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

This medicine is dispensed with a physician's prescription only

Jardiance Duo® 5 mg / 850 mg

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

Jardiance Duo® 5 mg / 1000 mg

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

Jardiance Duo® 12.5 mg / 850 mg

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

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Film-coated tablets

Inactive ingredients and allergens in this 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, consult your physician or pharmacist.

This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours. 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 serious side effect called lactic acidosis (a build-up of lactic acid in the blood), which may cause death. Lactic acidosis is a medical emergency and must be treated in a hospital. Stop taking Jardiance Duo and contact your physician right away or go to the nearest hospital emergency room if you experience symptoms of lactic acidosis (see also 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 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 empagliflozin and metformin, or to any of the other ingredients in this medicine (for the list of inactive ingredients, see section 6).

Symptoms of a serious allergic reaction to Jardiance Duo may include:

- swelling of the face, lips, throat and other areas of the skin
- difficulty with swallowing or breathing
- raised, red areas on the skin (hives).

If you have any of these symptoms, stop taking Jardiance Duo and contact your physician right away or go to the nearest hospital emergency room.

- You have severely reduced kidney function (your physician will establish the level of your kidney function damage).
- You suffer from moderate or severe kidney failure, end stage renal disease or are on dialysis treatment.
- You suffer from metabolic acidosis or diabetic ketoacidosis (increased ketones in the blood or urine).

Special warnings about using this medicine

Before using Jardiance Duo, tell your physician about your medical condition, including if:

- You have kidney problems.
- You have liver problems.
- You have heart problems, including heart failure.
- You are 65 years of age or older.
- You have a history of infection of the vagina or penis.
- You have a history of urinary tract infections or problems with urination.
- You are about to have surgery. Your physician may stop your treatment with Jardiance Duo before you have surgery. If you are about to have surgery, consult your physician about when to stop taking Jardiance Duo and when to start it 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 pancreas surgery.
- You drink alcohol very often, or drink a lot of alcohol in a short period of time ('binge' drinking) (see also section 'Using this medicine and alcohol consumption').
- You are going to receive an injection of dye or contrast agents for an x-ray procedure. Jardiance Duo administration may need to be stopped for a short time. Talk to your physician about when you should stop Jardiance Duo and when you should start Jardiance Duo again.
- You suffer from type 1 diabetes. Jardiance Duo is not indicated for the treatment of patients with type 1 diabetes.
- You have low levels of vitamin B12 in the blood.
- You are pregnant or plan to become pregnant (see section 'Pregnancy, breastfeeding, and fertility').
- You are breastfeeding or plan to breastfeed (see section 'Pregnancy, breastfeeding, and fertility').
- You are a woman who has not gone through menopause (premenopausal) who does not have periods regularly or at all (see section 'Pregnancy, breastfeeding, and fertility').

For additional special warnings related to the following serious side effects, see section 4 'Side effects':

- lactic acidosis
- ketoacidosis (increased levels of ketones in blood or urine)
- dehydration
- serious urinary tract infections
- low blood sugar levels (hypoglycemia)
- Fournier's gangrene (a rare but life-threatening bacterial infection of subcutaneous tissues in the genital area (all the way to the anus))
- vaginal yeast infection
- yeast infection of the penis (balanitis or balanoposthitis in uncircumcised men)
- allergic (hypersensitivity) reactions
- low vitamin B12 level (vitamin B12 deficiency)

Children and adolescents

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

Tests and follow-up

- During treatment, check your blood sugar levels as your physician tells you to.
- When taking Jardiance Duo, you may have sugar in your urine, which will show up in a urine test.
- Consult your physician about how to prevent, recognize and treat low blood sugar levels (hypoglycemia), high blood sugar levels (hyperglycemia), and complications of diabetes.
- Your physician will refer you for blood tests to check your kidney function before and during your treatment with Jardiance Duo.
- Your physician may refer you for certain blood tests before you start using the medicine and during treatment.
- Your physician may ask you to perform a blood test to check your vitamin B12 level.
- Diabetic foot: It is important to check your feet regularly according to the recommendations given by your healthcare professional.

