

Package leaflet: Information for the patient

CARDIURINE 50 mg/25 mg, scored tablets Captopril/ 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 or nurse.
- . This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- . If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What in this leaflet?:

1. What CARDIURINE is and what is used for?
2. Before you take CARDIURINE
3. How to take CARDIURINE?
4. Possible side effects
5. How to store CARDIURINE?
6. Content of the pack and other information.

1. WHAT CARDIURINE IS AND WHAT IT IS USED FOR?

Pharmacotherapeutic group: captopril and diuretics, ATC code: C09BA01.

CARDIURINE is a combination of two active substances, captopril and hydrochlorothiazide.

This medicine is used in the treatment of high blood pressure when your doctor considers it is necessary to use a combination of two active substances, captopril and hydrochlorothiazide.

Captopril belongs to a group of medicinal products called Angiotensin Converting Enzyme (ACE) Inhibitors. ACE inhibitors cause blood vessels to relax and the blood pressure to lower and ease pressure on the heart.

Hydrochlorothiazide is one of a group of medicinal products called thiazide diuretics (also known as water tablets). They increase urine output and hence decrease blood pressure.

The two active substances in CARDIURINE work together to decrease blood pressure further than if either was given alone.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE CARDIURINE

Do not take CARDIURINE

- . if you are allergic to captopril or to any of the other ingredients contained in this medicine, listed in section 6, or to any other ACE inhibitors.
- . if you are allergic to hydrochlorothiazide or to any of the other ingredients contained in this medicine, listed in section 6, or to a sulphonamide or to any other sulphonamide derivatives.
- . if you have diabetes or impaired kidney function and you are treated with a blood pressure lowering medicine containing aliskiren.
- . if you have previously been treated with CARDIURINE or a medicine in the same group as CARDIURINE (ACE inhibitors) and have had an allergic reaction which caused swelling of the arms, legs, ankles, lips, tongue and/or throat with difficulty in swallowing or breathing (angioedema) or if a member of your family has had a similar reaction.
- . if you are currently treated with the association sacubitril/valsartan, medication used to treat a type of long cardiac deficiency(chronic) in adults, because the higher risk of angioedema (fast swelling under the skin in the neck region) (see “warnings and precautions” and “other medicines and CARDIURINE”).
- . if you have severe liver or kidney problems (ask your doctor if you have any doubt).

- . if you are pregnant for more than 3 months (the use of CARDIURINE is not recommended during the first trimester of pregnancy-see section “Pregnancy and breast-feeding”).
- . CARDIURINE should not be given to children and adolescents (< 18 years).

Warnings and precautions

Talk to your doctor before using CARDIURINE:

- . if you suffer from excessive vomiting or diarrhoea.
- . if you are on a low-salt diet and you use salt substitutes or supplements containing potassium.
- . if you have any liver or kidney problems (ask your doctor if you have any doubt).
- . if you know that you have reduced blood circulation in the heart muscle or a narrowing of the aorta (aortic stenosis) or of the renal artery (renal artery stenosis).
- . if you have had shock following heart failure (cardiogenic shock).
- . if you suffer from diabetes. CARDIURINE may influence the effect of insulin or other anti-diabetic medicines. Please ask your doctor for advice.
- . if you take one of the following medicines used for treating hypertension:
 - An “angiotensin II receptor blocker” (ARBs) (also known as sartans – for example valsartan, telmisartan, irbesartan), especially if you have diabetes-related kidney problems.
 - Aliskiren.
- . if you are taking one of the following medicines, the risk of angioedema (sudden swelling occurring under the skin in areas like throat) is increased:
 - Racécadotril, medication to treat diarrhoea.
 - Medicines used to prevent transplant reject rejection and in cancer treatment (for example temsirolimus, sirolimus, everolimus).
 - Nephilysine inhibitors (NEP) as sacubitril (available in fixed dose association with valsartan), used in cardiac deficiency patients
 - Vildagliptine, an antidiabetic medication.
- . if you 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 type of skin and lip cancer (non-melanoma skin cancer). Protect your skin from sun exposure and UV rays while taking CARDIURINE.

