Package leaflet: Information for the user

Enalapril/Lercanidipine Krka 20 mg/10 mg film-coated tablets
enalapril maleate/lercanidipine hydrochloride

Read all of this 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 only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Enalapril/Lercanidipine Krka is and what it is used for

Enalapril/Lercanidipine Krka is a fixed combination of an ACE-inhibitor (enalapril) and a calcium channel blocker (lercanidipine), two medicines that lower blood pressure.

Enalapril/Lercanidipine Krka is used for the treatment of high blood pressure (hypertension) in patients whose blood pressure is not adequately controlled by enalapril 20 mg alone. Enalapril/Lercanidipine Krka should not be used for initial treatment of hypertension.

2. What you need to know before you take Enalapril/Lercanidipine Krka

Do not take Enalapril/Lercanidipine Krka
- if you are allergic to enalapril or lercanidipine or any of the other ingredients of this medicine (listed in section 6);
- if you have ever had an allergic reaction to a type of medicines similar to those contained in Enalapril/Lercanidipine Krka, i.e. medicines called ACE-inhibitors or calcium channel blockers;
- if you have ever developed angioedema (oedema of the face, lips, mouth, tongue or throat) which caused difficulty in swallowing or breathing (angioedema) after taking a type of medicine called ACE-inhibitors, or when the reason why was not known or it was inherited;
- if you have diabetes or impaired kidney function and you are treated with a blood pressure lowering medicine containing aliskiren;
- if you are more than 3 months pregnant. (It is also better to avoid Enalapril/Lercanidipine Krka in early pregnancy – see pregnancy section);
- if you suffer from certain heart diseases:
    - untreated heart failure;
    - obstruction to the flow of blood from the left ventricle of the heart, including a narrowing of the aorta (aortic stenosis);
    - chest discomfort occurring at rest or becoming worse or happening more often (unstable angina pectoris);

    - within one month after suffering a heart attack (myocardial infarction).
- if you have severe liver or kidney problems, or if you are undergoing dialysis;
- if you use medicines such as:
    - antifungals (e.g. ketoconazole, itraconazole);
    - macrolide antibiotics (e.g. erythromycin, troleandomycin, clarithromycin);
    - antivirals (e.g. ritonavir).
- if you are taking another drug called cyclosporin or ciclosporin (used after transplants to prevent organ rejection);
- together with grapefruit or grapefruit juice;
- if you have taken or are currently taking sacubitril/valsartan, a medicine used to treat a type of long-term (chronic) heart failure in adults, as the risk of angioedema (rapid swelling under the skin in an area such as the throat) is increased.

Warnings and precautions
Talk to your doctor or pharmacist before taking Enalapril/Lercanidipine Krka:
- if you have low blood pressure (you may notice this as faintness or dizziness, especially when standing);
- if you have been very sick (excessive vomiting) or have had diarrhoea recently, or are dehydrated;
- if you are on a salt restricted diet;
- if you have a heart problem;
- if you have a condition involving the blood vessels in the brain;
- if you have kidney problems (including kidney transplantation). This may lead to higher levels of potassium in your blood which can be serious. Your doctor may need to adjust your dose of enalapril or monitor your blood level of potassium;
- if you have liver problem;
- if you have a blood problem, such as low or lack of white blood cells (leucopenia, agranulocytosis), low platelet count (thrombocytopenia or a decreased number of red blood cells) (anaemia);
- if you have collagen vascular diseases (e.g. lupus erithematosus, rheumatoid arthritis or scleroderma), you are on therapy that suppresses your immune system, you are taking the medicines allopurinol or procainamide, or any combinations of these;
- if you are a black patient you should be aware that black patients are at increased risk of allergic reactions with swelling of the face, lips, tongue or throat with difficulty in swallowing or breathing when taking ACE-inhibitors;
- if you suffer from diabetes mellitus. You should monitor your blood for low blood glucose levels, especially during the first month of treatment. The level of potassium in your blood can also be higher;
- if you are taking potassium supplements, potassium-sparing agents, or potassium-containing salt substitutes;
- if you are over 70 years of age;
- if you have an intolerance to certain sugars (lactose);
- if you are taking any of the following medicines used to treat high blood pressure:
    - an angiotensin II receptor blocker (ARBs) (also known as sartans - for example valsartan, telmisartan, irbesartan), in particular if you have diabetes-related kidney problems;
    - aliskiren.

