PACKAGE LEAFLET

LOSAPRES PLUS 100 mg/25 mg Film Coated Tablets
Taken by mouth.

***Active substance*:** Each film-coated tablet contains 100 mg losartan potassium and 25 mg hydrochlorothiazide.
***Excipients*:** Lactose monohydrate (from bovine or cow's milk), microcrystalline cellulose PH 112 SLM, pregelatinized starch, magnesium stearate, colloidal silicon dioxide (Aerosil 200), Opadry 20A22156 Yellow: Hydroxypropyl cellulose, hypromellose, titanium dioxide, D&C Yellow #10 aluminum lacquer.

Read all of this PACKAGE LEAFLET carefully before you start taking this medicine because it contains important information for you.
- *Keep this leaflet. You may need to read it again.*
- *If you have any further questions, ask your doctor or pharmacist.*
- *This medicine has been prescribed for you. Do not pass it on to others.*
- *While you are taking this medicine, tell your doctor that you use this medicine, when you go to doctor or hospital.*
- *Exactly comply with what is written in this leaflet. Do not take this medicine in either* ***higher*** *or* ***lower*** *dose other than recommended to you.*

What is in this leaflet:

1. WHAT LOSAPRES PLUS IS AND WHAT IT IS USED FOR

LOSAPRES PLUS is a combination of an angiotensin II receptor antagonist (losartan) and a 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. Each film-coated tablet contains 100 mg losartan potassium and 25 mg hydrochlorothiazide.

LOSAPRES PLUS is presented in blister packs containing 28 film-coated tablets. They are yellow-colored film-coated tablets.

LOSAPRES PLUS is used in the following cases:
- LOSAPRES PLUS is used to reduce high blood pressure with unknown cause (essential hypertension) in patients whose blood pressure is not adequately controlled on losartan or hydrochlorothiazide alone.
- LOSAPRES PLUS is used to reduce the risk of disease and death in patients with high blood pressure (hypertension) and thickened left ventricle of the heart (left ventricle hypertrophy).
- LOSAPRES PLUS is used to reduce the risk of stroke in patients with high blood pressure (hypertension) and thickened left ventricle of the heart (left ventricle hypertrophy); however, this benefit does not apply to patients of Black race.

2. WHAT YOU NEED TO KNOW BEFORE YOU USE LOSAPRES PLUS

DO NOT USE LOSAPRES PLUS in the following situations:

- If you are allergic (hypersensitive) to losartan, hydrochlorothiazide or to any of the other ingredients of this medicine.
- If you are allergic to sulfonamide-derived medicines (e.g. other thiazides, some antibacterial medicines such as co-trimoxazole) (consult your doctor for information if you are not sure what sulfonamide-derived medicines are).
- If you have severely impaired liver function [such as cholestasis (slowing or stopping of bile flow) and bile duct obstruction disorders].
- If you have low sodium, low potassium and high calcium levels in your blood that cannot be corrected by treatment.
- If you have gout.
- If you are pregnant.
- If you have severely impaired kidney function or if your kidneys cannot produce urine.
- If you have diabetes or impaired kidney function and if you are being treated with aliskiren to lower your blood pressure.

USE LOSAPRES PLUS CAREFULLY in the following situations:

- If you have ever had any problem after using hydrochlorothiazide or if you have ever had lung problems (including inflammation or fluid retention in your lungs). If you experience any severe shortness of breath or difficulty in breathing following LOSAPRES PLUS use, seek immediate medical help.
- If you experience eye pain or decreased vision. These may be signs of fluid accumulation in the vascular lining of the eye (choroidal effusion) or increased pressure in the eye and they may occur within hours to weeks after receiving LOSAPRES PLUS. These can cause permanent loss of vision when left untreated. If you have ever had an allergy to penicillin or sulfonamide, you may have a higher risk of developing this.
- If you have previously suffered from swelling of the face, lips, throat or tongue.
- If you use diuretics (water pills).
- If you are on a salt-restricted diet.
- If you have or have had severe vomiting and/or diarrhea.
- If you have heart failure.
- If your liver function is impaired (see section 2 "**DO NOT USE LOSAPRES PLUS in the following situations**").
- If you have narrow arteries to your kidneys (renal artery stenosis) or only have one functioning kidney, or you have recently had a kidney transplant.
- If you have narrowing of the arteries (atherosclerosis), angina pectoris (chest pain due to poor heart function).
- If you have 'aortic or mitral valve stenosis' (narrowing of the valves of the heart) or 'hypertrophic cardiomyopathy' (a disease causing thickening of heart muscle).
- If you have diabetes.
- If you have gout.
- If you have or have had an allergic condition, asthma or a condition that causes joint pain, skin rashes and fever (systemic lupus erythematosus).
- If you have high calcium or low potassium levels or if you are on a low potassium diet.
- If you need to have an anesthetic (even at the dentist) or before surgery, or if you are going to have tests to check your parathyroid function, you must tell the doctor or medical staff that you are taking losartan potassium and hydrochlorothiazide tablets.