Interactions with other medicines

If you are taking or have recently taken other medicines, including nonprescription medicines and dietary supplements, tell your physician or 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:

- **Carbonic anhydrase inhibitors** (e.g. topiramate, zonisamide, acetazolamide or dichlorophenamide) - concomitant use may increase the risk of lactic acidosis.
- **Medicines reducing metformin clearance** (e.g. ranolazine, vandetanib, dolutegravir, and cimetidine) – may increase the blood levels of metformin and increase the risk of lactic acidosis.
- **Medicines used to remove fluids from the body (diuretics)** - co-administration with empagliflozin (one of the ingredients in Jardiance Duo) 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) - co-administration with Jardiance Duo increases the risk of low blood sugar levels (hypoglycemia) – your physician may consider reducing the doses of

these medicines (see section 4 'Side effects' for possible signs of low blood sugar levels).

- **Medicines that may cause high blood sugar levels** - thiazides and other diuretics, corticosteroids, phenothiazines, thyroid medicines, estrogens, oral contraceptives, phenytoin, nicotinic acid, sympathomimetics, calcium channel blockers, and isoniazid.
- **Lithium** - co-administration with lithium may decrease serum lithium concentrations. Your physician will monitor serum lithium concentration more frequently following Jardiance Duo initiation and during dosage changes.

Know the medicines you take. Keep a list of them to show your physician and pharmacist when you receive a new medicine.

Using this medicine and food

Take the medicine with a meal. Taking with food may lower the incidence of upset stomach.

Using this medicine and alcohol consumption

Avoid drinking alcohol very often, or drinking a lot of alcohol in a short period of time ("binge" drinking). This may increase your risk of experiencing serious side effects (see also section 2 under 'Special warnings about using this medicine').

Pregnancy, breastfeeding, and fertility

If you are pregnant, plan to become pregnant, breastfeeding or plan to breastfeed, consult your physician before using this medicine.

Do not use Jardiance Duo during pregnancy, the medicine may harm your fetus. If you become pregnant during treatment with Jardiance Duo, tell your physician as soon as possible.

Talk with your physician about the best way to control your blood sugar while you are pregnant.

Do not breastfeed while using Jardiance Duo. Jardiance Duo may pass into 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 woman who has not gone through menopause (premenopausal), who does not have periods regularly or at all, consult your physician before treatment with Jardiance Duo.

Jardiance Duo may cause the release of an egg from an ovary (ovulation). This may increase your chance of getting pregnant. Tell your physician right away if you become pregnant while taking Jardiance Duo.

3. How to use this medicine?

Always use this medicine according to your physician's instructions. Check with your physician or pharmacist if you are not sure about your dose or about how to take this medicine. The dosage and treatment will be determined only by the physician.

The usually recommended dosage is one tablet twice daily with a meal. Taking the tablets with food may lower your risk of upset stomach.

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

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 'Interactions with other medicines' and section 4 'Side effects').

If you have accidentally taken a higher dose, or if a child has accidentally swallowed some medicine, immediately see a physician or go to the nearest hospital emergency room and bring the medicine package with you.

If you forget to take the medicine at the scheduled time, take the dose immediately as you have remembered. If you have not remembered until 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.

Consult your physician if you have questions about the missed dose.

Adhere to the treatment as recommended by your physician.

Even if your health improves, do not stop taking this medicine without consulting your physician.

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

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

If you have any further questions about using this medicine, consult your physician or pharmacist.

4. Side effects

As with any medicine, using 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.

Jardiance Duo may cause serious side effects, including:

- **Lactic acidosis: Metformin hydrochloride, one of the ingredients in Jardiance Duo, may cause a rare but serious side effect called lactic acidosis (a build-up of lactic acid in the blood) that may cause death. Lactic acidosis is a medical emergency and must be treated in a hospital.**

Stop taking Jardiance Duo and contact your physician right away or go to the nearest hospital emergency room if you experience any of the following symptoms of lactic acidosis:

- You feel very weak and tired.
- You have unusual (not normal) muscle pain.
- You have trouble breathing.
- You have unexplained stomach or intestinal problems with nausea and vomiting, or diarrhea.
- You have unusual sleepiness or sleep longer than usual.
- You feel cold, especially in the arms and legs.
- You feel dizzy.

- You have a slow or irregular heartbeat.