  Your 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 under the heading “Do not take Enalapril/Lercanidipine Krka”.
- if you are taking any of the following medicines, the risk of angioedema (rapid swelling under the skin in area such as the throat) may be increased:
    - Racecadotril, used to treat diarrhoea,
    - Temsirolimus, sirolimus, everolimus and other medicines used to avoid rejection of transplanted organs and for cancer,
    - Vildagliptin, a medicine used to treat diabetes.

If you are about to have a procedure
If you are about to have any of the following, tell your doctor that you are taking Enalapril/Lercanidipine Krka:
- any surgery or receive anaesthetics (even at the dentist);
- a treatment to remove cholesterol from your blood called "LDL apheresis";
- a desensitization treatment, to lower the effect of any allergy to bee or wasp stings.

You must tell your doctor if you think you are (or might become) pregnant or breastfeeding (see pregnancy, breastfeeding and fertility section).

Children and adolescents
Do not give this medicine to children and adolescents under the age of 18 years as there is no information on if it works and if it is safe.

Other medicines and Enalapril/Lercanidipine Krka
Enalapril/Lercanidipine Krka must not be taken with certain medications.
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription. This is because when Enalapril/Lercanidipine Krka is taken simultaneously with certain other medicines, the effect of Enalapril/Lercanidipine Krka or of the other medicine may be intensified or weakened, or certain side effects may occur more frequently.

In particular, tell your doctor or pharmacist if you are taking any of the following medicines together with Enalapril/Lercanidipine Krka:
- potassium-sparing diuretics (e.g. triamterene, amiloride), potassium supplements or medicines containing potassium (including dietary salt substitutes), other drugs which can increase potassium in your body (such as heparin, a medicine used to thin blood to prevent clots; trimethoprim and co-trimoxazole also known as trimethoprim/sulfamethoxazole, for infections caused by bacteria; and ciclosporin, an immunosuppressant medicine used to prevent organ transplant rejection). See "Do not take Enalapril/Lercanidipine Krka";
- other medicines that lower blood pressure;
- lithium (a medicine used to treat a certain kind of depression);
- medicines for depression called 'tricyclic antidepressants';
- medicines for mental problems called 'antipsychotics';
- non-steroidal anti-inflammatory drugs, including COX-2-inhibitors (medicines that reduce inflammation and can be used to help relieve pain);
- certain pain or arthritis medicines including gold therapy (especially with intravenous administration);
- certain cough and cold medicines and weight reducing medicines which contain something called a 'sympathomimetic agent';
- medicines for diabetes (including insulin and oral antidiabetic medicines);
- astemizole or terfenadine (medicines for allergies);
- amiodarone or quinidine or sotalol (medicines to treat a fast heart beat);
- phenytoin, phenobarbital or carbamazepine (medicines for epilepsy);
- rifampicin (a drug for the treatment of tuberculosis);
- digoxin (a medicine to treat heart problems);
- midazolam (a medicine that helps you to sleep);
- beta-blockers, e.g. metoprolol (medicines to treat high blood pressure, heart failure and abnormal heart rhythm);
- cimetidine (a medicine for ulcers and heartburn, at daily doses of more than 800 mg).

Do not take enalapril/lercanidipine if you have taken or are currently taking sacubitril/valsartan, a medicine used to treat a type of long-term (chronic) heart failure in adults, as the risk of angioedema (rapid swelling under the skin in an area such as the throat) is increased.