- If 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 gland).
- If you have ever had skin cancer or develop a new skin lesion during treatment. Treatment with hydrochlorothiazide, especially long-term use at high doses, may increase the risk of certain types of skin and lip cancers (non-melanoma skin cancer). Protect your skin from exposure to sun and UV rays while using LOSAPRES PLUS.
- If you are using any of the following medicines used to treat high blood pressure:
  - ACE inhibitor (e.g. enalapril, lisinopril, ramipril), especially if you have diabetes-related kidney problems.
  - Aliskiren.
- If you are using another medicine that may increase serum potassium (see section 2 "**Using with other medicines**").

Your doctor may check your kidney function, blood pressure, and electrolytes (e.g. potassium) in your blood at regular intervals. Please also see the information under the heading "**DO NOT USE LOSAPRES PLUS in the following situations**".

If these warnings apply to you, even at any time in the past, please consult your doctor.

LOSAPRES PLUS with food and drink
LOSAPRES PLUS can be taken with or without food.

It is advisable to avoid alcohol consumption while using LOSAPRES PLUS tablets because alcohol and these tablets can increase each other's effect when taken together.

Dietary salt in excessive quantities may counteract the effect of LOSAPRES PLUS tablets.

Avoid consuming grapefruit juice during your treatment with LOSAPRES PLUS tablets.

Pregnancy
Consult your doctor or pharmacist before using this medicine.
You should use appropriate birth control methods during treatment with LOSAPRES PLUS.
If you are pregnant (or may be pregnant), you should tell your doctor. Your doctor will recommend that you stop using LOSAPRES PLUS before you become pregnant or as soon as you find out that you are pregnant and use another medicine instead of LOSAPRES PLUS. LOSAPRES PLUS should not be used during pregnancy.

If you realize that you are pregnant during the treatment, consult your doctor or pharmacist immediately.

Breastfeeding
Consult your doctor or pharmacist before using this medicine.
Tell your doctor if you are breast-feeding or about to start breast-feeding. LOSAPRES PLUS is not recommended for breastfeeding women, but if you absolutely wish to breastfeed, your doctor may choose another treatment for you.

Driving and using machines
When you begin treatment with this medication, you should not perform tasks that require special attention (e.g., driving a car or operating dangerous machinery) until you figure out how this medicine affects you.

Important information about some of the other ingredients of LOSAPRES PLUS
LOSAPRES PLUS contains lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before using this medicinal product.

Use with other medicines
If you are using potassium supplements, potassium-containing salt substitutes, potassium-sparing medicines such as some diuretics, or other medicines that may increase serum potassium (e.g. potassium-containing products), please inform your doctor, as the combination of these drugs with LOSAPRES PLUS is not recommended.

Diuretic substances such as hydrochlorothiazide contained in LOSAPRES PLUS may interact with other medications.

Preparations containing lithium (used to treat mania, depression and schizoaffective disorders) should not be taken with LOSAPRES PLUS without close supervision by your doctor.

If you are using potassium supplements, potassium-containing salt preparations or potassium-sparing drugs, other diuretics, some laxatives or glycyrrhizin found in licorice root, gout medications, medicines used to treat heart rhythm disorders or medicines used to lower blood sugar (oral antidiabetic medicines and insulin); it may be appropriate to take special precautions (such as blood tests).

