

Patient package insert according to Pharmacists' Regulations (Preparations) – 1986

This medicine can be sold with a physician's prescription only

LOSARDEX® PLUS, Tablets

Each tablet contains:

50 mg Losartan Potassium

12.5 mg Hydrochlorothiazide

Inactive ingredients and allergens in the medicine - see section 6 "Additional information" and in section 2 "Important information about some of the ingredients of the medicine".

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

This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their medical condition seems similar to yours.

Losardex Plus is not intended for children and adolescents under 18 years of age.

1. What is the medicine intended for?

For the treatment of hypertension for patients in whom combination therapy is appropriate, and to reduce the risk of stroke in patients with high blood pressure and a thickening of the left ventricle (the heart's main pumping chamber).

Therapeutic group: a combination of an angiotensin II receptor antagonist (losartan) and a thiazide diuretic (hydrochlorothiazide).

Angiotensin II is a substance produced in the body, which binds to receptors in blood vessels, causing them to tighten. This results in an increase in blood pressure. Losartan prevents the binding of angiotensin II to these receptors, causing the blood vessels to relax which in turn lowers the blood pressure. Hydrochlorothiazide works by making the kidneys pass more water and salt. This also helps to reduce blood pressure.

2. Before using the medicine

Do not use the medicine if you:

- are hypersensitive (allergic) to the active ingredients (losartan, hydrochlorothiazide), or to any of the other ingredients this medicine contains (see section 6),
- are hypersensitive (allergic) to other sulfonamide-derived substances (e.g. other thiazides, some antibacterial drugs such as co-trimoxazole). Ask your doctor if you are not sure.
- have severely impaired liver function.
- have low potassium, low sodium or high calcium levels, which cannot be corrected by treatment.
- are suffering from gout.
- are more than 3 months pregnant (it is also better to avoid **Losardex Plus** in early pregnancy, see section "Pregnancy and breast-feeding").
- have severely impaired kidney function or if your kidneys are not producing any urine.

- You have diabetes or impaired kidney function and you are treated with a blood pressure lowering medicine containing aliskiren.

Special warnings regarding the use of the medicine

Talk to your doctor, or pharmacist, before taking the medicine.

If you experience a decrease in vision or eye pain. These could be symptoms of fluid accumulation in the vascular layer of the eye (choroidal effusion) or an increase of pressure in the eye and can appear within hours to weeks of taking the medicine. If not treated, this can lead to permanent vision loss. If in the past you had an allergy to penicillin or sulfonamide, you may be at higher risk of developing these effects.

You must tell your doctor if you think you are (or may become) pregnant. **Losardex Plus** is not recommended in early pregnancy, and must not be taken after the third month of pregnancy, as it may cause serious harm to your baby if used at that stage (see section "Pregnancy and breastfeeding").

Before treatment with Losardex Plus, tell the doctor if:

- You had breathing or lung problems (including inflammation or fluid in the lungs) following hydrochlorothiazide intake in the past. If you develop severe shortness of breath or difficulty breathing after taking **Losardex Plus**, seek medical attention immediately;
- You have previously suffered from swelling of the face, lips, throat or tongue;
- You take diuretics ("water pills");
- You are on a salt-restricted diet;
- You have or have had severe vomiting and/or diarrhoea;
- You have heart failure;
- Your liver function is impaired (see in section 2 "Do not use the medicine if ");
- You have narrow arteries leading to your kidneys (renal artery stenosis), or if you only have one functioning kidney, or if you have recently had a kidney transplant;
- You have narrowing of the arteries (atherosclerosis), angina pectoris (chest pain due to poor heart function);
- You have aortic or mitral valve stenosis (narrowing of the valves of the heart) or hypertrophic cardiomyopathy (a disease causing thickening of heart muscle);
- You suffer from diabetes;
- You have had gout;
- You have or have had an allergic condition, asthma or a condition that causes joint pain, skin rashes and fever (systemic lupus erythematosus);
- You have high calcium or low potassium levels or you are on a low potassium diet;
- You need to have an anaesthesia (even at the dentist) or before surgery, or if you are about to have parathyroid gland function tests, you must tell your doctor or the medical staff that you are taking **Losardex Plus**;
- You suffer from primary hyperaldosteronism (a syndrome associated with increased secretion of the hormone aldosterone by the adrenal gland, caused by an abnormality within the adrenal gland);
- You are taking any of the following medicines used to treat high blood pressure:
 - an ACE-inhibitor (such as enalapril, lisinopril, ramipril), especially if you have diabetes-related kidney problems
 - aliskirenYour doctor may check your kidney function, blood pressure, and the amount of electrolytes (e.g., potassium) in your blood at regular intervals.
See also information in section 2 "Do not use the medicine if".

- You are taking other medicines that may increase serum potassium levels (see in section 2 "Drug interactions").
- You have had skin cancer in the past, or if you develop an unexpected skin lesion during the use of the medicine. Use of hydrochlorothiazide, especially in long-term use and in high doses may increase the risk of developing certain types of skin and lip cancer (non-melanoma skin cancer).