If you are taking any of the following medicines, the risk of angioedema may be increased:
- racecadotril, a medicine used to treat diarrhoea;
- medicines used to prevent organ transplant rejection and for cancer (e.g., temsirolimus, sirolimus, everolimus);
- vildagliptin, a medicine used to treat diabetes.

Your doctor may need to change your dose and/or to take other precautions:
- if you are taking an angiotensin II receptor blocker (ARB) or aliskiren (see also information under the headings "Do not take Enalapril/Lercanidipine Krka" and "Warnings and precautions").

Enalapril/Lercanidipine Krka with food, drink and alcohol
Enalapril/Lercanidipine Krka should be taken at least 15 minutes before a meal.
A high fat meal significantly increases blood levels of the medicine.
Alcohol can increase the effect of Enalapril/Lercanidipine Krka. Do not consume alcohol during treatment with Enalapril/Lercanidipine Krka.
Enalapril/Lercanidipine Krka should not be taken with grapefruit or grapefruit juice, as they can increase its hypotensive effect (see "Do not take Enalapril/Lercanidipine Krka").

Pregnancy, breast-feeding and fertility

Pregnancy and fertility
You must tell your doctor if you think you are (or might become) pregnant. Your doctor will normally advise you to stop taking Enalapril/Lercanidipine Krka before you become pregnant or as soon as you know you are pregnant and will advise you to take another medicine instead of Enalapril/Lercanidipine Krka. Enalapril/Lercanidipine Krka is not recommended in early pregnancy, and must not be taken when more than 3 months pregnant, as it may cause serious harm to your baby if used after the third month of pregnancy.

Breast-feeding
Enalapril/Lercanidipine Krka should not be used during breast-feeding.
Ask your doctor or pharmacist for advice before taking any medicines.

Driving and using machines
If you develop dizziness, weakness, tiredness, or drowsiness during treatment with this medicine, you must not drive a vehicle or operate machines.

Enalapril/Lercanidipine Krka contains lactose and sodium
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

3. How to take Enalapril/Lercanidipine Krka

Always take Enalapril/Lercanidipine Krka exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

Adults: unless otherwise prescribed by your doctor, the usual dose is one tablet once daily at the same time each day. The tablet should preferably be taken in the morning at least 15 minutes before breakfast. The tablets should be swallowed whole with water. See " Enalapril/Lercanidipine Krka with food, drink and alcohol".

Patients with kidney problems/elderly: your dose of medicine will be decided by your doctor and will be based on how well your kidneys are working.

If you take more Enalapril/Lercanidipine Krka than you should
If you have taken more than the dose prescribed by your doctor or in the event of overdosage, seek medical attention immediately and if possible take the tablets and/or the container with you to the doctor.
Taking more than the correct dose can cause your blood pressure to fall too far and your heart to beat irregularly or faster.

If you forget to take Enalapril/Lercanidipine Krka
If you forget to take your tablet, skip the missed dose.
Take the next dose as usual.
Do not take a double dose to make up for a forgotten dose.

If you stop taking Enalapril/Lercanidipine Krka
Do not stop taking your medicine unless your doctor tells you to.
If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. The following side effects may happen with this medicine:

Some side effects can be serious.
If any of the following happen, tell your doctor straight away:
- Allergic reaction with swelling of the face, lips, tongue or throat which may cause difficulty in breathing or swallowing.

When you start taking Enalapril/Lercanidipine Krka you might feel faint or dizzy or have blurred vision; this is caused by a sudden fall in blood pressure and if this happens, it will help if you lie down. If you are worried, please talk to your doctor.

<u>Side effects observed with Enalapril/Lercanidipine Krka</u>

Common (may affect up to 1 in 10 people)
Cough, feeling dizzy, headache.