It is important to tell your doctor if you are taking the following medications:
- Other medicines to reduce your blood pressure (e.g. spironolactone, amiloride, triamterene).
- Steroids (e.g. prednisone, hydrocortisone).
- Medicines used in cancer treatment (e.g. cyclophosphamide, methotrexate).
- Painkillers (acetylsalicylic acid).
- Medicines used to treat fungal infections (e.g. fluconazole).
- Arthritis (joint inflammation) medications (e.g. ibuprofen, diclofenac).
- Resins used for high cholesterol (e.g. cholestyramine, colestipol resins).
- Muscle relaxants (e.g. tubocurarine).
- Sleeping pills (e.g. barbiturates).
- Opioid medicines (painkillers) such as morphine.
- Pressor amines (medicines that can cause an increase in blood pressure) such as adrenaline or other medicines in this group.
- Oral medications used to treat diabetes (e.g. metformin) or insulin.
- Your doctor may want to change your dose and/or take other precautions.
- If you are using an ACE inhibitor or aliskiren (see section 2 "**DO NOT USE LOSAPRES PLUS in the following situations**" and "**USE LOSAPRES PLUS CAREFULLY in the following situations**")

Please inform your doctor you are taking LOSAPRES PLUS if you will be undergoing a radiographic procedure and will be given iodine contrast media.

If you are currently using or have recently used any prescription or non-prescription medication, please inform your doctor or pharmacist about them.

3. HOW TO TAKE LOSAPRES PLUS

Instructions for proper use and dose/administration frequency

- Always take LOSAPRES PLUS exactly as recommended by your doctor. Your doctor will decide the appropriate dose of LOSAPRES PLUS based on your condition and other medications you use.
- In order to maintain proper blood pressure control, it is important to continue taking LOSAPRES PLUS for the duration prescribed by your doctor.
- LOSAPRES PLUS has two forms on the market: LOSAPRES PLUS 50 mg/12.5 mg Film Coated Tablets and LOSAPRES PLUS 100 mg/25 mg Film Coated Tablets. To control blood pressure over a 24-hour period, the usual dose of losartan/hydrochlorothiazide in most patients with high blood pressure is 1 tablet of LOSAPRES PLUS 50 mg/12.5 mg per day. This can be increased to 2 tablets of LOSAPRES PLUS 50 mg/12.5 mg per day or changed to 1 tablet of LOSAPRES PLUS 100 mg/25 mg per day. The maximum daily dose to be taken is 2 tablets of 50 mg/12.5 mg losartan/hydrochlorothiazide or 1 tablet of 100 mg/25 mg losartan/ hydrochlorothiazide.

Route and method of administration

- LOSAPRES PLUS is only taken by mouth.
- It may be taken with or without food.
- Take the tablets without chewing and with plenty of liquid (e.g. a full glass of water).
- For your convenience and ease of remembering, take LOSAPRES PLUS at the same time every day.

Different age groups

Use in children

No experience regarding the use of losartan/hydrochlorothiazide combination in children and adolescents is available. Therefore, LOSAPRES PLUS is not recommended for patients under 18 years of age.

Use in elderly

In general, LOSAPRES 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.

Use in special conditions

Liver / Kidney failure

If you have moderate kidney failure, no dose change is needed. If you are undergoing dialysis, LOSAPRES PLUS is not recommended. Do not use LOSAPRES PLUS if you have severe liver or kidney failure.

Please talk to your doctor or pharmacist if you think that effect of LOSAPRES PLUS is too strong or too weak.

If you take more LOSAPRES PLUS than you should

If you have used more LOSAPRES PLUS than recommended, talk to a doctor or pharmacist.
An overdose can cause a drop in blood pressure, palpitations, slow pulse, changes in blood composition and dehydration (loss of fluid).

If you forget to take LOSAPRES PLUS
Try to take your medicine as recommended.
If you forget to take a dose, do not take it and then continue with your regular schedule.
Do not take a double dose to make up for a forgotten dose.

Effects that may occur when treatment with LOSAPRES PLUS is stopped
Do not stop your treatment on your own without consulting your doctor.

4. POSSIBLE SIDE EFFECTS

If any of the following happen, stop using LOSAPRES PLUS and IMMEDIATELY inform your doctor or go to the emergency department of the nearest hospital:
Hypersensitivity reactions (rare) such as:
- Anaphylactic reactions (serious, life-threatening allergic reactions).
- Difficulty in breathing, wheezing.
- Angioedema, including swelling of the larynx and glottis, causing airway obstruction and/or swelling of the face, lips, pharynx, and/or tongue.

Acute respiratory distress (symptoms include severe shortness of breath, fever, tiredness and confusion) (very rare).

