Package leaflet: Information for the user

COZAAR® 2.5 mg/ml powder and solvent for oral suspension

Losartan potassium

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, pharmacist, or nurse.
- This medicine has been prescribed for you. 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, pharmacist, or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What COZAAR is and what it is used for
2. What you need to know before you take COZAAR
3. How to take COZAAR
4. Possible side effects
5. How to store COZAAR
6. Contents of the pack and other information

1. What COZAAR is and what it is used for

Losartan (COZAAR) belongs to a group of medicines known as angiotensin-II receptor antagonists. Angiotensin-II is a substance produced in the body which binds to receptors in blood vessels, causing them to tighten. This results in an increase in blood pressure. Losartan prevents the binding of angiotensin-II to these receptors, causing the blood vessels to relax which in turn lowers the blood pressure. Losartan slows the decrease of kidney function in patients with high blood pressure and type 2 diabetes.

COZAAR is used
- to treat patients with high blood pressure (hypertension) in adults and in children and adolescents 6 – 18 years of age.
- to protect the kidney in hypertensive type 2 diabetic patients with laboratory evidence of impaired renal function and proteinuria ≥ 0.5 g per day (a condition in which urine contains an abnormal amount of protein).
- to treat patients with chronic heart failure when therapy with specific medicines called angiotensin-converting-enzyme inhibitors (ACE inhibitors, medicine used to lower high blood pressure) is not considered suitable by your doctor. If your heart failure has been stabilised with an ACE inhibitor you should not be switched to losartan.
- in patients with high blood pressure and a thickening of the left ventricle, COZAAR has been shown to decrease the risk of stroke ("LIFE indication").

2. What you need to know before you take COZAAR

Do not take COZAAR:
- if you are allergic to losartan or to any of the other ingredients of this medicine (listed in section 6),
- if you are more than 3 months pregnant (It is also better to avoid COZAAR in early pregnancy – see Pregnancy),
- if your liver function is severely impaired,

- if you have diabetes or impaired kidney function and you are treated with a blood pressure lowering medicine containing aliskiren.

Warnings and precautions
Talk to your doctor, pharmacist, or nurse before taking COZAAR.

You must tell your doctor if you think you are (or might become) pregnant. COZAAR 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).

It is important to tell your doctor before taking **COZAAR:**
- if you have had a history of angiooedema (swelling of the face, lips, throat, and/or tongue) (see also section 4 'Possible side effects'),
- if you suffer from excessive vomiting or diarrhoea leading to an extreme loss of fluid and/or salt in your body,
- if you receive diuretics (medicines that increase the amount of water that you pass out through your kidneys) or are under dietary salt restriction leading to an extreme loss of fluid and salt in your body (see section 3 'Dosage in special patient groups'),
- if you are known to have narrowing or blockage of the blood vessels leading to your kidneys or if you have received a kidney transplant recently,
- if your liver function is impaired (see sections 2 "Do not take COZAAR" and 3 'Dosage in special patient groups'),
- if you suffer from heart failure with or without renal impairment or concomitant severe life threatening cardiac arrhythmias. Special caution is necessary when you are treated with a ß-blocker concomitantly,
- if you have problems with your heart valves or heart muscle,
- if you suffer from coronary heart disease (caused by a reduced blood flow in the blood vessels of the heart) or from cerebrovascular disease (caused by a reduced blood circulation in the brain),
- if you suffer from primary hyperaldosteronism (a syndrome associated with increased secretion of the hormone aldosterone by the adrenal gland, caused by an abnormality within the gland),
- if you are taking any of the following medicines used to treat high blood pressure:
    - an ACE-inhibitor (for example enalapril, lisinopril, ramipril), 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 COZAAR**".

Children and adolescents
COZAAR has been studied in children. For more information, talk to your doctor.

COZAAR is not recommended for use in children suffering from kidney or liver problems, as limited data are available in these patient groups. COZAAR is not recommended for use in children under 6 years old, as it has not been shown to work in this age group.

