Package leaflet: Information for the patient

Perindopril tosilaat/Indapamide DOC 2,5 mg/0,625 mg, filmomhulde tabletten

perindopril tosilate/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 [Product name] 2.5 mg/0.625 mg is and what it is used for

[Product name] 2.5 mg/0.625 mg is a combination of two active ingredients, perindopril and indapamide. It is an anti-hypertensive and is used in the treatment of high blood pressure (hypertension) in adults.

Perindopril belongs to a class of medicines called ACE inhibitors. These work by widening the blood vessels, which makes it easier for your heart to pump blood through them. Indapamide is a diuretic. 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.

2. What you need to know before you take [Product name] 2.5 mg/0.625 mg

Do not take [Product name] 2.5 mg/0.625 mg
- if you are allergic to perindopril or any other ACE inhibitor, or to indapamide or any other sulfonamide or any of the other ingredients of this medicine (listed in section 6),
- 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 severe liver disease or suffer from a condition called hepatic encephalopathy (degenerative disease of the brain),
- if you have a severe kidney disease where the blood supply to your kidneys is reduced (renal artery stenosis),
- if you are receiving dialysis, or any other type of blood filtration. Depending on the machine that is used, [Product name] may not be suitable for you.
- if you have low blood potassium,
- if you are suspected of having untreated decompensated heart failure (severe water retention, difficulty in breathing),

- if you are more than 3 months pregnant (It is also better to avoid [Product name] in early pregnancy - see section "Pregnancy and breast-feeding"),
- 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 [Product name] 2.5 mg/0.625 mg

- if you have aortic stenosis (narrowing of the main blood vessel leading from the heart) or hypertrophic cardiomyopathy (heart muscle disease) or renal artery stenosis (narrowing of the artery supplying the kidney with blood),
- if you have heart failure or any other heart problems,
- if you have kidney problems or if you are receiving dialysis,
- 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 [Product name] 2.5 mg/0.625 mg. 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 aldosteronism),
- if you have liver problems,
- if you suffer from a collagen disease (skin disease) such as systemic lupus erythematosus or scleroderma,
- if you have atherosclerosis (hardening of the arteries),
- if you suffer from hyperparathyroidism (overactive parathyroid gland),
- if you suffer from gout,
- if you have diabetes,
- if you are on a salt restricted diet or use salt substitutes which contain potassium,
- if you take lithium or potassium-sparing drugs (spironolactone, triamterene) or potassium supplements as their use with [Product name] 2.5 mg/0.625 mg should be avoided (see section "Other medicines and [Product name] 2.5 mg/0.625 mg").
- if you are elderly,
- if you have had photosensitivity reactions,
- if you have a severe allergic reaction with swelling of the face, lips, mouth , tongue or throat which may cause difficulty in swallowing or breathing (angioedema). This may occur at any time during treatment. If you develop such symptoms, you should stop taking the treatment and see a doctor immediately.
- 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 [Product name] 2.5 mg/0.625 mg".
- if you are of black origin since you may have a higher risk of angioedema and this medicin may be less effective in lowering your blood pressure than in non-black patients,
- if you are a haemodialysis patient dialysed with high-flux membranes.
- if you are taking any of the following medicines, the risk of angioedema is increased:
  - racecadotril, a medicine used to treat diarrhoea;
  - medicines used to prevent organ transplant rejectionand for cancer (e.g., temsirolimus, sirolimus, everolimus);
  - 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).

<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 [Product name]. This may occur at any time during treatment. If you develop such symptoms, you should stop taking [Product name] and see a doctor immediately. See also section 4.

You must tell your doctor if you think that you are (or might become) pregnant. [Product name] 2.5 mg/0.625 mg 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 section "Pregnancy and breast-feeding").