You have a higher risk of developing lactic acidosis with Jardiance Duo if you:

- have moderate to severe kidney problems.
- have liver problems.
- drink a lot of alcohol (very often or a lot in a short period of time ('binge' drinking)) (see also section 'Using this medicine and alcohol consumption').
- get dehydrated (lose a large amount of body fluids). This may happen if you are sick with fever, vomiting, or diarrhea. Dehydration may also happen when you sweat a lot during activity or exercise and do not drink enough fluids.
- undergo certain x-ray tests with injectable dyes or contrast agents.
- have surgery or other procedure for which you need to restrict the amount of food and liquid you eat and drink.
- have congestive heart failure.
- have a heart attack, severe infection, or stroke.
- are 65 years of age or older, since patients of this age group may have problems with renal, hepatic or cardiac functions. You should ensure performing frequent renal function tests.

Tell your physician if you have any of the problems listed above.

Tell your physician that you are taking Jardiance Duo before you have surgery or x-ray tests. Your physician may need to stop your Jardiance Duo for a while if you have surgery or certain x-ray tests.

- **Ketoacidosis (increased ketones in blood or urine)** (unknown frequency): Ketoacidosis has occurred in people with **type 1 diabetes or type 2 diabetes** during treatment with empagliflozin, one of the ingredients in Jardiance Duo. Ketoacidosis has also occurred in people with diabetes who were sick or who had surgery during treatment with Jardiance Duo. Ketoacidosis is a serious condition, which needs to be treated in a hospital. Ketoacidosis may lead to death.

Ketoacidosis may happen with Jardiance Duo even if your blood sugar levels are less than 250 mg/dL. Stop taking Jardiance Duo and contact your physician right away or go to the nearest hospital emergency room if you experience any of the following symptoms:

nausea, vomiting, stomach area (abdominal) pain, tiredness, trouble breathing.

If you experience any of these symptoms during treatment with Jardiance Duo, if possible, check the level of ketones in the urine, even if your blood sugar levels are less than 250 mg/dL.

- **Dehydration** (an uncommon side effect – affects 1 to 10 of 1,000 users): Jardiance Duo may cause some people to become dehydrated (loss of body fluids and salts). Dehydration may cause you to feel dizzy, faint or weak, especially when you stand up (orthostatic hypotension). There have been reports of sudden worsening of kidney function in people who are taking Jardiance Duo. Dehydration may increase the risk of hypotension. Ensure adequate intake of fluids during the day. If you experience hypotension, tell your physician. You may be at higher risk of dehydration if you:
 - have kidney problems.
 - are 65 years of age or older.
 - are on low sodium (salt) diet.
 - take medicines to lower your blood pressure, including diuretics.

Consult your physician about what you can do to prevent dehydration, including how much fluid you should drink on a daily basis.

Consult 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 start to lose liquids from your body, for example due to vomiting, diarrhea or staying in the sun for too long.

- **Serious urinary tract infections:** Serious urinary tract infections, that may lead to hospitalization, have happened in patients who were 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 the abdomen (pelvis), or blood in urine. Sometimes patients may also have fever, back pain, nausea or vomiting.
- **Low blood sugar levels (hypoglycemia)** (a very common side effect – affects more than 1 of 10 users): If you take Jardiance Duo with another medicine that may cause low blood sugar levels, such as sulfonylurea or insulin, your risk of getting low blood sugar levels is higher.
The dose of your sulfonylurea medicine or insulin may need to be lowered while you take Jardiance Duo. Signs and symptoms of low blood sugar may include headache, drowsiness, weakness, irritability, hunger, fast heartbeat, confusion, shaking or feeling jittery, dizziness, sweating.
- **Fournier’s gangrene - a rare but life-threatening bacterial infection of subcutaneous tissues in the genital area (all the way to the anus)** (unknown frequency):
Contact your physician as soon as possible if you notice any of the following side effects:
redness, pain, tenderness or swelling in the genital area all the way to the anus, with fever above 38°C or feeling generally unwell and weakness. These side effects may indicate the development of Fournier’s gangrene. This is a rare but life-threatening bacterial infection of subcutaneous tissues in the genital area (all the way to the anus). There are a number of reports on the occurrence of this side effect in women and men taking medicines for diabetes from the same group to which Jardiance Duo belongs. This side effect may lead to hospitalization, require surgery and even lead to death. Fournier’s gangrene symptoms may deteriorate rapidly, so it is important to get medical treatment quickly if you notice any of these symptoms.
- **Vaginal yeast infection** (a common side effect – affects 1 to 10 of 100 users):
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 (balanitis or balanoposthitis in uncircumcised men)** (a common side effect – affects 1 to 10 of 100 users):
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 redness, itching or swelling of the penis, rash in the penis, foul smelling discharge from the penis, or pain in the skin around the penis.

