to your physician right away if you use an antifungal medication and your symptoms do not go away.

- **Allergic reactions (hypersensitivity):**

Serious allergic reactions have occurred in patient who took Jardiance Duo. Symptoms of allergic reactions may include:

- Swelling of the face, lips, throat, or other areas of your skin.
- Difficulty swallowing or breathing.
- Lumpy, red skin lesions (hives).

If you experience any symptom on this list, stop taking Jardiance Duo and immediately consult your physician or go to the nearest emergency room.

- **Low level of vitamin B₁₂ (vitamin B₁₂ deficiency):**

Using metformin (one of the ingredients in Jardiance Duo) 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 blood levels before. Your physician may do blood tests to check your vitamin B₁₂ levels.

- **Increased cholesterol levels in your blood.**

Very common side effects (affecting more than 1 user out of 10) include: low levels of blood sugar (hypoglycemia), urinary tract infections in women.

Common side effects (affecting 1 to 10 users out of 100) include: common cold (runny nose and throat ache), urinary tract infections in men, fungal infections of the female genitals, infection of the upper respiratory system, increased urination, impaired levels of fats in the blood, joint pains, fungal infections of the male genitals,

nausea, thirst, drop in vitamin B₁₂ levels, increased level of blood cholesterol (LDL), increased level hematocrits in the blood.

Uncommon side effects (affecting 1 to 10 users out of 1,000): low blood pressure, dehydration, decrease in blood volume, drop in blood pressure when standing from sitting, fainting, increase in urine volume, increased frequency of urination during the day, increased night urination, and tightened foreskin.

Side effects reported after marketing and whose frequency cannot be defined: ketoacidosis (see under "Serious side effects" above), an infection of the kidney and renal pelvis (pyelonephritis), and sepsis as a result of the urinary tract infection (urosepsis), swelling of the face, lips, throat (angioedema), skin reactions (such as rash or hives), damage to the liver, necrotizing fasciitis.

If a side effect occurs, if any side effect gets worse, or if you suffer from a side effect not mentioned in the leaflet, you should consult the physician.

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Medication' on the Ministry of Health 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! This medicine and any other medicine should be kept in a closed place out of the sight and reach of children and/or infants in order to avoid poisoning. Do not induce vomiting without an explicit instruction from your physician.
- Do not use the medicine after the expiration date (exp. date) that appears on the box. The expiration date refers to the last day of that month.
- Store below 25°C.

6. Additional information

In addition to the active ingredients, the medicine also contains: copovidone, maize starch, magnesium stearate and silica colloidal anhydrous.

The tablet coating is composed of:

- 5 mg / 500 mg, 5 mg / 850 mg, 5 mg / 1000 mg doses: hypromellose 2910, titanium dioxide, macrogol 400, talc, iron oxide yellow.
- 12.5 mg / 500 mg, 12.5 mg / 850 mg, 12.5 mg / 1000 mg doses: hypromellose 2910, titanium dioxide, macrogol 400, talc, iron oxide red and iron oxide black.

What does the medicine look like and what are the contents of the package:

- **Jardiance Duo 5 mg / 500 mg** – coated, oval tablets, convex on both sides, orange-yellow in color. One side is stamped with the logo of Boehringer Ingelheim and "S5" and the other side bears the number "500".
- **Jardiance Duo 5 mg / 850 mg** – coated, oval tablets, convex on both sides, yellowish white in color. One side is stamped with the logo of Boehringer Ingelheim and "S5" and the other side bears the number "850".
- **Jardiance Duo 5 mg / 1000 mg** – coated, oval tablets, convex on both sides, yellowish brown in color. One side is stamped with the logo of Boehringer Ingelheim and "S5" and the other side bears the number "1000".

- **Jardiance Duo 12.5 mg / 500 mg** – coated, oval tablets, convex on both sides, purple in color. One side is stamped with the logo of Boehringer Ingelheim and “S12” and the other side bears the number “500”.
- **Jardiance Duo 12.5 mg / 850 mg** – coated, oval tablets, convex on both sides, pinkish white in color. One side is stamped with the logo of Boehringer Ingelheim and “S12” and the other side bears the number “850”.
- **Jardiance Duo 12.5 mg / 1000 mg** – coated, oval tablets, convex on both sides, purplish dark brown in color. One side is stamped with the logo of Boehringer Ingelheim and “S12” and the other side bears the number “1000”.

The medicine is marketed in packs of 14, 60, 180 tablets. Not all pack sizes may be marketed.

- **Registration holder’s name and address:** Boehringer Ingelheim Israel Ltd., 89 Medinat Ha-Yehudim, P.O.B. 4124, Hertzliya-Pituach 4676672.
- **Manufacturer’s name and address:**
Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim am Rhein, Germany
or Boehringer Ingelheim Ellas A.E. Koropi, Greece
- This patient leaflet was formatted according to Ministry of Health guidelines. This patient leaflet was reviewed and approved in November 2017 and revised in March 2020 in accordance with Ministry of Health guidelines
- Registration number of the medicine in the National Drug Registry of the Ministry of Health:

Jardiance Duo 5 mg / 500 mg:	159-25-34922
Jardiance Duo 5 mg / 850 mg:	155-26-34512
Jardiance Duo 5 mg / 1000 mg:	155-28-34533
Jardiance Duo 12.5 mg / 500 mg:	159-26-34923
Jardiance Duo 12.5 mg / 850 mg:	155-29-34534
Jardiance Duo 12.5 mg / 1000 mg:	155-27-34532