When you are taking [Product name] 2.5 mg/0.625 mg, you should also inform your doctor or the medical staff:
- if you are to undergo anaesthesia and/or surgery,
- if you have recently suffered from diarrhoea or vomiting, or are dehydrated,
- if you are to undergo dialysis or LDL apheresis (which is removal of cholesterol from your blood by a machine),
- 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)
- if you have changes in your vision or pain in one or both of your eyes while taking [Product name]. This could be a sign that you are developing glaucoma, increased pressure in your eye(s). You should discontinue [Product name] treatment and seek medical attention.

Athletes should be aware that [Product name] 2.5 mg/0.625 mg contains an active ingredient (indapamide) which may give a positive reaction in drug tests.

Children and adolescents

[Product name] 2.5 mg/0.625 mg should not be given to children and adolescents.

Other medicines and [Product name] 2.5 mg/0.625 mg
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

You should avoid [Product name] 2.5 mg/0.625 mg with:
- lithium (used to treat mania or depression),
- aliskiren (medicine used to treat hypertension) if you have no diabetes mellitus or kidney problems,
- potassium supplements (including salt substitutes), potassium-sparing diuretics (e.g. triamterene, 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).
- estramustine (used in cancer therapy),
- other medicines used to treat high blood pressure: angiotensin-converting-enzyme inhibitors and angiotensin receptor blockers.

Treatment with [Product name] 2.5 mg/0.625 mg can be affected by other medicines. Your doctor may need to change your dose and/or to take other precautions. Make sure to tell your doctor if you are taking any of the following medicines as special care may be required:
- other medicines for treating high blood pressure, including angiotensin II receptor blocker (ARB) or aliskiren (see also information under the headings "Do not take [Product name] 2.5 mg/0.625 mg" and "Warnings and precautions") or diuretics (medicines which increase the amount of urine produced by the kidneys),
- potassium-sparing drugs used in the treatment of heart failure: eplerenone and spironolactone at doses between 12.5 mg to 50 mg per day,

- medicines, which is 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 [Product name] 2.5 mg/0.625 mg” and “Warnings and precautions”.
- anaesthetic medicines,
- iodinated contrast agent,
- antibiotics used to treat bacterial infections (e.g moxifloxacin, sparfloxacin, erythromycin by injection),
- methadone (used to treat addiction),
- procainamide (for the treatment of an irregular heartbeat),
- allopurinol (for the treatment of gout),
- antihistamines used to treat allergic reactions, such as hay fever (e.g mizolastine, terfenadine, astemizole),
- corticosteroids used to treat various conditions including severe asthma and rheumatoid arthritis,
- immunosuppressants used for the treatment of auto-immune disorders or following transplant surgery to prevent rejection (e.g. ciclosporin, tacrolimus),
- halofantrine (used to treat certain types of malaria),
- pentamidine (used to treat pneumonia),
- injectable gold (used to treat rheumatoid polyarthritis),
- vincamine (used to treat symptomatic cognitive disorders in elderly including memory loss),
- bepridil (used to treat angina pectoris),
- medicines used for heart rhythm problems (e.g. quinidine, hydroquinidine, disopyramide,amiodarone, sotalol, ibutilide, dofetilide, digitalis, bretylium),
- cisapride, diphemanil (used to treat gastric and digestive problems),
- digoxin or other cardiac glycosides (for the treatment of heart problems),
- baclofen (to treat muscle stiffness occurring in diseases such as multiple sclerosis),
- medicines to treat diabetes such as insulin, metformin or gliptins,
- calcium including calcium supplements,
- stimulant laxatives (e.g. senna),
- non-steroidal anti-inflammatory drugs (e.g. ibuprofen) or high dose salicylates (e.g. acetylsalicylic acid (a substance presents in many medicines used to relieve pain and lower fever, as well as to prevent blood clotting)),
- amphotericin B by injection (to treat severe fungal disease),
- medicines used to treat mental disorders such as depression, anxiety, schizophrenia…(e.g. tricyclic antidepressants, neuroleptics (such as amisulpride, sulpiride, sultopride, tiapride, haloperidol, droperidol),
- tetracosactide (to treat Crohn’s disease),
- trimethoprim (for the treatment of infections),
- vasodilators including nitrates (products that make the blood vessels become wider),
- medicines used for the treatment of low blood pressure, shock or asthma (e.g. ephedrine, noradrenaline or adrenaline).