Uncommon (may affect up to 1 in 100 people)
Changes in blood values such as a lower number of blood platelets, increased blood potassium level, nervousness (anxiety), feeling dizzy when standing up, vertigo, fast heartbeat, fast or uneven heartbeat (palpitations), sudden reddening of your face, neck or upper chest (flushing), low blood pressure, abdominal pain, constipation, feeling sick (nausea), higher levels of liver enzymes, redness of the skin, joint pain, increased number of times one urinates, feeling weak, tiredness, feeling hot, ankle swelling.

Rare (may affect up to 1in 1,000 people)
Anaemia, allergic reactions, ringing in your ears (tinnitus), fainting, dry throat, sore throat, indigestion, salty sensation on the tongue, diarrhoea, dry mouth, swelling of gums, allergic reaction with swelling of the face, lips, tongue or throat with difficulty in swallowing or breathing, skin rash, hives, getting up at night to urinate, producing large amounts of urine, impotence.

<u>Additional side effects observed with enalapril or lercanidipine alone</u>

Enalapril

Very common (may affect more than 1 in 10 people)
Blurred vision, feeling dizzy, weak, feeling sick (nausea) and cough.

Common (may affect up to 1 in 10 people)
Depression, headache, fainting (syncope), chest pain, light-headedness due to low blood pressure, changes in heart rhythm, fast heartbeat, angina, shortness of breath, change in sense of taste, increased levels of creatinine in your blood (usually detected by a test), high levels of potassium in the blood, diarrhoea, abdominal pain, tiredness (fatigue), rash, allergic reaction with swelling of the face, lips, tongue or throat with difficulty in swallowing or breathing.

Uncommon (may affect up to 1 in 100 people)
Anaemia (including aplastic and haemolytic), sudden fall in blood pressure, confusion, sleeplessness or sleepiness, feeling your skin prickling or being numb, vertigo (spinning sensation), ringing in your ears (tinnitus), fast or uneven heartbeat (palpitations), heart attack (possibly due to very low blood pressure in certain high-risk patients, including those with blood flow problems of the heart or brain), stroke (possibly due to very low blood pressure in high-risk patients), runny nose, sore throat and hoarseness, asthma-associated tightness in chest, slow movement of food through your intestine (ileus), inflammation of your pancreas, being sick (vomiting), indigestion, constipation, irritated stomach (gastric irritations), dry mouth, ulcer, anorexia, increased sweating, itch, nettle rash, hair loss, impaired kidney function, kidney failure, high level of proteins in your urine (measured in a test), impotence, muscle cramps, generally feeling unwell (malaise), high temperature (fever), increased urea level in blood, reduced sugar or sodium level in blood (all measured in a blood test), sudden reddening of your face, neck or upper chest (flushing).

Rare (may affect up to 1 in 1,000 people)
Changes in blood values such as a lower number of white blood cells, reduced bone marrow function, autoimmune diseases, strange dreams, swollen glands in neck, armpit or groin, sleep problems, 'Raynaud's phenomenon' (where your hands and feet may become very cold and white due to low blood flow), pulmonary infiltrates, accumulation of fluid or other substances in the lungs (as seen on X-rays), inflammation of your nose, pneumonia, inflammation of the cheeks, gums, tongue, lips, throat, liver problems such as lower liver function, inflammation of your liver, jaundice (yellowing of the skin and/or the whites of the eyes), higher levels of bilirubin (measured in a blood test), erythema multiforme (red spots of different shapes on the skin), Stevens-Johnson syndrome or toxic epidermal necrolysis (a serious skin conditions where you have reddening and scaling of your skin, blistering or raw sores, or detachment of the top layer of skin from bottom layers), exfoliative dermatitis /erythroderma (severe skin rash with flaking or peeling the skin), or pemphigus (small fluid-filled bumps on the skin), reduced urine output, enlargement of the mammary glands in males (gynaecomastia).

Very rare (may affect up to 1 in 10,000 people)
Intestinal swelling (intestinal angioedema).

