Package leaflet: Information for the patient

Enalaprilmaleaat/Hydrochloorthiazide 20/12,5, tabletten 20/12,5 mg

enalapril maleate/hydrochlorothiazide

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 [nationally completed name] is and what it is used for

[nationally completed name] tablets contain a combination of enalapril and hydrochlorothiazide and are used as a treatment for high blood pressure when treatment with enalapril as a single agent on its own has proven insufficient.

Your doctor may also prescribe [nationally completed name] tablets instead of separate tablets of the same doses of enalapril and hydrochlorothiazide.
This fixed dose combination is not suitable for initial therapy.

You must talk to a doctor if you do not feel better or if you feel worse.

Enalapril belongs to a group of medicines called angiotensin converting enzyme inhibitors (ACE inhibitors) and lowers blood pressure by widening the blood vessels.

Hydrochlorothiazide belongs to a group of medicines called diuretics ("water tablets") and lowers blood pressure by increasing urine output.

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

Do not take [nationally completed name]:
- if you are allergic to enalapril maleate, hydrochlorothiazide or any of the other ingredients of this medicine (listed in section 6).
- if you are allergic to sulphonamide-derived medicines (mostly antibiotics e.g. sulphamethoxazole)

- if you have previously suffered from swelling of the extremities, face, lips, throat, mouth or tongue (angioedema) when treated with other medicines belonging to a group of medicines called ACE inhibitors (angiotensin-converting enzyme inhibitors)
- if you have previously suffered from swelling of the extremities, face, lips, throat, mouth or tongue (angioedema) under any other circumstances
- if anyone among your blood relatives has previously suffered from swelling of the extremities, face, lips, throat, mouth or tongue (angioedema)
- if you have severe kidney problems
- if you are not passing urine
- if you have diabetes or impaired kidney function and you are treated with a blood pressure lowering medicine containing aliskiren
- if you have severe liver problems or a neurological disorder as a result of severe liver problems (hepatic encephalopathy)
- if you are more than 3 months pregnant. (It is also better to avoid [nationally completed name] in early pregnancy – see pregnancy section).
- 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 [nationally completed name] if you:
- have narrowing of the arteries (atherosclerosis), cerebrovascular problems such as a stroke or transient ischemic attack (TIA, a “mini-stroke”)
- suffer from a disease, distinguished by reduced blood supply of the heart muscle, usually due to coronary blood vessel diseases (ischemic heart disease)
- have heart failure
- have low blood pressure, are on a salt restricted diet or are taking diuretics (“water tablets”)
- have abnormal levels of water and minerals in your body (fluid/electrolyte imbalance) distinguished by nausea, abdominal cramping, and/or vomiting, headache, edema (swelling), muscle weakness and/or tremor amongst others
- have heart muscle disease (hypertrophic cardiomyopathy), a narrowing of the main artery carrying blood away from the heart, the aorta (aortic stenosis), or a narrow of the artery to the only functioning kidney, have a kidney transplantation or other forms of a heart problem called outflow obstruction
- undergo LDL apheresis (removal of cholesterol from the blood by a machine)
- undergo desensitization therapy to some insect venoms, such as bee or wasp stings
- have diabetes
- suffer from gout, have high levels of uric acid in your blood or are being treated with allopurinol
- need to have an anesthetic
- have recently suffered from prolonged, violent vomiting and/or serious diarrhoea
- are going to have tests to check your parathyroid function
- have or have had liver or kidney problems, or you have narrow arteries to your kidneys (renal artery stenosis) or only have one functioning kidney, or you are undergoing dialysis
- have collagen vascular disease such as systemic lupus erythematosus (SLE) or scleroderma, which may be associated with skin rashes, joint pain and fever
- take an agent capable of suppressing immune responses (immunosuppressant) or procainamide, which is used to treat heart rhythm disturbances amongst others
- have had skin cancer or if you develop an unexpected skin lesion during the treatment. Treatment with hydrochlorothiazide, particularly long term use with high doses, may increase the risk of some types of skin and lip cancer (non-melanoma skin cancer). Protect your skin from sun