Protect your skin from sun exposure and ultraviolet radiation (UV) while using **Losardex Plus**.

Drug interactions:

If you are taking, have recently taken, or might take other medicines including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.

Tell your doctor if you are taking potassium supplements, salt substitutes containing potassium, potassium-sparing medicines, or other medicines that may increase serum potassium levels (e.g., trimethoprim-containing medicines), as the combination with **Losardex Plus** is not recommended.

Diuretic agents such as the hydrochlorothiazide contained in **Losardex Plus** may interact with other medicines.

Do not take **Losardex Plus** in combination with medicines containing lithium without close supervision by your doctor.

Special precautions (e.g., blood tests) may be appropriate if you take other diuretics ("water tablets"), certain laxatives, medicines for the treatment of gout, medicines to control heart rhythm or for diabetes (oral agents or insulin).

It is also important for your doctor to know if you are taking:

- other medicines to reduce your blood pressure
- steroids
- medicines to treat cancer
- pain killers
- medicines to treat fungal infections
- medicines to treat arthritis
- preparations containing resins to treat high cholesterol such as cholestyramine
- medicines which relax your muscles
- sleeping medicines
- opioid medicines such as morphine
- 'pressor amines' such as adrenaline or other medicines of the same group
- oral medicines for diabetes or insulin

Your doctor may need to change your dose and/or to take other precautions:

If you are taking an ACE-inhibitor or aliskiren (see also in section 2 "Do not use the medicine if you" and "Special warnings regarding the use of the medicine").

Please also inform your doctor you are taking **Losardex Plus** if you are about to undergo a radiographic procedure and will be given iodine contrast media.

Use of this medicine with food and drink

Excessive amounts of salt in the diet may counteract the effect of **Losardex Plus**.

Losardex Plus tablets may be taken with or without food.

Grapefruit juice should be avoided while taking **Losardex Plus** tablets.

Use of this medicine and alcohol consumption

You are advised not to drink alcohol whilst taking these tablets: alcohol and **Losardex Plus** may increase each other's effects.

Pregnancy and breastfeeding

Pregnancy

You must tell your doctor if you think you are (or may become) pregnant. Your doctor will normally advise you to stop taking **Losardex Plus** before you become pregnant or as soon as you know you are pregnant and will advise you to take another medicine instead of **Losardex Plus**. **Losardex Plus** is not recommended during pregnancy, and must not be taken after the third month of pregnancy, as it may cause serious harm to your baby if taken after the third month of pregnancy.

Breast-feeding

Tell your doctor if you are breast-feeding or about to start breast-feeding. **Losardex Plus** is not recommended for breast-feeding mothers, and your doctor may choose another treatment for you if you wish to breast-feed.

Children and adolescents

There is no information regarding the use of **Losardex Plus** in children. Therefore, do not give **Losardex Plus** to children.

Use in elderly

Losardex Plus works equally well in and is equally well tolerated by most older and younger adult patients. Most older patients require the same dose as younger patients.

Driving and using machines

When you begin treatment with this medication, do not perform tasks which may require special attention (such as: driving a car or operating dangerous machinery) until you know how you react to the medicine.

Important information about some of the ingredients of the medicine

This medicine contains lactose. If you have been told by the doctor that you have an intolerance to some sugars, contact a doctor before starting treatment with this medicine.

3. How to use the medicine?

Always use the medicine as instructed by the doctor. You should check with the doctor or pharmacist if you are not sure about the dosage and the manner of treatment with the medicine.

Losardex Plus can be taken with or without food. Swallow the medicine with a glass of water.

The dosage and manner of treatment will be determined by the doctor only.

The usual recommended dosage is:

High blood pressure

The usual dose of **Losardex Plus** for most patients with high blood pressure is one tablet of **Losardex Plus** per day, to control blood pressure over the 24 hour period. The maximum daily dose is two tablets per day of **Losardex Plus**, once daily.

Patients with high blood pressure and a thickening of the left ventricle

The dosage will be determined by the doctor only.

Do not exceed the recommended dose.

Do not halve the tablets, since there is no score line. There is no information regarding crushing and chewing.

If you have accidentally taken a higher dosage

Overdose can cause a drop in blood pressure, palpitations, slow pulse, changes in blood composition, and dehydration.

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

If you forgot to take the medicine

Try to take **Losardex Plus** daily as prescribed for you. However, if you forgot to take a dose, do not take an extra dose. Just resume your usual schedule.

Continue with the treatment as recommended by the doctor in order to maintain proper control of your blood pressure.

Even if there is an improvement in your health, do not stop treatment with this medicine without consulting the doctor.

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 on the use of this medicine, consult the doctor or pharmacist.

4. Side effects

Like any medicine, the use of **Losardex Plus** may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

Stop taking the medicine and refer to the doctor or to the nearest hospital emergency room immediately if the following appears:

A severe allergic reaction (rash, itching, swelling of the face, the lips, the mouth or the throat that may cause difficulty in swallowing or breathing).

