Package leaflet: Information for the patient

Perindopril/amlodipine Krka 4 mg/5 mg tablets
Perindopril/amlodipine Krka 4 mg/10 mg tablets
Perindopril/amlodipine Krka 8 mg/5 mg tablets
Perindopril/amlodipine Krka 8 mg/10 mg tablets
perindopril tert-butylamine/amlodipine

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 Perindopril/amlodipine Krka is and what it is used for

Perindopril/amlodipine Krka is prescribed for treatment of high blood pressure (hypertension) and/or treatment of stable coronary artery disease (a condition where the blood supply to the heart is reduced or blocked).
Patients already taking perindopril and amlodipine from separate tablets may instead receive one tablet of Perindopril/amlodipine Krka which contains both ingredients.

Perindopril/amlodipine Krka is a combination of two active ingredients, perindopril and amlodipine. Perindopril is an ACE (angiotensin converting enzyme) inhibitor. Amlodipine is a calcium antagonist (which belongs to a class of medicines called dihydropyridines). Together they work to widen and relax the blood vessels so that blood passes through them more easily and makes it easier for your heart to maintain a good blood flow.

2. What you need to know before you take Perindopril/amlodipine Krka

Do not take Perindopril/amlodipine Krka
- if you are allergic (hypersensitive) to perindopril or any other ACE inhibitor, or to amlodipine or any other calcium antagonists, or any of the other ingredients of Perindopril/amlodipine Krka,
- if you are more than 3 months pregnant (It is also better to avoid Perindopril/amlodipine Krka in early pregnancy – see pregnancy section),
- if you have experienced symptoms such as wheezing, swelling of the face or tongue, intense itching or severe skin rashes with previous ACE inhibitor treatment or if you or a member of your family have had these symptoms in any other circumstances (a condition called angioedema),
- if you have diabetes or impaired kidney function and you are treated with a blood pressure lowering medicine containing aliskiren,
- if you have narrowing of the aortic heart valve (aortic stenosis) or cardiogenic shock (a

condition where your heart is unable to supply enough blood to the body),
- if you have severe low blood pressure (hypotension),
- if you suffer from heart failure after a heart attack,
- if you are having dialysis or any other type of blood filtration. Depending on the machine that is used, Perindopril/amlodipine Krka may not be suitable for you,
- if you have kidney problems where the blood supply to your kidneys is reduced (renal artery stenosis),
- 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
If you have any of the following please talk to your doctor before taking Perindopril/amlodipine Krka:
- hypertrophic cardiomyopathy (cardiac muscle disease) or renal artery stenosis (narrowing of the artery which supplies the kidney with blood),
- heart failure,
- severe increase in blood pressure (hypertensive crisis),
- any other heart problems,
- liver problems,
- kidney problems or if you are receiving dialysis,
- abnormally increased levels of a hormone called aldosterone in your blood (primary aldosteronism),
- collagen vascular disease (disease of the connective tissue) such as systemic lupus erythematosus or scleroderma,
- diabetes,
- if you are on a salt restricted diet or use salt substitutes which contain potassium (a well balanced potassium blood level is essential),
- if you are elderly and your dose needs to be increased,
- 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 Perindopril/amlodipine Krka".
- if you are taking any of the following medicines, the risk of angioedema is increased:
  - racecadotril (used to treat diarrhea),
  - sirolimus, everolimus, temsirolimus and other drugs belonging to the class of so-called mTor inhibitors (used to avoid rejection of transplanted organs),
  - sacubitril (available as fixed dose combination with valsartan) used to treat long-term heart failure,
  - linagliptin, saxagliptin, sitagliptin, vildagliptin and other drugs belonging to the class of the also called gliptins (used to treat diabetes),
- are of black origin since you may have a higher risk of angioedema and this medicine may be less effective in lowering blood pressure than in non-black patients.

<u>Angioedema</u>
Angioedema (a severe allergic reaction with swelling of the face, lips, tongue or throat with difficulty in swallowing or breathing) has been reported in patients treated with ACE inhibitors, including perindopril. This may occur at any time during treatment. If such symptoms develop, you should stop taking Perindopril/amlodipine Krka and see a doctor immediately. See also Section 4.

You must tell your doctor if you think you are (or might become) pregnant. Perindopril/amlodipine Krka is not recommended in early pregnancy, and must not be taken if you are more than 3 months pregnant, as it may cause serious harm to your baby if used at that stage (see pregnancy section).

When you are taking Perindopril/amlodipine Krka, you should also inform your doctor or the medical staff if you:
- are going to have a general anaesthetic and/or major surgery,
- have recently suffered from diarrhoea or vomiting (being sick),
- are to undergo LDL apheresis (the removal of cholesterol from your blood by a machine),
- are going to have desensitisation treatment to reduce the effects of an allergy to bee or wasp stings.