Not known (frequency cannot be estimated from the available data)
Over production of antidiuretic hormone, which causes fluid retention, resulting in weakness, tiredness or confusion.
A symptom complex has been reported which may include some or all of the following: fever, inflammation of blood vessels (serositis/vasculitis), muscle pain (myalgia/myositis), joint pain (arthralgia/arthritis). Rash, photosensitivity or other skin manifestations may occur.

Lercanidipine

Some side effects can be serious.
If any of the following happen, tell your doctor straight away:

Rare (may affect up to 1 in 1,000 people)

Angina pectoris (chest pain due to lack of blood to your heart), allergic reactions (symptoms include itching, rash, urticaria), fainting.
Patients with pre-existing angina pectoris may experience increased frequency, duration or severity of the attacks with the group of medicines to which lercanidipine belongs. Isolated cases of heart attack may be observed.

Other possible side effects:
Common (may affect up to 1 in 10 people)
Headache, fast heart rate, feeling of fast or uneven heart beat (palpitations), sudden reddening of your face, neck or upper chest (flushing), ankle swelling.

Uncommon (may affect up to 1 in 100 people)
Dizziness, low blood pressure, heartburn, feeling sick (nausea), stomach pain, skin rash, itching, muscle pain, passage of large amounts of urine, feeling weak or feeling tired.

Rare (may affect up to 1 in 1,000 people)
Sleepiness, fainting (syncope), vomiting, diarrhoea, hypersensitivity, hives, increase in the usual number of times one urinates, chest pain (angina).

Not known (frequency cannot be estimated from the available data)
Swelling of gums, changes in liver function (detected by blood tests), cloudy fluid (when performing dialysis through a tube into your abdomen), swelling of your face, lip, tongue or throat which may cause difficulty in breathing or swallowing (angiooedema).

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist. You can ask your doctor or pharmacist for more information about side effects. Both have a more complete list of side effects.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance.Website: www.hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Enalapril/Lercanidipine Krka

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the packaging after EXP. The expiry date refers to the last day of that month.

Do not store above 30 °C.
Store in the original package in order to protect from moisture.

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.

6. Contents of the pack and other information

What Enalapril/Lercanidipine Krka contains
- The active substances are enalapril maleate and lercanidipine hydrochloride. Each film-coated tablet contains 20 mg enalapril maleate (equivalent to 15.29 mg enalapril) and 10 mg lercanidipine hydrochloride (equivalent to 9.44 mg lercanidipine).
- The other ingredients are povidone K30, maleic acid, sodium starch glycolate type A, lactose

monohydrate and sodium stearyl fumarate in the tablet core and hypromellose, titanium dioxide (E171), talc, macrogol 6000, yellow iron oxide (E172) and quinoline yellow (E104) in film coating. See section 2 “Enalapril/Lercanidipine Krka contains lactose and sodium”.

What Enalapril/Lercanidipine Krka looks like and contents of the pack
The film-coated tablets are yellow, round, slightly biconvex with bevelled edges, tablet diameter 10 mm.

Enalapril/Lercanidipine Krka is available in blister packs containing 10, 14, 15, 28, 30, 50, 56, 60, 84, 90, 98 or 100 film-coated tablets in a box.

Enalapril/Lercanidipine Krka is available in blister calendar packs: 14, 28, 56 or 98 film-coated tablets in a box.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
KRKA, d.d., Novo mesto, Šmarješka cesta 6, 8501 Novo mesto, Slovenia

This medicinal product is authorised in the Member States of the European Economic Area under the following names:

Hungary, Bulgaria, Estonia, Latvia, Slovakia	Elernap
Portugal	Enalapril + Lercanidipina Generis
Austria	Enalapril/Lercanidipin Krka
Spain	Enalapril/Lercanidipino Krka
Finland, Ireland, Belgium, France, Norway	Enalapril/Lercanidipine Krka
Slovenia	Elyrno
Italy	Enalapril e Lercanidipina Krka
Germany	EnaCanpin

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