This is a serious but rare side effect, which appears in a frequency of 1-10 users out of 10,000. You may need urgent medical attention or hospitalisation.

Very rare (may affect up to 1 in 10,000 people):

acute respiratory distress (signs include severe shortness of breath, fever, weakness and confusion).

The following side effects have been reported:

Common side effects (effects that occur in 1-10 out of 100 users):

- Cough, upper airway infection, nasal congestion, sinusitis, sinus disorders
- Diarrhoea, abdominal pain, nausea, indigestion
- Muscle pain or cramps, leg pain, back pain
- Insomnia, headache, dizziness
- Weakness, tiredness, chest pain
- Increased blood potassium levels (which may cause an abnormal heart rhythm), decreased haemoglobin levels
- Changes in kidney function, including kidney failure
- Too low blood sugar levels (hypoglycaemia)

Uncommon side effects (effects that occur in 1-10 out of 1,000 users):

- Anaemia, red or brown spots on the skin (sometimes especially on the feet, legs, arms and buttocks, with joint pain, swelling of the hands and feet and stomach pain), bruising, decrease in white blood cells level, blood clotting problems, reduced number of platelets
- Loss of appetite, increased uric acid levels or gout, increased blood sugar levels, abnormal blood electrolyte levels
- Anxiety, nervousness, panic disorder (recurring panic attacks), confusion, depression, abnormal dreams, sleep disorders, sleepiness, memory impairment
- "Pins and needles" or similar sensations, pain in the extremities, trembling, migraine, fainting
- Blurred vision, burning or stinging in the eyes, conjunctivitis, worsening eyesight, seeing things in yellow
- Ringing, buzzing, roaring or clicking in the ears, vertigo
- Low blood pressure, which may be associated with changes in posture (feeling light-headed or weak when standing up), angina pectoris (chest pain), abnormal heartbeat, cerebrovascular accident (TIA – transient ischemic attack, "mini-stroke"), heart attack, palpitations
- Inflammation of blood vessels, which is often associated with a skin rash or bruising
- Sore throat, breathlessness, bronchitis, pneumonia, water in the lungs (which causes difficulty breathing), nosebleed, runny nose, congestion
- Constipation, severe constipation, wind, stomach upsets, stomach spasms, vomiting, dry mouth, inflammation of the salivary gland, toothache
- Jaundice (yellowing of the eyes and skin), inflammation of the pancreas
- Hives, itching, inflammation of the skin, rash, redness of the skin, sensitivity to light, dry skin, flushing, sweating, hair loss
- Pain in the arms, shoulders, hips, knees or other joints, joint swelling, stiffness, muscle weakness
- Frequent urination including at night, abnormal kidney function including inflammation of the kidneys, urinary tract infection, sugar in the urine
- Decreased sexual desire, impotence
- Swelling of the face, localised swelling (oedema), fever

Rare side effects (effects that occur in 1-10 out of 10,000 users):

- Hepatitis (inflammation of the liver), abnormal liver function tests

Side effects with unknown frequency (effects for which a frequency has not yet been determined):

- Flu-like symptoms
- Unexplained muscle pain with dark (tea-coloured) urine (rhabdomyolysis)
- Low levels of sodium in the blood (hyponatremia)
- Generally feeling unwell
- Disturbed taste
- Skin and lip cancer (non-melanoma skin cancer)
- Decrease in vision or pain in your eyes due to high pressure (possible signs of fluid accumulation in the vascular layer of the eye (choroidal effusion) or acute angle-closure glaucoma).

If a side effect occurs,, if any of the side effects worsens or if you suffer from a side effect not mentioned in this leaflet, consult the doctor.

Reporting of side effects

Side effects can be reported to the Ministry of Health by clicking the link "דיווח על תופעות לוואי עקב טיפול תרופתי" that can be found on the home page of the Ministry of Health website (www.health.gov.il) directing to the online form of adverse events reporting, or via the following link: <https://sideeffects.health.gov.il>

5. How to store the medicine?

- Avoid poisoning! This medicine and any other medicine must be stored in a closed place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use this medicine after the expiry date (תאריך תפוגה) stated on the package. The expiry date refers to the last day of that month.
- **Storage conditions:** Store in the original package, at a temperature not above 25°C.
- Do not throw away any medicines via wastewater or household waste. Ask the pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Additional information

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

Cellulose microcrystalline, lactose monohydrate, starch pregelatinised, hypromellose 2910, silica colloidal anhydrous, magnesium stearate, titanium dioxide, macrogol 400, carnauba wax.

What the medicine looks like and what the package contains: white round tablet. Pack sizes: 2, 10, 14, 20, 28, 30 tablets. Not all pack sizes may be marketed.

Manufacturer and address: Dexcel Ltd., 1 Dexcel street, Or Akiva, 3060000, Israel. Revised in January 2023 according to MOH guidelines

Drug registration number at the national medicines registry of the Ministry of Health:

141 56 31892 00

Registration holder: Dexcel Pharma Technologies Ltd., 21 Haftzadi Nahum Street, Jerusalem 9548402, Israel