These are all very serious side effects. If you have any of these, it means you are seriously allergic to LOSAPRES PLUS. You may require urgent medical attention or hospitalization.

In some patients, angioedema had been reported in the past in connection with the administration of other medicines, including ACE inhibitors.

Like all other medicines, side effects may occur in individuals who are sensitive to the ingredients contained in LOSAPRES PLUS.

Side effects are classified in the following frequencies:
Very common : may occur in at least 1 in 10 patients.
Common : may occur in less than 1 in 10 patients, but more than 1 in 100 patients.
Uncommon : may occur in less than 1 in 100 patients, but more than 1 in 1,000 patients.
Rare : may occur in less than 1 in 1,000 patients, but more than 1 in 10,000 patients.
Very rare : may occur in less than 1 in 10,000 patients.
Not known : frequency cannot be estimated from the available data.

Common
- Cough, upper airway infection, congestion in the nose, sinusitis (sinus inflammation), and sinus disorder.
- Diarrhea, abdominal pain, nausea, indigestion.
- Muscle pain or cramps, leg pain, back pain.
- Insomnia, headache, dizziness.
- Tiredness and weakness, chest pain.
- Increased potassium levels (which can cause an abnormal heart rhythm), decreased hemoglobin and hematocrit levels.
- Changes in kidney function including kidney failure.
- Too low sugar in the blood (hypoglycemia).
- Increased calcium levels in the blood.

Uncommon
- Anemia, red or brownish 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, reduction in white blood cells, clotting problems, reduced number of platelets.
- Loss of appetite, increased uric acid levels or frank gout, increased blood sugar levels, abnormal blood electrolyte levels.
- Anxiety, anxiety disorder, 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 (inflammation of the eye), worsening eyesight, seeing things in yellow.
- Ringing, buzzing, roaring or clicking in the ears.
- Low blood pressure, which may be associated with changes in posture (feeling light-headed or weak when you stand up, angina (chest pain), abnormal heartbeat, cerebrovascular accident (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 on the lungs (which causes difficulty breathing), nosebleed, runny nose, congestion, inflammation of the vocal cords.
- Constipation, obstipation, wind, stomach upsets, stomach spasms, vomiting, dry mouth, inflammation of a 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 appetite, impotence.
- Swelling of the face, localized swelling (edema), and fever.

Rare
- Hepatitis (liver inflammation), abnormalities in liver function tests (increased ALT enzymes), allergy (hypersensitivity), a sudden hypersensitivity reaction that may cause difficulty in breathing and swallowing due to swelling of the face, lips or throat (anaphylactic reaction).

Very rare
- Increase in bilirubin (the dark yellow substance that gives bile its color) and liver enzymes.
- Acute respiratory distress (symptoms include severe shortness of breath, fever, weakness and confusion).

Not known
- Flu-like symptoms.
- Unexplained muscle pain with dark (tea-colored) urine (rhabdomyolysis, damage to muscle tissue).
- Low levels of sodium in the blood (hyponatremia).
- Generally feeling unwell.
- Disturbed taste (dysgeusia).

- Skin flaking (lupus erythematosus).
- Inflammation of the pancreas.
- Skin and lip cancer (non-melanoma skin cancer).
- Liver function abnormalities and thrombocytopenia (reduced platelet count).
- 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 you feel any side effects not listed in this package leaflet, inform your doctor or pharmacist.

Reporting of side effects
If you get any side effects including any possible side effects not listed in this leaflet, talk to your doctor, pharmacist or nurse. You can also report side effects directly via the national reporting system. By reporting side effects, you can help provide more information on the safety of this medicine.

5. HOW TO STORE LOSAPRES PLUS

Keep LOSAPRES PLUS out of the sight and reach of children and in its original package.

Store at room temperature below 25°C.

Do not open blister pack until you are ready to take the medicine.

Use it in accordance with the expiry date.

Do not use LOSAPRES PLUS after the expiry date, which is stated on the package.

Do not use LOSAPRES PLUS if you notice any defect on the product and/or its package.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

Marketing Authorization Holder:
DEVA Holding A.Ş.
Küçükçekmece – İSTANBUL / TÜRKİYE

Manufacturer:
DEVA Holding A.Ş.
Kapaklı – TEKİRDAĞ / TÜRKİYE

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