Package leaflet: Information for the patient

Dalnecombi 7 mg/5 mg/2.5 mg tablets
perindopril arginine/amlodipine/indapamide

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 Dalnecombi is and what it is used for

Dalnecombi is a combination of three active ingredients: perindopril, amlodipine and indapamide. Dalnecombi is an anti-hypertensive medicine used in the treatment of high blood pressure (hypertension) in adults.

Patients already taking perindopril/amlodipine as fixed dose combination and indapamide from separate tablets may instead receive one tablet of Dalnecombi, which contains the three active ingredients in the same strength.

Each of the active ingredients reduces blood pressure and they work together to control your blood pressure:
- Perindopril belongs to a class of medicines called Angiotensin Converting Enzyme (ACE) inhibitors. It works by widening the blood vessels, which makes it easier for your heart to pump blood through them.
- Amlodipine is a calcium channel blocker (which belongs to a class of medicines called dihydropyridines). It works by relaxing blood vessels, so blood passes through easily.
- Indapamide is a diuretic (which belongs to a class of medicines called sulphonamide derivatives with an indole ring). Diuretics increase the amount of urine produced by the kidneys. However, indapamide is different from other diuretics, as it only causes a slight increase in the amount of urine produced.

2. What you need to know before you take Dalnecombi

Do not take Dalnecombi
- if you are allergic to perindopril or any other ACE inhibitor, to amlodipine or any other calcium antagonists, and to indapamide or any other sulfonamide or any of the other ingredients of this medicine (listed in section 6),
- if you have severe kidney disease,
- if you are having dialysis or any other type of blood filtration. Depending on the machine that

is used, Dalnecombi 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 for heart failure, as the risk of angioedema (rapid swelling under the skin in an area such as the throat) is increased (see "Warning and Precaution" and "Other medicines and Dalnecombi").
- if you have severe liver disease or suffer from a condition called hepatic encephalopathy (liver problems which affect the brain and central nervous system),
- if you have low potassium levels in your blood,
- 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 are more than 3 months pregnant (it is also better to avoid Dalnecombi in early pregnancy – see pregnancy section),
- if you have severe low blood pressure (hypotension),
- 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 suffer from heart failure after a heart attack,
- if you have diabetes or impaired kidney function and you are treated with a blood pressure lowering medicine containing aliskiren.

Warnings and precautions

Talk to your doctor or, pharmacist before taking Dalnecombi:
- if you have had photosensitivity reactions,
- if you have hypertrophic cardiomyopathy (cardiac muscle disease),
- if you have heart failure or any heart rhythm problems,
- if you have severe increase in blood pressure (hypertensive crisis),
- if you have any other heart problems,
- if you have liver problems,
- if you have kidney problems (including kidney transplantation),
- 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 your eye and can happen within hours to weeks of taking Dalnecombi. This can lead to permanent vision loss, if not treated. If you earlier have had a penicillin or sulfonamide allergy, you can be at higher risk of developing this,
- if you have muscle disorders including muscle pain, tenderness, weakness or cramps,
- if you have abnormally increased levels of a hormone called aldosterone in your blood (primary aldosternism),
- if you have collagen vascular disease (disease of the connective tissue) such as systemic lupus erythematosus or scleroderma,
- if you have 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,
- 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 Dalnecombi".
- if you are of black origin since you may have a higher risk of angioedema and this medicine may be less effective in lowering your blood pressure than in non-black patients,

- if you suffer from gout,
- if you need to have a test to check how well your parathyroid gland is working,
- if you are taking any of the following medicines, the risk of angioedema is increased:
  - racecadotril (used to treat diarrhoea),
  - sirolimus, everolimus, temsirolimus and other drugs belonging to the class of so- called mTor inhibitors (used to avoid rejection of transplanted organs and for cancer),
  - 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).

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

You must tell your doctor if you think you are (or might become) pregnant. Dalnecombi 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 and breast-feeding sections).