exposure and UV rays while taking [nationally completed name]
- have allergy problems or asthma.
- experienced breathing or lung problems (including inflammation or fluid in the lungs) following hydrochlorothiazide intake in the past. If you develop any severe shortness of breath or difficulty breathing after taking [nationally completed name], seek medical attention immediately.
- are taking lithium, used for the treatment of some psychiatric illness
- are taking any of the following medicines, the risk of angioedema (rapid swelling under the skin in area such as the throat) is increased:
  - racecadotril, a medicine used to treat diarrhoea;
  - medicines used to prevent organ transplant rejection and for cancer (e.g., temsirolimus, sirolimus, everolimus and other medicines belonging to the class of mTOR inhibitors);
  - vildagliptin, a medicine used to treat diabetes.
- 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 [nationally completed name]".

You must tell your doctor if you think you are (or might become) pregnant. [nationally completed name] 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). Breast-feeding is not recommended when you take [nationally completed name]

[nationally completed name] is not generally recommended if the following apply, so talk to your doctor before starting to take this medicine:
- if you have recently had a kidney transplant
- if you have too much potassium in the blood, your potassium values should be supervised during the treatment. Risk factors for raised potassium values include a reduced kidney function, age (> 70 years), dehydration, acute heart failure, acidification of the blood (metabolic acidose), diabetes (diabetes mellitus), concurrent taking of potassium sparing water tablet (diuretic), a potassium supplement or potassium-containing salt substitutes or taking medicines that increase the concentration of potassium in the blood. It is also possible that you can develop low levels of potassium in your blood distinguished by elevated blood pressure, disturbed heart rhythm etc. (e.g. to be caused by drug interactions, excessive loss of urine etc.).

Refer also to "Other medicines and [nationally completed name]" below.

Talk to your doctor if you are an athlete taking a doping test, as [nationally completed name] contains an active substance that can cause positive results in a doping test.

Elderly (> 70 years) or malnourished patients should be particularly careful when using [nationally completed name].

[nationally completed name] may be less effective in black people.

Children and adolescents
This medicine is not recommended for use in children.

While taking [nationally completed name] if you develop any of the following symptoms you should let your doctor know immediately:

- You feel dizzy after your first dose. A few people react to their first dose or when their dose is increased by feeling dizzy, weak faint and sick.
- Sudden swelling of the lips and face neck, possibly also hands and feet, or wheezing or hoarseness. This condition is called angioedema. This may occur at any time during treatment. ACE inhibitors cause a higher rate of angioedema in black patients than in non-black patients.
- High temperature, sore throat or mouth ulcers (these may be symptoms of infection caused by the lowering of the number of white blood cells).
- Yellowing of the skin and whites of eyes (jaundice) that may be sign of liver disease.
- A dry cough which is persistent for a long time. Cough has been reported with the use of ACE inhibitors but may be also a symptom of other upper respiratory track disease.
- Sudden short sightedness.
- 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 [nationally completed name]. This can lead to permanent vision loss, if not treated. If you earlier have had a penicillin or sulphonamide allergy, you can be at higher risk of developing this.

Other medicines and [nationally completed name]

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

You should not take [nationally completed name] at the same time as the following medicines:

- potassium supplements (including salt substitutes), diuretics ("water tablets") which are used to treat high blood pressure including potassium-sparing diuretics such as spironolactone, triamterene or amiloride, and other medicines that can increase the amount of potassium in your blood (e.g. trimethoprim and co-trimoxazole also known as trimethoprim/sulfamethoxazole 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).
- other medicines used to treat high blood pressure.
  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 [nationally completed name]" and "Warnings and precautions").
- anesthetics and medicines for mental disorders or depressions, medicines to treat psychoses, tricyclic antidepressants or sedatives
- lithium (medicine for treatment of psychic disorders)
- painkillers and anti-inflammatory medicines, such as acetylsalicylic acid, indomethacin and selective cyclooxygenase-2 inhibitors (COX-2 inhibitors)
- gold injections (sodium aurothiomalat), a medicine to injection against rheumatic arthritis
- medicines such as ephedrine, used in some cough and cold remedies, or noradrenaline and adrenaline used for low blood pressure, shock, cardiac failure, asthma or allergies.
- blood sugar lowering medicines, such as insulin or those taken orally.
- colestyramine resin and colestipol, active substances for lowering blood lipid values
- corticosteroids, anti-inflammatory hormone-like substances
- corticotropin (ACTH), it is used mainly to test whether your adrenal glands are working properly
- muscle relaxants (e.g., tubocurarine chloride, medicines for relaxing muscles that are used in operations)
- allopurinol, probenecide, sulfinpyrazone, medicines used to treat gout
- medicines such as atropine or biperiden which are used to treat a variety of disorders such as gastrointestinal cramps, urinary bladder spasm, asthma, motion sickness, muscular spasms and as an

