Package leaflet: Information for the patient

[Invented name] 5 mg/1.25 mg, capsules, hard
[Invented name] 5 mg/2.5 mg, capsules, hard
[Invented name] 10 mg/1.25 mg, capsules, hard
[Invented name] 10 mg/2.5 mg, capsules, hard

ramipril/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 [Invented name] is and what it is used for

[Invented name] contains two active substances called ramipril and indapamide.
Ramipril belongs to a group of medicines called ACE inhibitors (Angiotensin Converting Enzyme Inhibitors). These work by decreasing your body's production of substances that could raise your blood pressure and widening the blood vessels, which makes it easier for your heart to pump blood through them.
Indapamide belongs to a class of medicines called "diuretics". 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.
Each of the active ingredients reduces blood pressure and they work together to control your blood pressure.

This medicine is used for treatment of hypertension (high blood pressure) as substitution therapy in adult patients whose blood pressure is adequately controlled by the use of ramipril and indapamide given concurrently at the same dose level as in the combination, but as separate medicines.

2. What you need to know before you take [Invented name]

Do not take [Invented name]
- if you are allergic to ramipril or indapamide, to other ACE inhibitors, or to other sulphonamides or any of the other ingredients of this medicine (listed in section 6). Signs of an allergic reaction may include a rash, swallowing or breathing problems, swelling of your lips, face, throat or tongue.
- if you have ever had a serious allergic reaction called "angioedema". The signs include itching, hives (urticaria), red marks on the hands, feet and throat, swelling of the throat and tongue, swelling around the eyes and lips, difficulty breathing and swallowing.

- if you are having dialysis or any other type of blood filtration. Depending on the machine that is used, [Invented name] treatment may not be suitable for you.
- if you have kidney problems where the blood supply to your kidney is reduced (kidney artery stenosis);
- during the last 6 months of pregnancy (see section below on “Pregnancy and breast-feeding”);
- if you are breast-feeding;
- if your blood pressure is abnormally low or unstable. Your doctor will need to make this assessment;
- if you have diabetes or impaired kidney function and you are treated with a blood pressure lowering medicine containing aliskiren;
- 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 have severe liver disease or suffer from a condition called hepatic encephalopathy (damage to the brain and nerves which can occur as a complication of liver problems);
- if you have severe kidney disease;
- if you have been told by your doctor that you have low levels of potassium in your blood;
- if you have decompensated heart failure (especially untreated).

Do not take [Invented name] if any of the above apply to you. If you are not sure, talk to your doctor before taking this medicine.

Warnings and precautions
Talk to your doctor or pharmacist before taking [Invented name]:
- if you have lost a lot of body salts or fluids (through being sick (vomiting), having diarrhoea, sweating more than usual, being on a low salt diet, taking diuretics (water tablets) for a long time or having had dialysis);
- if you are going to receive an anaesthetic. This may be given for an operation or any dental work. You may need to stop your [Invented name] treatment one day beforehand; ask your doctor for advice.
- if you are going to have treatment to reduce your allergy to bee or wasp stings (desensitization);
- if you have high amounts of potassium or low amounts of sodium in your blood (shown in blood test results);
- if you have collagen vascular disease (when problems with the immune system affect the collagen in your body) such as scleroderma (a chronic disease mainly affecting the skin) or systemic lupus erythematosus (a long-lasting inflammatory disease in which the immune system attacks healthy tissues);
- if you are dark-skinned. You have a higher risk of sudden, mostly painful severe swelling of deep skin layers, mainly in the face and reduced effect of ramipril.
- if you have a cough. Inform your doctor if this becomes worse.
- 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;
- if you are taking any of the following medicines, the risk of angioedema may be increased:
  - racecadotril, a medicine used to treat diarrhea;
  - medicines used to prevent organ transplant rejection and for cancer (e.g., temsirolimus, sirolimus, everolimus);
  - vildagliptin, a medicine used to treat diabetes;
- if you have heart, liver or kidney problems;
- if you have diabetes (please check your blood sugar levels regulary);
- if you suffer from gout;
- if you have had photosensitivity reactions (reactions of immune system to sunlight);
- 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 a weeks of taking [Invented name]. 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 disorders of blood electrolyte levels or body water depletion.
- if you need to have a test to check how well your parathyroid gland is working.

You must tell your doctor if you think that you are (or might become) pregnant. [Invented name] is not recommended in the first 3 months of pregnancy and may cause serious harm to your baby after 3 months of pregnancy (see section "Pregnancy and breast-feeding").

If any of the above apply to you (or if you are not sure), talk to your doctor before taking [Invented name].