When you are taking Dalnecombi, you should also inform your doctor or the medical staff:
- if you are going to have a general anaesthetic and/or major surgery,
- if you have recently suffered from diarrhoea or vomiting (being sick),
- if you are going to have desensitisation treatment to reduce the effects of an allergy to bee or wasp stings,
- if you are to undergo a medical test that requires injection of an iodinated contrast agent (a substance that makes organs like kidney or stomach visible on an X-ray).

Your doctor may give you blood tests to check for low sodium or potassium levels or high calciumlevels.
Athletes should be aware that Dalnecombi contains an active ingredient (indapamide) which may give a positive reaction in drug tests.

Children and adolescents
Dalnecombi should not be given to children and adolescents.

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

You should avoid Dalnecombi with:
- lithium (used to treat mania or depression),
- estramustine (used in cancer therapy),
- potassium-sparing drugs (e.g. 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),
- aliskiren (used to treat high blood pressure), (see also information under the headings "Do not take Dalnecombi" and "Warnings and precautions"),
- angiotension II-receptor blockers (ARB) (used to treat high blood pressure) (e.g. valsartan, telmisartan, irbesartan…),
- dantrolene (infusion) (used to treat muscle stiffness in diseases such as multiple sclerosis or to treat malignant hyperthermia during anaesthesia, symptoms including very high fever and muscle stiffness),

- medicines, which are most often used to treat diarrhoea (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 Dalnecombi" and "Warnings and precautions".

Treatment with Dalnecombi 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 diuretics (medicines which increase the amount of urine produced by the kidneys) and angiotensin converting enzyme (ACE) inhibitors (used to treat high blood pressure and heart failure),
- medicines used for heart rhythm problems (e.g. quinidine, hydroquinidine, disopyramide, amiodarone, sotalol, ibutilide, dofetilide, digitalis, bretylium),
- procainamide (for the treatment of an irregular heart beat),
- ephedrine, noradrenaline or adrenaline (medicines used to treat low blood pressure, shock or asthma),
- medicines used to treat mental disorders such as depression, anxiety, schizophrenia etc (e.g. tricyclic antidepressants, antipsychotics, imipramine-like antidepressants, neuroleptics (such as amisulpride, sulpiride, sultopride, tiapride, haloperidol, droperidol)),
- antibiotics used to treat bacterial infections (e.g rifampicin, erythromycin by injection, clarithromycin, sparfloxacin, moxifloxacin),
- bepridil (used to treat angina pectoris, a condition causing chest pain),
- cisapride (used to treat reduced movement of the gullet and stomach),
- diphemanil (used to treat gastro-intestinal problems such as ulcers, too much acid, overactive digestive system),
- vincamine by injection (used to treat symptomatic cognitive disorders in elderly including memory loss),
- halofantrine (antiparasitic drug used to treat certain types of malaria),
- pentamidine (used to treat certain types of pneumonia),
- antihistamines used to treat allergic reactions, such as hay fever (e.g mizolastine, astemizole, terfenadine),
- antifungal medicines (e.g itraconazole, ketoconazole, amphotericin B by injection),
- tetracosactide (to treat Crohn’s disease),
- stimulant laxatives,
- medicines to treat diabetes (such as insulin, gliptins, metformin),
- baclofen used to treat muscle stiffness in diseases such as multiple sclerosis,
- potassium-sparing drugs used in the treatment of heart failure: eplerenone and spironolactone at doses between 12.5 mg to 50 mg by day, amiloride, triamterene,
- non-steroidal anti-inflammatory drugs (e.g. ibuprofen) for pain relief or high dose acetylsalicylic acid, a substance presents in many medicines used to relieve pain and lower fever, as well as to prevent blood clotting,
- hypericum perforatum (St John’s wort, an herbal medicine used to treat depression),
- vasodilators including nitrates (products that widen the blood vessels),
- corticosteroids (used to treat various conditions including severe asthma and rheumatoid arthritis),
- 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),
- ritonavir, indinavir, nelfinavir (so called protease inhibitors used to treat HIV),
- gold salts, especially with intravenous administration (used to treat symptoms of rheumatoid arthritis),
- iodinated contrast media (used for tests involving X-rays),
- calcium tablets or other calcium supplements,
- 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),
- allopurinol (for the treatment of gout),
- antiepileptic agents such as carbamazepine, phenobarbital, phenytoin, fosphenytoin, primidone,
- trimethoprim (for the treatment of infections),
- methadone (used to treat addiction).