aid to anesthesia
- medicines to treat cancer, such as cyclophosphamide or methotrexate
- medicines that inhibit your body's immune system, medicines to prevent rejection reactions after organ or bone marrow transplants such as ciclosporin
- cardiac glycosides (e.g., digoxin, medicines for strengthening the heart)
- medicines that as a side effect may cause abnormalities in the stimulus conduction in the heart such as medicines for disturbances for heart rhythm, some medicines for psychosis and other medicines such as medicines used to treat bacterial infections
- calcium salts and vitamin D, elevated calcium levels in the blood (can lead to gastrointestinal disorders, excessive thirst, excessive urination, tiredness, weakness and decrease in weight)
- carbamazepine, medicine used primarily in the treatment of epilepsy and bipolar disorder
- amphotericin B, medicines against fungal infections
- laxatives, medicines to promote defecation
- iodinated contrast media, enhances the visibility of vascular structures and organs during radiographic procedures
- barbiturates, medicines that act as central nervous system depressant resulting in sedation
- opioid analgesics, strong pain killers with no anti-inflammatory effect
- carbenoxolone, medicine to treat inflammation of the intestinal tract
- salicylates, medicines to treat pain and/or inflammatory diseases
- medicines which are most often used to avoid rejection of transplanted organs (sirolimus, everolimus and other medicines belonging to the class of mTOR inhibitors). See section "Warnings and precautions".

[nationally completed name] with food, drink and alcohol

[nationally completed name] can be taken without regard to meals. Drinking alcohol together with this medicine can increase the blood pressure-lowering effect (and can then cause dizziness on standing up, among other things).

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 [nationally completed name] before you become pregnant or as soon as you know you are pregnant and will advise you to take another medicine instead of [nationally completed name]. [nationally completed name] 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
Tell your doctor if you are breast-feeding or about to start breast-feeding. [nationally completed name] is not recommended for mothers who are breast-feeding.

Driving and using machines
Dizziness and tiredness have been reported by people taking [nationally completed name]. If you experience either of these do not drive a car and do not operate machinery (see also "4. Possible side effects").

[nationally completed name] contains lactose

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

[Nationally completed name] 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 [nationally completed name]

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

The recommended dose is:

Adults
The recommended dose is one tablet taken once a day.

Elderly
Your doctor may adjust the dose of enalapril and hydrochlorothiazide carefully.

Renal impairment
Your doctor will adjust the dose of enalapril and hydrochlorothiazide carefully.

If you are taking other diuretic tablets
If you are currently taking other diuretic tablets (water tablets) your doctor will inform you to stop taking them 2-3 days before starting to take [nationally completed name].

Method of administration
The tablets should be swallowed with a glass of water.
[nationally completed name] can be taken with meal or to empty stomach.

The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

If you take more [nationally completed name] than you should
If you (or someone else) swallow a lot of the tablets all together, or if you think a child has swallowed any of the tablets, seek medical advice immediately. An overdose is likely to cause low blood pressure, an excessively fast or slow heart beat, palpitations (a feeling of unduly rapid or irregular heart beat), shock, rapid breathing, cough, feeling and being sick, cramps, dizziness, feeling sleepy and confused or anxious, excessive urination or not being able to urinate. Please take this leaflet, any remaining tablets and the container with you to the hospital or doctor so that they know which tablets were consumed.

If you forget to take [nationally completed name]
Do not take a double dose to make up for a forgotten tablet, take your next dose at the normal time.
If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

If you stop taking [nationally completed name]
The treatment of hypertension is a long term treatment and interruption of treatment must be discussed with the doctor. Interruption or stopping your treatment could cause your blood pressure to increase.