It is recommended that your doctor monitor the white blood cell count. More frequent monitoring is advised:
- at the beginning of treatment
- in patients with reduced kidney function or collagen vascular diseases or
- when medicines that influence the blood cell count are used.

Your doctor may check your kidney function, blood pressure, and the amount of electrolytes (such as sodium, potassium) in your blood at regular intervals.

Athletes should be aware that [Invented name] contains an active ingredient (indapamide) which may give a positive reaction in drug tests.

See also information under the heading "Do not take [Invented name]".

Children and adolescents
[Invented name] is not recommended for use in children and adolescents.

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

You should avoid [Invented name] with:
- lithium (used to treat depression).

Treatment with [Invented name] 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:
- sacubitrile in combination with valsartan - used to treat a long-term (chronic) heart failure in adults (see section 2 "Do not take [Invented name]");
- medicines used to relieve pain and inflammation (for example Non-Steroidal Anti-Inflammatory Drugs [NSAIDs] such as ibuprofen or indometacin and acetylsalicylic acid);
- potassium supplements (including salt substitutes), potassium-sparing diuretics (e.g. spironolactone, triamterene, amiloride) and other medicines that can increase the amount of potassium in your blood (e.g. trimethoprim and co-trimoxazole for infections caused by bacteria; ciclosporin, an immunosuppressant medicine used to prevent organ transplant rejection and heparin, a medicine used to thin blood to prevent clots);
- diuretics (tablets promoting the production of urine) such as furosemide;
- medicines that decrease blood pressure;
- medicines used for the treatment of low blood pressure, shock, cardiac failure, asthma or allergies such as ephedrine, noradrenaline or adrenaline and also dopamine, dobutamine, epinephrine, isoprenaline;
- steroid medicines for inflammation such as prednisolone;
- allopurinol (used to lower the uric acid in your blood);
- procainamide (for heart rhythm problems);
- temsirolimus (used to treat cancer);
- sirolimus, everolimus and other mTOR inhibitors (used to prevent organ transplant rejection);

- vildagliptin (used to treat type 2 diabetes);
- racecadotril (used to treat diarrhoea);
- medicines that may change the blood cell count;
- erythromycin by injection (antibiotic used to treat infections);
- medicines used for heart rhythm problems (quinidine, hydroquinidine, disopyramide, amiodarone, sotalol, dofetilide, ibutilide, digitalis preparations);
- medicines used to treat mental disorders such as depression, anxiety, schizophrenia (like tricylic antidepressants, antipsychotic medicines, neuroleptics);
- 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 gastric problems such as ulcers, too much acid, overactive digestive system);
- sparfloxacin, moxifloxacin (antibiotics used to treat infections);
- 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);
- mizolastine (used to treat allergic reactions, such as hay fever);
- amphotericin B by injection (anti-fungal medicines);
- oral corticosteroids used to treat various conditions including severe asthma and rheumatoid arthritis;
- stimulant laxatives;
- baclofen (to treat muscle stiffness occurring in diseases such as multiple sclerosis);
- medicines for diabetes (such as metformin) and insulin;
- iodinated contrast media (used for tests involving X-rays);
- calcium tablets or other calcium supplements;
- tetracosactide (to treat Crohn's disease).

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 [Invented name]” and “Warnings and precautions”).

[Invented name] with alcohol
Drinking alcohol during [Invented name] treatment may make you feel dizzy or light-headed. If you are concerned about how much you can drink while you are taking [Invented name], discuss this with your doctor as medicines used to reduce blood pressure and alcohol can have additive effects.

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 [Invented name] before you become pregnant or as soon as you know you are pregnant and will advise you to take another medicine instead of [Invented name]. This medicine 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
You must not take [Invented name] if you are breast-feeding. Tell your doctor immediately if you are breast-feeding or about to start breast-feeding.

Driving and using machines
[Invented name] has minor or moderate influence on the ability to drive and use machines. You may experience dizziness, headaches, fatigue (tiredness), weariness or nausea while taking [Invented

name]. This is more likely to happen when you start taking this medicine. If this happens, do not drive or use any tools or machines.

3. How to take [Invented name]

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

Use in adults
The recommended dose is one capsule once a day, preferably to be taken in the morning with a sufficient amount of fluid (such as with a glass of water).

Use in children and adolescents
[Invented name] is not recommended for use in children and adolescents due to a lack of data on safety and efficacy.

If you take more [Invented name] than you should
Tell a doctor or go to the nearest hospital casualty department straight away. Do not drive to the hospital, get somebody else to take you or call for an ambulance. Take the medicine pack with you. This is so the doctor knows what you have taken.