Your doctor may need to monitor regularly your renal function, blood pressure and the amount of electrolytes (e.g. potassium) in your blood. See information in section “Do not take CARDIURINE”:

- . if you undergo dialysis. There have been some reports of allergic-type reactions when people using medicinal products such as CARDIURINE undergo dialysis with certain dialysis membranes [so called High-flux-Haemodialysis-Membranes or low-density lipoprotein (LDL)-apheresis with dextran sulphate absorption]. Tell your doctor before your next dialysis treatment.
- . if you are to have desensitisation treatment for wasp or bee stings. There have been some reports of allergic-type reactions when people using medicinal products such as CARDIURINE have such desensitisation treatment. Tell your doctor before taking your treatment.
- . if you suffer from lupus or lupus-like disorders.
- . if you notice a decrease in your vision or feel eye pains in one or both your eyes during treatment with CARDIURINE. These signs can be signs of fluid accumulation in vascular layer of the eye (choroidal effusion), increase in the intraocular pressure and may develop after few hours or one week after taking CARDIURINE. Without treatment, it may lead to definitive sight loss. If you are allergic to medicines containing penicillin or sulfonamide, you are more at risk. You must stop your treatment and talk to your doctor.

Tell your doctor if you experience photosensitive skin reactions (such as rash after sun or UV exposure).

In case photosensitivity develops under treatment, it is recommended to discontinue it. If réadministration has been proven necessary, it is recommended to protect areas exposed to sunlight or artificial UVAs.

You must tell your doctor if you think you are (or might become) pregnant. CARDIURINE 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 breastfeeding”). Medicinal products containing lithium should not be taken with CARDIURINE without medicinal advice.

If you develop one of the following, contact your doctor immediately:

- . Swelling of the arms, legs, ankles, face, lips, tongue and/or throat with difficulty swallowing or breathing,
- . Any sign of infection (such as sore throat or fever) not readily responding to the usual treatment,
- . Severe dizziness or fainting,
- . Severe abdominal pain,
- . Unusually fast or irregular heartbeat,
- . Jaundice (yellow skin/eyes),
- . Any sudden, unexplained rash or burning, red or peeling skin.

Please inform following persons that you take CARDIURINE

- . the medical staff, especially the anaesthetist (if you are having an operation) if you are hospitalised.
- . your dentist before you have an anaesthetic for a dental procedure.

If you are taking CARDIURINE for the first time you may feel light-headed or dizzy for a short time and it may help to sit or lie down. This is unlikely to happen when you are taking the tablets regularly. If you are worried, contact your doctor.

Children and adolescents

CARDIURINE should not be given to children and adolescents (< 18 years old).

Other medicines and CARDIURINE

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicinal products, including medicinal products obtained without a prescription. These include medicines for a cold, cough, hay fever or sinus problems as these may increase your blood pressure.

Your doctor may need to modify your medication doses and/or take other precautions.

If you take angiotensin II receptor blocker or aliskiren see also information in section “Do not take CARIURINE” and “Warnings and precautions”.

This applies in particular if you are also taking:

- . some pain-killers which are also called 'anti-inflammatories' (e.g. indomethacin, ibuprofen),
- . salicylic acid (if you take more than 1 g per intake and/or 3 g daily) (pain and inflammation relief medicine),
- . lithium (for the treatment of mental disorders),
- . carbenoxolone (for the treatment of gastrointestinal ulcers),
- . corticosteroids, corticotrophin (ACTH),
- . some laxatives,
- . antifungal (amphotericin injectable),
- . muscle relaxants (given at the time of surgery),
- . colestyramine resin, colestipol (for lowering blood cholesterol),
- . allopurinol (for gout treatment),
- . procainamide and digoxin or other cardiac glycosides (treatment for irregular pulse),
- . medication that can cause torsade de pointes (aggravated cardiac rhythm disorder),
- . cytostatic or immunosuppressive agents (e.g. azathioprine and cyclophosphamide),
- . sympathomimetics medication (used in cardiac or artery hypotension disorders),
- . calcium salts,
- . estramustine (chemotherapy medication),