Consult your physician about what to do if you experience symptoms of a yeast infection of the vagina or penis. Your physician may suggest you to use an over-the-counter antifungal medicine. Contact your physician right away if you use an over-the-counter antifungal medicine and your symptoms do not go away.

- **Allergic (hypersensitivity) reactions** (unknown frequency): Serious allergic reactions have occurred in people who are taking empagliflozin, one of the ingredients in Jardiance Duo. Symptoms may include:
 - swelling of the face, lips, throat and other areas of your skin
 - difficulty with swallowing or breathing
 - raised, red areas on the skin (hives)If you experience any of these symptoms, stop taking Jardiance Duo and contact your physician right away or go to the nearest hospital emergency room.
- **Low vitamin B12 level (vitamin B12 deficiency)** (a common side effect – affects 1 to 10 of 100 users):
Using metformin for long periods of time may cause a decrease in the levels of vitamin B12 in your blood, especially if you have had low vitamin B12 levels previously. Your physician may ask you to perform blood tests to check your vitamin B12 levels.

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

Urinary tract infections in women.

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

Stuffy or runny nose and sore throat, diarrhea, nausea or vomiting, gas, stomach discomfort, indigestion, weakness, headache, upper respiratory tract infection, increased urination (polyuria (excessive urination), urinary frequency and nocturia (excessive urination at night)), impaired blood lipid level, joint pain, thirst (including excessive thirst), urinary tract infections in men, increased LDL-cholesterol level in blood, increased hematocrit level in blood.

Uncommon side effects (affect 1 to 10 of 1,000 users):

Decreased blood pressure, hypotension, hypovolemia, foreskin narrowing.

Additional side effects:

Increase in serum creatinine levels (in blood test) and decrease in estimated glomerular filtration rate (eGFR), constipation, pyelonephritis and sepsis due to urinary system infection (urosepsis), acute kidney injury, skin reactions (e.g. rash, urticaria), liver injury.

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

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

5. How to store the medicine?

- Prevent poisoning! To prevent poisoning, keep this and all other medicines in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by your physician.
- Do not use the medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.
- **Storage conditions:**
Store below 25°C.

6. Additional information

In addition to the active ingredients, this medicine also contains:

copovidone, maize starch, magnesium stearate, silica colloidal anhydrous.

The tablet coating is composed of:

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

What the medicine looks like and contents of the pack:

- **Jardiance Duo 5 mg / 850 mg** - film-coated, oval, biconvex, yellowish-white tablets. One side debossed with the logo of Boehringer Ingelheim company and "S5" and the other side is debossed with "850".
- **Jardiance Duo 5 mg / 1000 mg** - film-coated, oval, biconvex, brownish-yellow tablets. One side debossed with the logo of Boehringer Ingelheim company and "S5" and the other side is debossed with "1000".
- **Jardiance Duo 12.5 mg / 850 mg** - film-coated, oval, biconvex, pinkish-white tablets. One side debossed with the logo of Boehringer Ingelheim company and "S12" and the other side is debossed with "850".
- **Jardiance Duo 12.5 mg / 1000 mg** - film-coated, oval, biconvex, dark brownish-purple tablets. One side debossed with the logo of Boehringer Ingelheim company and "S12" and the other side is debossed with "1000".

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

- **Registration holder's and importer's name and address:** Boehringer Ingelheim Israel Ltd., 89 Medinat Ha-Yehudim, P.O. Box 4124, Herzliya Pituach 4676672.
- This leaflet was revised in July 2023 according to Ministry of Health guidelines.
- Registration number of the medicine in the Ministry of Health National Drug Registry:

Jardiance Duo 5 mg / 850 mg:	155-26-34512
Jardiance Duo 5 mg / 1000 mg:	155-28-34533
Jardiance Duo 12.5 mg / 850 mg:	155-29-34534
Jardiance Duo 12.5 mg / 1000 mg:	155-27-34532