If you forget to take [Invented name]
If you miss a dose, take your normal dose when it is next due. Do not take a double dose to make up for a forgotten capsule.

If you stop taking [Invented name]
Do not stop taking this medicine abruptly or change the prescribed dose before consulting your doctor, as in such cases your disease may worsen.

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 [Invented name] and see a doctor straight away, if you notice any of the following serious side effects - you may need urgent medical treatment:
- swelling of the face, lips or throat which makes it difficult to swallow or breathe, as well as itching and rashes. This could be a sign of a severe allergic reaction to [Invented name].
- severe skin reactions including rash, ulcers in your mouth, worsening of a pre-existing skin disease, reddening, blistering or detachment of skin (such as Stevens-Johnson syndrome, toxic epidermal necrolysis or erythema multiforme).

Tell your doctor immediately if you experience:
- faster heart rate, uneven or forceful heartbeat (palpitations), chest pain, tightness in your chest or more serious problems including heart attack and stroke;
- shortness of breath or a cough. These could be signs of lung problems.
- bruising more easily, bleeding for longer than normal, any sign of bleeding (for example bleeding from the gums), purple spots blotching on the skin or getting infections more easily than usual, sore throat and fever, feeling tired, faint, dizzy or having pale skin. These can be signs of blood or bone marrow problems.
- severe stomach pain which may reach through to your back. This could be a sign of inflammation of the pancreas (pancreatitis).

- fever, chills, tiredness, loss of appetite, stomach pain, feeling sick, yellowing of your skin or eyes (jaundice). These can be signs of liver problems such as inflammation of the liver (hepatitis) or liver damage.
- concentrated urine (dark in colour), feel or are sick, have muscle cramps, confusion and fits which may be due to inappropriate ADH (anti-diuretic hormone) secretion.

Other side effects
Tell your doctor if any of the following gets serious or lasts longer than a few days.

Common (may affect up to 1 in 10 people)
- blood tests showing more potassium than usual in your blood, low potassium in the blood;
- headache and feeling dizzy;
- fainting (syncope), hypotension (abnormally low blood pressure), especially when you stand or sit up quickly;
- dry tickly cough, inflammation of your sinuses (sinusitis) or bronchitis, shortness of breath;
- stomach and/or bowel inflammation, stomach or gut pain, diarrhoea, indigestion, feeling or being sick;
- allergic reaction (especially in people who tend to have allergic or asthmatic reactions) leading to skin rashes with macules and papules;
- cramps or pain in your muscles;
- chest pain or feeling tired.

Uncommon (may affect up to 1 in 100 people)
- increased number of certain white blood cells (eosinophilia) found during a blood test;
- loss or decrease of appetite (anorexia), low sodium in the blood that may lead to dehydration and low blood pressure;
- feeling depressed, anxious, more nervous than usual or restless, sleep problems including somnolence;
- balance problems (vertigo), itching and unusual skin sensations such as numbness, tingling, pricking, burning or creeping on your skin (paraesthesia), loss or change in the way things taste;
- visual disturbances (including blurred vision);
- myocardial ischaemia including angina pectoris or myocardial infarction, increased or irregular heartbeats, palpitations, swelling of the ankles, feet or fingers;
- flushing;
- blocked nose, difficulty breathing or worsening of asthma;
- inflammation of the pancreas (pancreatitis), swelling in your gut called “intestinal angioedema” presenting with symptoms like abdominal pain, vomiting and diarrhoea;
- heartburn, constipation or dry mouth;
- blood tests showing changes in the way your liver, pancreas or kidneys are working;
- swelling of the face, lips or throat. See first bullet point at the beginning of chapter 4.
- sweating more than usual;
- exanthema, purple spots blotching on the skin (purpura), skin discolouration;
- joint pain;
- kidney impairment including acute kidney failure, increased need to urinate;
- sexual inability in men, reduced sexual desire in men or women, impotence (inability to obtain or maintain an erection);
- fever.

Rare (may affect up to 1 in 1,000 people)
- blood tests showing a decrease in the number of red blood cells, white blood cells or platelets or in the amount of haemoglobin;
- low chloride in the blood, low magnesium in the blood;
- feeling shaky or confused;
- tremor, balance disorder;
- fatigue (tiredness);
- conjunctivitis (“pink eye”);
- hearing impaired, tinnitus (sensation of noises in the ears);

- narrowed blood vessels, hypoperfusion (reduced amount of blood flow), inflammation of blood vessels;
- glossitis (swelling of the tongue);
- jaundice (yellowing of the skin and whites of the eye), damaged liver cells;
- severe flaking or peeling of the skin, urticaria, nail problem (for example loosening or separation of a nail from its bed);
- feeling of weakness (asthenia).