- . amifostine (protective medicine used in cancer treatment),
- . alpha-blocker for high blood pressure or prostate hypertrophy,
- . gold (use to treat rheumatoid polyarthritis),
- . ciclosporin (transplantation medication to avoid graft rejection),
- . drugs that reduce blood pressure by widening of the blood vessels (e.g. minoxidil),
- . cardiac infarct treatment medicines,
- . carbamazepine (for the treatment of epilepsy),
- . any other potassium lowering medicines (medicines that can decrease potassium quantity in blood),
- . any other sodium lowering medicines (medicines that can decrease sodium quantity in blood),
- . drugs used in diabetes (insulin and oral antidiabetics such as sulphonyl ureas or gliptines),
- . iodinated contrast agents (products used for radiology imagery),
- . drugs used to treat psychotic conditions and some old antidepressants,
- . any other treatment for high blood pressure,
- . medicines used to prevent transplant rejection (sirolimus, everolimus and other medicines of the mTOR protein inhibitors as temsirolimus (for cancer treatment)). See section “Warnings and precautions”.
- . potassium supplements (including salt substitutes containing potassium), potassium sparing diuretics and any other medication that can increase potassium in your body (such as trimethoprim and co-trimoxazole), to treat infection caused by bacteria,
- . cyclosporin, immunosuppressant used to prevent organ transplant rejection, heparin blood thinner to avoid clot formation),
- . if you take NEP inhibitors, as sacubitril (available in fixed dose association with valsartan) and racecadotril: angioedema risk may be increased (sudden swelling under the skin in the throat region). See section “Warnings and precautions”.

CARDIURINE with food and drink

Not applicable.

Pregnancy and breast-feeding

If you are pregnant, breastfeeding, if you think you may be pregnant or planning to have a baby, ask your doctor 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 CARDIURINE before you become pregnant or as soon as you know you are pregnant and will advise you to take another medicine instead of CARDIURINE. CARDIURINE 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.

Breast-feeding

Tell your doctor if you are breast-feeding or about to start breast-feeding. Breast-feeding new-born babies (first few weeks after birth), and especially for premature babies, is not recommended whilst taking CARDIURINE. In the case of an older baby your doctor should advise you on the benefits and risks of taking CARDIURINE whilst breast-feeding, compared with other treatments.

Ask your doctor or your pharmacist for advice before taking any medicines.

Athletes

Hydrochlorothiazide contained in this medicine can induce a false positive result in anti-doping test.

Driving and using machines

Caution is necessary when driving or operating machinery if side effects occur such as light-headedness, dizziness or tiredness. This applies in particular at the start of the treatment, when the dosage is changed or if you have had any alcohol.

CARDIURINE contains lactose monohydrate (see “Content of the pack and other information”).

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

3. HOW TO TAKE CARDIURINE?

Always take CARDIURINE exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure how to take these tablets.

Your doctor has prescribed CARDIURINE since previous treatment for high blood pressure did not provide appropriate blood pressure reduction. Your doctor will inform you how to switch from the previous treatment to CARDIURINE.

Dosage:

The usual dose is 1 tablet CARDIURINE a day (corresponding to 50 mg captopril and 25 mg hydrochlorothiazide). The maximum daily dose of 1 tablet CARDIURINE should not be exceeded.

Method of administration:

CARDIURINE tablets are for oral use only.

The tablets should be swallowed with a sufficient amount of fluid (e.g. one glass of water). You can take CARDIURINE with or without food. You should try to take your daily dose at about the same time each day, preferably in the morning. It is important that you continue to take CARDIURINE until your doctor tells you otherwise.

Special populations:

If you suffer from moderate kidney disease, diabetes, or if you have less salt or water in your body, your doctor may prescribe a lower dose of CARDIURINE for you, such as 1/2 tablet CARDIURINE (corresponding to 25 mg captopril and 12.5 mg hydrochlorothiazide).