[Product name] 2.5 mg/0.625 mg with food and drink
It is preferable to take [Product name] 2.5 mg/0.625 mg before a meal.

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 [Product name] 2.5 mg/0.625 mg before you become pregnant or as soon as you know you are pregnant and will advise you to take another medicine instead of [Product name] 2.5 mg/0.625 mg.

[Product name] 2.5 mg/0.625 mg 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
[Product name] 2.5 mg/0.625 mg is not recommended for mothers if you are breast-feeding. Tell your doctor immediately if you are breast-feeding or about to start breast-feeding.
See your doctor immediately.

Driving and using machines
[Product name] 2.5 mg/0.625 mg does not usually affect alertness but different reactions such as dizziness or weakness in relation to the decrease in blood pressure may occur in certain patients. If affected, your ability to drive or to operate machinery may be impaired.

[Product name] 2.5 mg/0.625 mg contains lactose
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

[Product name] 2.5 mg/0.625 mg 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 [Product name] 2.5 mg/0.625 mg

Always take this medicine 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 daily. Your doctor may decide to increase the dose to 2 tablets daily or to modify the dosage regimen if you suffer from renal impairment.
Take your tablet preferably in the morning and before a meal. Swallow the tablet with a glass of water.

The score line is only there to help you break the tablet if you have difficulty swallowing it whole.

If you take more [Product name] 2.5 mg/0.625 mg 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. If marked low blood pressure occurs (associated with nausea, vomiting, cramps, dizziness, sleepiness, mental confusion, changes in the amount of urine produced by kidneys), lying down with your legs raised can help.

If you forget to take [Product name] 2.5 mg/0.625 mg
It is important to take your medicine every day as regular treatment is more effective. However, if you forget to take a dose of [Product name] 2.5 mg/0.625 mg, 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 [Product name] 2.5 mg/0.625 mg
As the treatment for high blood pressure is usually life-long, you should discuss with your doctor before stopping 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:

- Severe dizziness or fainting due to low blood pressure (Common - may affect up to 1 in 10 people),
- Bronchospasm (tightening of the chest, wheezing and shortness of breath (Uncommon) (may affect up to 1 in 100 people),
- Swelling of the face, lips, mouth, tongue or throat, difficulty in breathing, (angioedema) (See section 2 "Warning and precaution"), (Uncommon) (may affect up to 1 in 100 people),
- Severe skin reactions including erythema multiforme (a skin rash which often starts with red itchy patches on your face, arms or legs) or 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) or other allergic reactions (Very rare) (may affect up to 1 in 10,000 people),
- Cardiovascular disorders (irregular heartbeat, angina pectoris (pains to the chest, jaw and back, brought on by physical effort), heart attack) (Very rare) (may affect up to 1 in 10,000 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),
- Inflamed pancreas which may cause severe abdominal and back pain accompanied with feeling very 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) (may affect up to 1 in 10,000 people),
- Life-threatening irregular beat (Not known),
- Disease of the brain caused by liver illness (Hepatic encephalopathy) (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 (Not known).

In decreasing order of frequency, side effects can include:

- Common: (may affect up to 1 in 10 people)
  Low potassium in the blood, skin reactions in subjects predisposed to allergic and asthmatic reactions, headache, dizziness, vertigo, pins and needles, vision disturbances, tinnitus (sensation of noises in the ears), cough, shortness of breath (dyspnoea), gastro-intestinal disorders (nausea, vomiting, abdominal pain, taste disturbances, dyspepsia or difficulty of digestion, diarrhoea, constipation), allergic reactions (such as skin rashes, itching), cramps, feeling of tiredness.