Children and adolescents
Perindopril/amlodipine Krka is not recommended for use in children and adolescents.

Other medicines and Perindopril/amlodipine Krka
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

You should avoid Perindopril/amlodipine Krka with:
- lithium (used to treat mania or depression),
- estramustine (used in cancer therapy),
- potassium-sparing drugs (triamterene, amiloride), potassium supplements or potassium-containing 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),
- potassium-sparing drugs used in the treatment of heart failure: eplerenone and spironolactone at doses between 12.5 mg to 50 mg by day.

Treatment with Perindopril/amlodipine Krka can be affected by other medicines. Make sure to tell your doctor if you are taking any of the following medicines as special care may be required:
- other medicines for high blood pressure, including angiotensin II receptor blocker (ARB), aliskiren (see also information under the headings "Do not take Perindopril/amlodipine Krka" and "Warnings and precautions"), or diuretics (medicines which increase the amount of urine produced by the kidneys),
- medicines, which are most often used to treat diarrhea (racecadotril) or avoid rejection of transplanted organs (sirolimus, everolimus, temsirolimus and other drugs belonging to the class of so-called mTor inhibitors). See section “Warnings and precautions”,
- sacubitril/valsartan (used to treat long-term heart failure): See sections “Do not take Perindopril/amlodipine Krka” and “Warnings and precautions”,
- non-steroidal anti-inflammatory drugs (e.g. ibuprofen) for pain relief or high dose acetylsalicylic acid, a substance present in many medicines used to relieve pain and lower fever, as well as to prevent blood clotting,
- medicines to treat diabetes (such as insulin),
- medicines to treat mental disorders such as depression, anxiety, schizophrenia etc (e.g. tricyclic antidepressants, antipsychotics, imipramine-like antidepressants, neuroleptics),
- immunosuppressants (medicines which reduce the defence mechanism of the body) used for the treatment of auto-immune disorders or following transplant surgery (e.g. ciclosporin, tacrolimus),
- trimethoprim and Co-trimoxazole (for the treatment of infections),
- allopurinol (for the treatment of gout),
- procainamide (for the treatment of an irregular heart beat),
- vasodilators including nitrates (products that widen the blood vessels),
- ephedrine, noradrenaline or adrenaline (medicines used to treat low blood pressure, shock or asthma),
- baclofen or dantrolene (infusion) both used to treat muscle stiffness in diseases such as multiple sclerosis; dantrolene is also used to treat malignant hyperthermia during anaesthesia (symptoms including very high fever and muscle stiffness),
- some antibiotics such as rifampicin, erythromycin, clarithromycin (for infections caused by bacteria),

- *Hypericum perforatum* (St John's wort, an herbal medicine used to treat depression),
- simvastatin (cholesterol lowering medicine),
- antiepileptic agents such as carbamazepine, phenobarbital, phenytoin, fosphenytoin, primidone,
- itraconazole, ketoconazole (medicines used for treatment of fungal infections),
- alpha-blockers used for the treatment of enlarged prostate such as prazosin, alfuzosin, doxazosin, tamsulosin, terazosin,
- amifostine (used to prevent or reduce side effects caused by other medicines or radiation therapy that are used to treat cancer),
- corticosteroids (used to treat various conditions including severe asthma and rheumatoid arthritis),
- gold salts, especially with intravenous administration (used to treat symptoms of rheumatoid arthritis),
- ritonavir, indinavir, nelfinavir (so called protease inhibitors used to treat HIV).

Perindopril/amlodipine Krka with food and drink
Perindopril/amlodipine Krka should be taken before a meal.
Grapefruit juice and grapefruit should not be consumed by people who are taking Perindopril/amlodipine Krka. This is because grapefruit and grapefruit juice can lead to an increase in the blood levels of the active ingredient amlodipine, which can cause an unpredictable increase in the blood pressure lowering effect of Perindopril/amlodipine Krka.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Pregnancy
You must tell your doctor if you think you are (or might become) pregnant. Your doctor will normally advise you to stop taking Perindopril/amlodipine Krka before you become pregnant or as soon as you know you are pregnant and will advise you to take another medicine instead of Perindopril/amlodipine Krka. Perindopril/amlodipine 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
Amlodipine has been shown to pass into breast milk in small amounts. Tell your doctor if you are breast-feeding or about to start breast-feeding. Perindopril/amlodipine Krka is not recommended for mothers who are breast-feeding, and your doctor may choose another treatment for you if you wish to breast-feed, especially if your baby is newborn, or was born prematurely.

Driving and using machines
Perindopril/amlodipine Krka may affect your ability to drive or use machines. If the tablets make you feel sick, dizzy, weak or tired, or give you a headache, do not drive or use machines and contact your doctor immediately.