Elderly patients:

Your doctor may prescribe a lower dose of CARDIURINE for you, such as 1/2 tablet CARDIURINE (corresponding to 25 mg captopril and 12.5 mg hydrochlorothiazide).

If you have the impression that the effect of CARDIURINE is too strong or too weak, talk to your doctor or pharmacist.

If you take more CARDIURINE than you should:

If you have accidentally taken too many tablets, or a child has swallowed some, contact your doctor or pharmacist immediately. Take the empty container and any remaining tablets with you.

If you take more CARDIURINE than you should, you may experience the following effects: passing urine more frequently, a change in the levels of some components in your blood, a large drop in your blood pressure, a reduced awareness of yourself or of your surrounding (including coma), fits, a weakness in the muscles, an irregular or slower heartbeat or reduced kidney function.

If another person has taken too many tablets and has fainted, lay the person down with feet higher than the person's head.

If you forget to take CARDIURINE:

If you accidentally miss a daily dose, just take the next dose as prescribed. Do not take a double dose to make up for the missed tablet.

If you have any further questions about the use of this medicinal product, ask your doctor or pharmacist or nurse.

4. POSSIBLE SIDE EFFECTS

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Stop taking CARDIURINE and seek medical attention immediately if you experience any of the following:

- . swelling of the arms, legs, ankles, face, lips, tongue and/or throat with difficulty in swallowing or breathing, sore throat or fever,
- . dizziness or fainting,
- . severe abdominal pain,
- . unusual fast or irregular heartbeat,
- . jaundice (yellow skin/eyes),
- . sudden unexplained skin reactions such as rash, burning, red or peeling skin.

Below you will find separated side effects presented in order of decreasing seriousness that were observed with captopril and/or other ACE inhibitors and side effects that were observed with hydrochlorothiazide.

Following side effects were commonly observed (occurring in more than 1 in 100 but fewer than 1 in 10 patients) with captopril and other ACE inhibitors:

- . sleep disorders,
- . taste perversion, dizziness,
- . dry, irritating (non-productive) cough, breathing problems,
- . nausea, vomiting, gastric irritations, abdominal pain, diarrhoea, constipation, dry mouth, peptic ulcer,
- . skin disorders such as itching and rash, hair loss.

Following uncommon side effects were observed (occurring in more than 1 in 1000 but fewer than 1 in 100 patients) with captopril and other ACE inhibitors:

- . loss of appetite (anorexia),
- . headache, an abnormal sensation on your skin (such as a burning or prickle),
- . heart problems such as unusual fast or irregular heartbeat, chest pain (angina), feeling your heartbeat,
- . low blood pressure, impaired circulation in the fingers (Raynaud's syndrome), flushing or pale skin,
- . swelling of the hands, face, lips or tongue,
- . chest pain, tiredness, feeling unwell.

Following rare side effects were observed (occurring in less than 1 in 1000 but more than 1 in 10.000 patients) with captopril and other ACE inhibitors:

- . drowsiness,
- . mouth problems such as sore mouth and mouth ulcers,
- . allergic reaction in the gut causing severe abdominal pain (intestinal angioedema),
- . kidney problems, increased or decreased urination.

Following very rare side effects were observed (occurring in 1 or less in 10.000 patients including isolated reports) with captopril and other ACE inhibitors:

- . side effects affecting the blood and its components such as:
 - anaemia (reduced red blood cell count that may cause decrease in performance and tiredness),
 - lack of certain types of white blood cells which may cause infection, sore throat, fever or bleeding (neutropenia, agranulocytosis, pancytopenia),
 - a reduced ability of the blood to clot (thrombocytopenia) which may cause bleeding or bruising
- . confusion, depression,
- . stroke including cerebral vascular deficiency, fainting,
- . blurred vision,
- . heart attack,
- . chest problems including:
 - difficulty in breathing or wheezing,
 - a blocked or runny nose, a type of pneumonia, caused by changes in the blood or a condition which causes cough, fever, shortness of breath and wheezing,
- . swollen tongue, pancreatitis (inflammation of the pancreas which may cause a stomach ache),
- . impaired liver function, including jaundice which causes the skin and eyes to turn yellow, and inflammation of the liver (hepatitis),
- . severe skin reactions such as:
 - allergic reactions which cause the skin to itch and turn red (urticaria),
 - a severe rash all over the body (Stevens-Johnson-syndrome),
 - an allergic rash which causes pink-red patches which may have clear centres (erythema multiforme),
 - increased sensitivity of the skin to the sunlight,
 - a reddening of the skin (erythroderma),
 - a series of skin reactions which can cause fluid-filled patches to form (pemphigoid reactions),
 - a condition causing the skin to scale or peel (exfoliative dermatitis),
- . pains in the muscles and joints,
- . kidney problems,
- . impotence, swelling of the breasts in men,
- . fever,
- . changes in laboratory test values.

Following side effects that were observed with hydrochlorothiazide, the second active substance contained in CARDIURINE include:

- . swollen salivary glands,
- . side effects affecting the blood and its components which may cause:
 - decrease in performance,
 - tiredness,
 - infection,
 - sore throat or fever due to a lack of white blood cells,
 - a reduced ability for the blood to clot which may cause bleeding or bruising.
- . loss of appetite (anorexia), sugar in the urine, abnormal changes in your blood components such as sugar, uric acid (gout), sodium, potassium, high levels of cholesterol and other lipids in the blood,
- . restlessness, depression, sleep disorders,
- . abnormal skin feelings (pins and needles),
- . problems with the eyes and vision such as 'yellow vision' and blurred vision, decreasing in visual acuity and ocular pain [possible sign of fluid accumulation in the eye vascular layer (choroidal effusion) or acute angle-closure glaucoma],
- . dizziness,
- . low blood pressure, heart problems such as an irregular heartbeat,
- . circulation problems such as inflamed blood vessels including those in the skin and other organs (necrotising angiitis),
- . lung and breathing problems such as respiratory distress,
- . gastric irritation, diarrhoea, constipation, pancreatitis,
- . jaundice which causes the skin and eyes to turn yellow,
- . severe skin reactions such as:
 - sensitivity of the skin to light,
 - rash,
 - a condition that causes a characteristic red, blotchy, butterfly-shaped rash over the cheeks and nose (lupus and lupus-like reactions),
 - allergic reactions which cause the skin to itch and turn red (urticaria),
- . an over-reaction of the body's natural defence system (hypersensitivity reactions),
- . muscle spasm,
- . kidney problems,
- . fever, weakness.
- . skin and lip cancer (non melanoma skin cancer) – *unknown frequency*.

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. By reporting side effects, you can help provide more information on the safety of this medicine.

5. HOW TO STORE CARDIURINE?

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. The expiry date refers to the last day of that month.

Store below 30°C.

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 CARDIURINE contains

The active substances are: captopril and hydrochlorothiazide. Each tablet of CARDIURINE contains 50 mg captopril and 25 mg hydrochlorothiazide.

The other ingredients are: maize starch, lactose, microcrystalline cellulose, colloidal anhydrous silica, talc, magnesium stearate, croscarmellose sodium.

What CARDIURINE looks like and contents of the pack

CARDIURINE tablets are white, round; with a break line on one side. The tablet can be divided into equal halves.

CARDIURINE tablets are supplied in PVC/Aluminium foil blisters, in boxes containing 30 tablets.

CARDIURINE® is a trademark of Exphar s.a.

Exphar s.a.

Zoning Industriel de Nivelles Sud, zone II - Av. Thomas Edison 105 - 1402 Thines (Belgium)

Manufacturer

Gracure Pharmaceuticals Ltd.,

E-1105 Industrial area, Phase III, Bhiwadi (Raj) India.

This leaflet was last revised in 07/2021.