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 the following, stop taking [nationally completed name] and tell your doctor immediately or go to the emergency department of your nearest hospital:
- A severe allergic reaction called angioedema (rash, itching, swelling of the extremities, face, lips, mouth or throat that may cause difficulty in swallowing or breathing). This is a serious and common side effect (may affect up to 1 in 10 people). You may need urgent medical attention or hospitalization.
- A serious allergic reaction called anaphylactic reaction which causes difficulty in breathing or dizziness. This is a rare side effect (may affect up to 1 in 1,000 people).
- Severe blisters, Stevens Johnson syndrome (blistering of the skin, mouth, eyes and genitals), skin looking as if it were burnt and peeling off, sensitivity of the skin to light, skin conditions with red scaly patches over the nose and cheeks (lupus erythematosus), pemphigus (a condition causing blisters and lesions normally starting in the mouth, nettle rash, hair loss and itching). These are rare side effects (may affect up to 1 in 1,000 people).
- Jaundice (yellowing of the skin and the whites of the eyes). This is a potentially serious but rare side effect (may affect up to 1 in 1,000 people) indicative of inflammation of the liver. You may need urgent medical attention or hospitalization.
- Sudden short sightedness. The frequency of this side effect is not known (cannot be estimated from the available data).
- 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). The frequency of this side effect is not known (cannot be estimated from the available data).
- Acute respiratory distress (signs include severe shortness of breath, fever, weakness, and confusion). This is a very rare side effect (may affect up to 1 in 10,000 people).

[nationally completed name] commonly (may affect up to 1 in 10 people) causes low blood pressure which may be associated with feelings of light-headedness and weakness. In some patients, this may occur after the first dose or when the dose is increased. If you experience these symptoms, you should contact your doctor immediately.

[nationally completed name] rarely (may affect up to 1 in 1,000 people) causes a reduction in the number of white blood cells and your resistance to infection may be decreased. If you experience an infection with symptoms such as fever and serious deterioration of your general condition, or fever with local infection symptoms such as sore throat/pharynx/mouth or urinary problems you should see your doctor immediately. A blood test will be taken to check possible reduction of white blood cells (agranulocytosis). It is important to inform your doctor about your medicine.

A dry cough, which may persist for a long time, has been reported very commonly (may affect more than 1 in 10 people) with the use of [nationally completed name] and other ACE inhibitors, but may be also a symptom of other upper respiratory tract disease. You should contact your doctor if you develop this symptom.

The following side effects have also been reported:

Very common (may affect more than 1 in 10 people)
- blurred vision
- dizziness
- nausea
- weakness
- cough

Common (may affect up to 1 in 10 people)
- low level of potassium in the blood, which can cause muscle weakness, twitching or abnormal heart rhythm
- high level of fat or uric acid in the blood
- headache, depression
- fainting, low blood pressure associated with changes in posture (such as feeling light-headed or weak when you stand up after lying down), chest pain, abnormal heart rhythm, excessively fast heart beat (tachycardia)
- shortness of breath
- diarrhoea, abdominal pain
- a distorted sense of taste
- rash
- tiredness
- high level of potassium in the blood, which can cause an abnormal heart rhythm; increase in the amount of creatinine in the blood
- muscle cramps

Uncommon (may affect up to 1 in 100 people)
- reduction in the number of red blood cells, which can make the skin pale and cause weakness or breathlessness (anaemia)
- hypoglycaemia (low blood sugar levels) (see “Warnings and precautions” in section 2)
- low level of magnesium in the blood
- uric acid crystals in the joints (gout)
- confusion, sleepiness, insomnia, nervousness, restlessness, tingling feeling or numbness, vertigo, decreased sexual desire
- predominance of yellow in vision due to a yellowing of the optic media of the eye (xanthopsia)
- palpitations (a sensation of a fast or particularly strong or irregular heart beat)
- heart attack or cerebrovascular accident (“mini-stroke”) (mainly in patients suffering from low blood pressure)
- inflammation of your blood vessels (necrotising vasculitis)
- runny nose, sore throat, hoarseness, difficulty breathing, wheezing
- intestinal obstruction, inflammation of the pancreas which causes severe pain in the abdomen and back (pancreatitis), vomiting, indigestion, constipation, loss of appetite, stomach irritation, dry mouth, peptic ulcer, flatulence
- sweating, itching, hives, hair loss
- increased sensitivity of the skin to sun
- joint pain
- kidney problems, protein in the urine
- impotence
- hot flushes, ringing in the ears
- feeling unwell, fever
- inflammation of a salivary gland
- abnormal amount of salts in the body (disturbance of the electrolyte balance), including low levels of sodium in the blood, which can cause tiredness and confusion, muscle twitching, fits or coma, also leading to dehydration and low blood pressure that makes you feel dizzy when you stand up
- increase in the amount of urea in the blood