Very rare (may affect up to 1 in 10,000 people)
- increase in the levels of calcium in blood;
- reduction in levels of certain blood cells which can cause weakness, bruising or make infections more likely (haemolytic anaemia); aplastic anaemia (a bone marrow depression);
- irregular heart beat;
- pancreatitis (inflammation of the pancreas);
- abnormal liver function;
- photosensitivity reactions (change in skin appearance) after exposure to the sun or artificial UV light;
- severe skin reactions. See second bullet point at the beginning of chapter 4.

Not known (frequency cannot be estimated from the available data)
- bone marrow failure, pancytopenia (low levels of red, white blood cells and platelets), haemolytic anaemia;
- severe allergic reactions;
- syndrome of inappropriate antidiuretic hormone secretion;
- difficulty concentrating;
- circulation disorders in the brain including stroke, burning sensations, change in the way things smell;
- 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);
- life-threatening irregular beat (torsade de pointes);
- fingers and toes changing colour when you are cold and then tingling or feeling painful when you warm up (Raynaud's phenomenon);
- inflammation of oral mucosa (mucous membrane lining inside the mouth) with small ulcerations;
- acute liver failure, hepatitis (inflammation of the liver). If you have existing liver problems, taking [Invented name] may cause a condition called hepatic encephalopathy (damage to the brain and nerves which can occur as a complication of liver disease);
- hair loss;
- breast enlargement in men (gynecomastia);
- abnormal ECG heart tracing;
- changes may occur in your blood and your doctor may need to give you blood tests to check your condition. The following changes in your blood test results may occur:
    - increase in blood glucose levels in diabetic patients;
    - increase in uric acid, a substance which may cause or worsen gout (painful joint(s) especially in the feet);
    - increased levels of liver enzymes.

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 the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store [Invented name]

Keep this medicine out of the sight and reach of children.
Do not store above 25°C.

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

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 [Invented name] contains
- The active substances are ramipril and indapamide.
  Each capsule 5 mg/1.25 mg contains 5 mg ramipril and 1.25 mg indapamide.
  Each capsule 5 mg/2.5 mg contains 5 mg ramipril and 2.5 mg indapamide.
  Each capsule 10 mg/1.25 mg contains 10 mg ramipril and 1.25 mg indapamide.
  Each capsule 10 mg/2.5 mg contains 10 mg ramipril and 2.5 mg indapamide.
- The other excipients are:
  capsule content: microcrystalline cellulose, mannitol, magnesium stearate
  capsule shell: gelatin (bovine); The 5 mg/2.5 mg; 10 mg/1.25 mg; 10 mg/2.5 mg capsules contain: iron oxide red (E172); The 5 mg/1.25 mg; 5 mg/2.5 mg; 10 mg/1.25 mg capsules contain: iron oxide yellow (E172).

What [Invented name] looks like and contents of the pack
[Invented name] 5 mg/1.25 mg, hard gelatin yellow capsules, with overprint on the body 5+1,25; size of capsules - no. 3 (approximately 16 mm in length), containing a filling in the form of a white or almost white powder or slightly compacted larger agglomerates.
[Invented name] 5 mg/2.5 mg, hard gelatin capsules, yellow body, orange cap, with overprint on the body 5 mg+2,5 mg; size of capsules - no.1 (approximately 19.5 mm in length), containing a filling in the form of a white or almost white powder or slightly compacted larger agglomerates.
[Invented name] 10 mg/1.25 mg, hard gelatin capsules, orange body, red cap, with overprint on the body 10 mg+1,25 mg; size of capsules - no. 1 (approximately 19.5 mm in length), containing a filling in the form of a white or almost white powder or slightly compacted larger agglomerates.
[Invented name] 10 mg/2.5 mg, hard gelatin red capsules, with overprint on the body 10 mg+2,5 mg; size of capsules - no. 1 (approximately 19.5 mm in length), containing a filling in the form of a white or almost white powder or slightly compacted larger agglomerates.

The medicine is supplied in Aluminium/OPA/Aluminium/PVC blisters packed in cartons containing 28 and 84 capsules.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
[To be completed nationally]

This medicinal product is authorised in the Member States of the European Economic Area under the following names:
<{Name of the Member State}> <{Name of the medicinal product}>
<{Name of the Member State}> <{Name of the medicinal product}>

This leaflet was last revised in