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

3. How to take Perindopril/amlodipine Krka

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Swallow your tablet with a glass of water, preferably at the same time each day, in the morning, before a meal. Your doctor will decide on the correct dose for you. This will normally be one tablet per day.

Perindopril/amlodipine Krka will usually be prescribed for patients already taking perindopril and amlodipine from separate tablets.

Use in children and adolescents
Use in children and adolescents is not recommended.

If you take more Perindopril/amlodipine Krka than you should
If you take too many tablets, contact your nearest accident and emergency department or tell your doctor immediately. The most likely symptoms of overdose are low blood pressure which can make you feel dizzy or faint. If this happens, lying down with your legs raised can help.

Excess fluid may accumulate in your lungs (pulmonary oedema) causing shortness of breath that may develop up to 24-48 hours after intake.

If you forget to take Perindopril/amlodipine Krka
It is important to take your medicine every day as regular treatment works better. However, if you forget to take a dose of Perindopril/amlodipine Krka, take the next dose at the usual time. Do not take a double dose to make up for a forgotten dose.

If you stop taking Perindopril/amlodipine Krka
As the treatment with Perindopril/amlodipine Krka is usually life-long, you should discuss with your doctor before you stop taking your tablets.

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.

If you experience any of the following, stop taking the medicinal product at once and tell your doctor immediately:
- sudden wheeziness, chest pain, shortness of breath, or difficulty in breathing,
- swelling of eyelids, face or lips,
- swelling of the tongue and throat, which causes great difficulty breathing,
- severe skin reactions including intense skin rash, hives, reddening of the skin over your whole body, severe itching, blistering, peeling and swelling of the skin, inflammation of mucous membranes (Stevens Johnson Syndrome, toxic epidermal necrolysis) or other allergic reactions,
- severe dizziness or fainting,
- heart attack, unusual fast or abnormal heart beat, or chest pain.
- inflamed pancreas which may cause severe abdominal and back pain accompanied with feeling very unwell.

The following common side effects have been reported. If any of these cause you problems or if they last for more than one week, you should contact your doctor.
- Very common side effects (may affect more than 1 in 10 people): oedema (fluid retention).

- Common side effects (may affect up to 1 in 10 people): headache, dizziness, sleepiness (especially at the beginning of treatment), vertigo, numbness or tingling sensation in your limbs, vision disturbances (including double vision), tinnitus (sensation of noises in the ears), palpitations (awareness of your heartbeat), flushing, light-headedness due to low blood pressure, cough, shortness of breath, nausea (feeling sick), vomiting (being sick), abdominal pain, taste disturbances, dyspepsia or difficulty of digestion, change of bowel habit, diarrhoea, constipation, allergic reactions (such as skin rashes, itching), muscle cramps, tiredness, weakness, ankle swelling (oedema peripheral).

Other side effects that have been reported include the following list. If any of these get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

- Uncommon side effects (may affect up to 1 in 100 people): mood swings, anxiety, depression, sleeplessness, sleep disturbances, trembling, fainting, loss of pain sensation, irregular heart beat, rhinitis (blocked up or runny nose), hair loss, red patches on skin, skin discoloration, back pain, arthralgia (joint pain), myalgia (muscle pain), chest pain, disorder in passing urine, increased need to urinate at night, increased number of times of passing urine, pain, feeling unwell, bronchospasm (tightening of the chest, wheezing and shortness of breath), dry mouth, angioedema (symptoms such as wheezing, swelling of the face or tongue), formation of blister clusters over the skin, kidney problems, impotence, increased sweating, an excess of eosinophils (a type of white blood cells), discomfort or enlargement of the breasts in men, weight increase or decrease, tachycardia, vasculitis (inflammation of blood vessels), photosensitivity reaction (increased sensitivity of the skin to sun), fever, fall, change in laboratory parameters: high blood level of potassium reversible on discontinuation, low level of sodium, hypogycemia (very low blood sugar level) in case of diabetic patients, increased blood urea, and increased blood creatinine.

- Rare side effects (may affect up to 1 in 1,000 people): acute renal failure, symptoms of a condition called SIADH (inappropriate antidiuretic hormone secretion): dark urine, feeling sick (nausea) or being sick (vomiting), muscle cramps, confusion and seizures, decreased or absent urine output, psoriasis worsening, changes in laboratory parameters: increased level of liver enzymes, high level of serum bilirubin.