- Uncommon: (may affect up to 1 in 100 people)
  Mood swings, sleep disturbances, depression, urticaria, purpura (red pinpoints on skin), blister cluster, kidney problems, impotence, sweating, an excess of eosinophils (a type of white blood cells), change in laboratory parameters: high blood level of potassium reversible on discontinuation, low blood level of sodium, somnolence, fainting, palpitations (awareness of your heartbeat), tachycardia (fast heartbeat), hypoglycaemia (very low blood sugar level) in case of diabetic patients, vasculitis (inflammation of blood vessels), dry mouth, photosensitivity reactions (increased sensitivity of the skin to sun), arthralgia (joint pain), myalgia (muscle pain), chest pain, malaise, oedema peripheral, fever, increased blood urea, increased blood creatinine, fall.

- Rare: (may affect up to 1 in 1000 people)
  Psoriasis worsening, changes in laboratory parameters: low chloride in the blood, low magnesium in the blood, increased level of liver enzymes, high level of serum bilirubin, fatigue flushing, 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)
  Confusion, eosinophilic pneumonia (a rare type of pneumonia), rhinitis (blocked up or runny nose), severe kidney problems, changes in blood values such as a lower number of white and red blood cells, lower haemoglobin, lower number of blood platelets, high level of calcium in the blood, abnormal hepatic function.

- Not known: (frequency cannot be estimated from the available data)
  Abnormal ECG heart tracing, changes in laboratory parameters: high uric acid levels and high sugar levels in the blood, short sightedness (myopia), vision blurred, visual impairment, 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), discoloration, numbness and pain in fingers or toes (Raynaud's phenomenon). If you suffer from systemic lupus erythematosus (a type of collagen disease), this might get worse.

Disorders of the blood, kidney, liver or pancreas and changes in laboratory parameters (blood tests) can occur. Your doctor may need to give you blood tests to monitor your condition.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any 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 [Product name] 2.5 mg/0.625 mg

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 carton and bottle label EXP. The expiry date refers to the last day of that month.

Keep the container tightly closed in order to protect from 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 [Product name] 2.5 mg/0.625 mg contains

- The active substances are perindopril tosilate and indapamide.
  Each film-coated tablet contains 2.5 mg perindopril tosilate (corresponding to 1.704 mg perindopril) and 0.625 mg indapamide.

- The other ingredients are lactose monohydrate, maize starch, sodium hydrogen carbonate (E 500 (ii)), pregelatinized starch (maize), Povidone K30 (E 1201), magnesium stearate (E 470b), polyvinyl alcohol - part hydrolized, titanium dioxide (E171), macrogol/PEG 3350 and talc.

What [Product name] 2.5 mg/0.625 mg looks like and contents of the pack

[Product name] 2.5 mg/0.625 mg film-coated tablets are white, capsule shaped biconvex film-coated tablet of approximately 4 mm width and 8 mm length, debossed breakline on one side and plain on the other side.
The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

Tablets are available in polypropylene (PP) containers with polyethylene (PE) stopper with desiccant, containing 30 film-coated tablets.

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

Vergunninghouder:
DOC Generici S.r.l.
Via Filippo Turati 40
Milano 20121
Italië

Fabrikant:
Teva Gyogyszergyar Zrt.
Pallagi Ut 13
Hajdu-Bihar 4042 Debrecen
Hongarije

Teva Operations Poland Sp. z o.o.
Ul. Mogilska 80
Małopolskie 31-546 Kraków
Polen

In het register ingeschreven onder RVG 130956

Dit medicijn is geregistreerd in lidstaten van de Europese Economische Ruimte onder de volgende namen:

Nederland: Perindopril tosilaat/Indapamide DOC 2,5 mg/0,625 mg, filmomhulde tabletten
Italië: PERINDOPRIL E INDAPAMIDE DOC

Deze bijsluiter is voor het laatst goedgekeurd in maart 2024.