Rare (may affect up to 1 in 1,000 people)
- reduction in the number of white blood cells, which makes infection more likely, reduction in the number of other blood cells, changes in blood composition, poor production of bone marrow, disease of the lymph nodes, autoimmune disease, in which the body attacks itself.
- strange dreams, sleep disorders

- paresis
- Raynaud's syndrome, a blood vessel disorder which may cause your fingers and toes to tingle, and turn pale, then bluish, then reddish.
- lung problems including pneumonia, inflammation of the lining of the nose causing the nose to run (rhinitis)
- mouth ulcers, inflammation of the tongue
- liver problems, inflammation of the gallbladder
- skin rash, redness of the skin
- reduced urine production
- inflammation in the kidneys (interstitial nephritis)
- breast enlargement including in men
- increase in the amount of enzymes and waste products produced by the liver
- increased blood sugar levels

Very rare (may affect up to 1 in 10,000 people)
- swelling in the intestines
- high levels of calcium in the blood (see "Other medicines and [nationally completed name]" in section 2)

Not known (frequency cannot be estimated from the available data)
- A complex side effect has also been reported which may include some or all of the following signs:
  - fever, inflammation of your blood vessels, pain and inflammation of muscles or joints
  - blood disorders affecting the components of your blood (usually detected by a blood test)
  - rash, hypersensitivity to sunlight and other effects on your skin.
- inappropriate antidiuretic hormone secretion (known as SIADH) causing amongst others the general symptoms confusion, nausea, altered mood, seizures and loss of consciousness
- excretion of glucose into the urine (glycosuria)
- decreased appetite, light-headedness
- skin and lip cancer (non-melanoma skin cancer)

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 [nationally completed name]

Keep 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.

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 [nationally completed name] contains

The active substances are enalapril maleate and hydrochlorothiazide.

Each tablet contains 20 mg of enalapril maleate and 12.5 mg of hydrochlorothiazide.

The other ingredients are sodium hydrogen carbonate, maize starch, lactose monohydrate, calcium hydrogen phosphate dihydrate, talc, magnesium stearate.

What [nationally completed name] looks like and contents of the pack

[nationally completed name] 20 mg/12.5 mg tablets are white, oval, biconvex, with a break-line on one side of the tablet and the stamp “E H” on the other side of the tablet.

The tablets are packed in OPA-Al-PVC/Al blisters which are inserted into a carton folder.

[nationally completed name] 20 mg/12.5 mg tablets are available in pack sizes of 10, 14, 20, 28 , 30, 49, 50, 50x1, 60, 84, 90, 98 and 100 tablets.

Not all pack sizes may be marketed.

Houder van de vergunning voor het in de handel brengen en fabrikant

Houder van de vergunning voor het in de handel brengen
Hexal AG
Industriestrasse 25
D-83607 Holzkirchen
Duitsland

Fabrikant
Salutas Pharma GmbH
Otto-von-Guericke Allee 1
39179 Barleben
Duitsland

Sandoz A/S
Edvard Thomsens
2300 Kopenhagen S
Denemarken

In het register ingeschreven onder:
Enalaprilmaleaat/Hydrochloorthiazide 20/12,5, tabletten 20/12,5 mg - RVG 34510

Dit geneesmiddel is geregistreerd in lidstaten van de EEA onder de volgende namen:
Nederland: Enalaprilmaleaat/Hydrochloorthiazide 20/12,5, tabletten 20/12,5 mg
Duitsland Enalapril plus – 1A Pharma 20/12,5 mg Tabletten

Deze bijsluiter is voor het laatst goedgekeurd in april 2022