Dalnecombi with food and drink
See section 3.

Grapefruit juice and grapefruit should not be consumed by people who are taking Dalnecombi. 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 Dalnecombi.

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 that you are (or might become) pregnant.
Your doctor will normally advise you to stop taking Dalnecombi before you become pregnant or as soon as you know you are pregnant and will advise you to take another medicine instead of Dalnecombi. Dalnecombi 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. Dalnecombi 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 new-born, or was born prematurely.

Driving and using machines
Dalnecombi 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.

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

3. How to take use Dalnecombi

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

The recommended dose is one tablet of Dalnecombi once daily.
Take your tablet preferably at the same time each day, in the morning, before a meal.
Do not exceed the prescribed dose.

If you take more Dalnecombi than you should
If you take too many tablets, contact your nearest accident and emergency department or tell your doctor immediately.

The most likely effect in case of overdose is low blood pressure which can make you feel dizzy or faint. If this happens, lying down with your legs raised can help.

It could cause nausea (feeling sick), vomiting, cramps, drowsiness, confusion and changes in the amount of urine produced by the kidneys.
You may feel lightheaded, faint, or weak. If your blood pressure drop is severe enough, shock can occur. Your skin could feel cool and clammy and you could lose consciousness.

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 Dalnecombi
It is important to take your medicine every day as regular treatment works better. However, if you forget to take a dose of Dalnecombi, 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 Dalnecombi
As the treatment with Dalnecombi is usually life-long, you should consult your doctor before you stop taking this medicinal product.

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.

Stop taking the medicinal product and see a doctor immediately, if you experience any of the following side effects that can be serious:
- sudden wheeziness, chest pain, shortness of breath, or difficulty in breathing (bronchospasm) (uncommon - may affect up to 1 in 100 people),
- swelling of eyelids, face or lips (uncommon - may affect up to 1 in 100 people),
- swelling of the mouth, tongue and throat, which causes great difficulty breathing (angioedema) (uncommon - may affect up to 1 in 100 people),
- severe skin reactions including intense skin rash, hives, reddening of the skin over your whole body, severe itching (erythema multiforme) (very rare - may affect up to 1 in 10 000 people), blistering, peeling and swelling of the skin (exfoliative dermatitis) (very rare - may affect up to1 in 10 000 people), inflammation of mucous membranes (Stevens Johnson Syndrome) (very rare - may affect up to 1 in 10 000 people) or other allergic reactions (common - may affect upto 1 in 10 people), toxic epidermal necrolysis (Not known - frequency cannot be estimated from the available data),
- severe dizziness or fainting (common - may affect up to 1 in 10 people),
- weakness of arms or legs, or problems speaking which could be a sign of a possible stroke (very rare - may affect up to 1 in 10 000 people),
- heart attack, chest pain (angina) (very rare - may affect up to 1 in 10 000 people), unusual fast or abnormal heartbeat (common - may affect up to 1 in 10 people),
- inflamed pancreas which may cause severe abdominal and back pain accompanied with feelingvery unwell (very rare - may affect up to 1 in 10 000 people),
- yellowing of the skin or eyes (jaundice) which could be a sign of hepatitis (very rare - mayaffect up to 1 in 10 000 people),
- disease of the brain caused by liver illness (Hepatic encephalopathy) (frequency not known),
- muscle weakness, cramps, tenderness or pain and particularly, if at the same time, you feel unwell or have a high temperature it may be caused by an abnormal muscle breakdown. (frequency not known).

In decreasing order of frequency, side effects can include:

Very common (may affect more than 1 in 10 people):
oedema (fluid retention).