- Very rare side effects (may affect up to 1 in 10,000 people): cardiovascular disorders (angina, heart attack and stroke), eosinophilic pneumonia (a rare type of pneumonia), swelling of eyelids, face or lips, swelling of the tongue and throat, which causes great difficulty in breathing, severe skin reactions including intense skin rash, hives, reddening of the skin over your whole body, severe itching, blistering, peeling and swelling of the skin, inflammation of mucous membranes (Stevens Johnson Syndrome), erythema multiforme (a skin rash which often starts with red itchy patches on your face, arms or legs), sensitivity to light, changes in blood values such as a lower number of white and red blood cells, lower haemoglobin, lower number of blood platelets, disorders of the blood, inflamed pancreas which may cause severe abdominal and back pain accompanied with feeling very unwell, abnormal liver function, inflammation of the liver (hepatitis), yellowing of the skin (jaundice), liver enzyme increase which may have an effect on some medical tests, abdominal bloating (gastritis), disorder of the nerves which can cause weakness, tingling or numbness, increased muscle tension, swelling of the gums, excess sugar in blood (hyperglycaemia).

- Side effects with not known frequency: (frequency cannot be estimated from the available data): trembling, rigid posture, mask-like face, slow movements and a shuffling, unbalanced walk, discoloration, numbness and pain in fingers or toes (Raynaud’s phenomenon).

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 Perindopril/amlodipine 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 blister and carton after EXP. The

expiry date refers to the last day of that month.

Store in the original package in order to protect from light and moisture.
This medicine does not require any special temperature storage conditions.

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 Perindopril/amlodipine Krka contains

- The active substances are perindopril tert-butylamine and amlodipine.
  Perindopril/amlodipine Krka 4 mg/5 mg tablets
  Each tablet contains 4 mg perindopril tert-butylamine (equivalent to 3.34 mg perindopril) and 5 mg amlodipine (as besilate).
  Perindopril/amlodipine Krka 4 mg/10 mg tablets
  Each tablet contains 4 mg perindopril tert-butylamine (equivalent to 3.34 mg perindopril) and 10 mg amlodipine (as besilate).
  Perindopril/amlodipine Krka 8 mg/5 mg tablets
  Each tablet contains 8 mg perindopril tert-butylamine (equivalent to 6.68 mg perindopril) and 5 mg amlodipine (as besilate).
  Perindopril/amlodipine Krka 8 mg/10 mg tablets
  Each tablet contains 8 mg perindopril tert-butylamine (equivalent to 6.68 mg perindopril) and 10 mg amlodipine (as besilate).
- The other ingredients are sodium hydrogen carbonate, microcrystalline cellulose (E460), pregelatinised maize starch, sodium starch glycolate (type A), colloidal anhydrous silica and magnesium stearate (E470b). See section 2 "Perindopril/amlodipine Krka contains sodium".

What Perindopril/amlodipine Krka looks like and contents of the pack

Perindopril/amlodipine Krka 4 mg/5 mg tablets
This medicinal product is presented as white to almost white, round, slightly biconvex tablets with bevelled edges, engraved with mark U 1 on one side of the tablet. Diameter: 7 mm.
Perindopril/amlodipine Krka 4 mg/10 mg tablets
This medicinal product is presented as white to almost white, capsule shaped, biconvex tablets scored on one side. The tablets are engraved with mark U on one side and mark 2 on the other side of the breaker score. Dimensions: 12.5 mm × 5.5 mm. The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.
Perindopril/amlodipine Krka 8 mg/5 mg tablets
This medicinal product is presented as white to almost white, round, biconvex tablets with bevelled edges, engraved with mark U 3 on one side of the tablet. Diameter: 9 mm.
Perindopril/amlodipine Krka 8 mg/10 mg tablets
This medicinal product is presented as white to almost white, round, biconvex tablets with bevelled edges and a score line on one side. The tablets are engraved with mark U on one side and mark 4 on the other side of the breaker score. Diameter: 9 mm. The tablet can be divided into equal doses.

The tablets are available in carton boxes containing:

- 10, 30, 60, 90 and 100 tablets in blisters,
- 10 x 1, 30 x 1, 60 x 1, 90 x 1 and 100 x 1 tablets in perforated unit dose blisters.

Not all pack sizes may be marketed.

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

Manufacturer
KRKA, d.d., Novo mesto, Šmarješka cesta 6, 8501 Novo mesto, Slovenia
TAD Pharma GmbH, Heinz-Lohmann-Straβe 5, 27472 Cuxhaven, Germany

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

Portugal	Perindopril + Amlodipina TAD
Italy	PERINDOPRIL E AMLODIPINA HCS
Belgium	Perindopril/Amlodipine Krka
Germany	Amlessa
Finland	Perindopril/amlodipin Krka
Netherlands	Perindopril tert-butylamine/Amlodipine Krka
France	PERINDOPRIL/AMLODIPINE HCS
Ireland	Perindopril/amlodipine Krka

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