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

Uncommon (may affect up to 1 in 100 people):
rhinitis (blocked up or runny nose), increase in some white blood cells (eosinophilia), low sugar level in the blood (hypoglycaemia), high levels of blood potassium which can cause abnormal heart rhythm (hyperkalaemia), low sodium level in the blood (hyponatraemia) that may lead to dehydration and low blood pressure, sleeplessness, mood swings, anxiety, depression, sleep disturbances, loss of pain sensation, trembling, fainting, vasculitis (inflammation of blood vessels), dry mouth, hair loss, red patches on skin (purpura), skin discolouration, increased sweating, photosensitivity reaction (change in skin appearance) after exposure to the sun or artificial UVA, formation of blister clusters over the skin, muscle or joint pain, back pain, disorder in passing urine, increased need to urinate at night, increased number of times of passing urine, kidney problems, impotence(inability to obtain or maintain an erection), discomfort or enlargement of the breasts in men, chest pain, pain, feeling unwell (malaise), fever, weight increase or decrease, increased blood urea, increased blood creatinine, fall.

Rare (may affect up to 1 in 1 000 people):
low chloride in the blood, low magnesium in the blood, confusion, psoriasis worsening, high level of serum bilirubin, increased level of liver enzymes, decrease or absence urine output, acute renal failure.
Dark urine, feeling sick (nausea) or being sick (vomiting), muscle cramps, confusion and seizures. These may be symptoms of a condition called SIADH (inappropriate antidiuretic hormone secretion).

Very rare (may affect up to 1 in 10 000 people):
changes in blood values such as a lower number of white and red blood cells, lower haemoglobin, lower number of blood platelets, excess sugar in the blood (hyperglycaemia), high level of calcium in blood (hypercalcaemia), increased muscle tension, disorders of the nerves which can cause weakness, eosinophilic pneumonia (a rare type of pneumonia), swelling of the gums, abdominal bloating (gastritis), yellowing of the skin (jaundice), acute renal failure.

Not known (frequency cannot be estimated from the available data):
short sightedness (myopia), blurred vision, 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 suffer from systemic lupus erythematosus (a type of collagen disease), this might get worse, abnormal ECG heart tracing, trembling, rigid posture, mask-like face, slow movements and a shuffling, unbalanced walk, increase in uric acid, a substance which may cause or worsen gout (painful joint(s) especially in the feet), discoloration, numbness and pain in fingers or toes (Raynaud's phenomenon).

If you have these symptoms contact your doctor as soon as possible.

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 Dalnecombi

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 box and blister after EXP. The expiry date refers to the last day of that month.

This medicine does not require any special temperature storage conditions.
Store in the original package in order to protect from light and 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 Dalnecombi contains
- The active substances are perindopril arginine, amlodipine and indapamide. Each tablet contains 7 mg perindopril arginine (equivalent to 4.75 mg perindopril), amlodipine besilate equivalent to 5 mg amlodipine and 2.5 mg indapamide.
- The other ingredients are calcium chloride hexahydrate, microcrystalline cellulose, pregelatinised maize starch, sodium starch glycolate (Type A), sodium hydrogen carbonate, colloidal hydrated sillica and magnesium stearate. See section 2 "Dalnecombi contains sodium".

What Dalnecombi looks like and contents of the pack
Dalnecombi are white or almost white, round (8 mm in diameter), biconvex tablets, marked with K4 on one side.

Dalnecombi is available in blisters containing 10, 30, 60, 90, 100 or 120 tablets, in a box.

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-Straße 5, 27472 Cuxhaven, Germany

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

Ireland	Dalnecombi
Germany	Co-Amlessa
Spain	Perindopril/Amlodipino/Indapamida Krka
Cyprus	CO-APERNEVA
Poland	COARAMLESSA

Latvia	Perindopril arginine/Amlodipine/Indapamide TAD
Lithuania	Perindopril arginine/amlodipine/indapamide Krka
Slovenia	Argininijev perindoprilat/indapamid/amlodipin Krka

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