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

Take particular care if you are taking the following medicines while under treatment with COZAAR:
- other blood pressure lowering medicines as they may additionally reduce your blood pressure. Blood pressure may also be lowered by one of the following drugs/ class of drugs: tricyclic antidepressants, antipsychotics, baclofene, amifostine,

- medicines which retain potassium or may increase potassium levels (e.g. potassium supplements, potassium-containing salt substitutes or potassium-sparing medicines such as certain diuretics [amiloride, triamteren, spironolactone] or heparin),
- non-steroidal anti-inflammatory drugs such as indomethacin, including cox-2-inhibitors (medicines that reduce inflammation, and can be used to help relieve pain), as they may reduce the blood pressure lowering effect of losartan.

Your doctor may need to change your dose and/or to take other precautions:
If you are taking an ACE-inhibitor or aliskiren (see also information under the headings "**Do not take COZAAR**" and "**Warnings and precautions**")

If your kidney function is impaired, the concomitant use of these medicines may lead to a worsening of the kidney function.

Lithium containing medicines should not be taken in combination with losartan without close supervision by your doctor. Special precautionary measures (e.g. blood tests) may be appropriate.

COZAAR with food and drink
COZAAR may be taken with or without food.

Pregnancy and breast-feeding
Pregnancy
You must tell your doctor if you think you are (or might become) pregnant. Your doctor will normally advise you to stop taking COZAAR before you become pregnant or as soon as you know you are pregnant and will advise you to take another medicine instead of COZAAR. COZAAR 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. COZAAR is not recommended for mothers who are breast-feeding, and your doctor may choose another treatment for you if you wish to breast-feed. Especially if your baby is a new-born, or born prematurely.

Ask your doctor or pharmacist for advice before taking this medicine.

Driving and using machines
No studies on the effects on the ability to drive and use machines have been performed.

COZAAR is unlikely to affect your ability to drive or use machines. However, as with many other medicines used to treat high blood pressure, losartan may cause dizziness or drowsiness in some people. If you experience dizziness or drowsiness, you should consult your doctor before attempting such activities.

COZAAR contains lactose and preservatives
COZAAR contains lactose monohydrate and sorbitol. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

COZAAR also contains methylhydroxybenzoate and propylhydroxybenzoate, which may cause allergic reactions (possibly delayed).

3. How to take COZAAR

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure. Your doctor will decide on the appropriate dose of COZAAR, depending on your condition and whether you are taking other medicines. It is important to continue taking COZAAR for as long as your doctor prescribes it in order to maintain smooth control of your blood pressure.

Adult patients with High Blood Pressure
Treatment usually starts with 50 mg losartan (20 ml of COZAAR suspension) once a day. The maximal blood pressure lowering effect should be reached 3-6 weeks after beginning treatment. - In some patients the dose may later be increased to 100 mg losartan (40 ml of COZAAR suspension) once daily.

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

Use in children and adolescents

Children below 6 years of age
COZAAR is not recommended for use in children under 6 years old, as it has not been shown to work in this age group.

Children aged 6-18 years old
The recommended starting dose in patients who weigh between 20 and 50 kg is 0.7 mg of losartan per kg of body weight administered once a day (up to 25 mg or 10 ml of COZAAR suspension). The doctor may increase the dose if blood pressure is not controlled.

Adult patients with high blood pressure and type 2 diabetes
Treatment usually starts with 50 mg losartan (20 ml of COZAAR suspension) once a day. The dose may later be increased to 100 mg losartan (40 ml of COZAAR suspension) once daily depending on your blood pressure response.

Losartan may be administered with other blood pressure lowering medicines (e.g. diuretics, calcium channel blockers, alpha- or beta-blockers, and centrally acting agents) as well as with insulin and other commonly used medicines that decrease the level of glucose in the blood (e.g. sulfonylureas, glitazones and glucosidase inhibitors).

Adult patients with Heart Failure
Treatment usually starts with 12.5 mg losartan (5 ml of COZAAR suspension) once a day. Generally, the dose should be increased weekly step-by-step (i.e., 12.5 mg daily during the first week, 25 mg daily during the second week, 50 mg daily during the third week, 100 mg daily during the fourth week, 150 mg daily during the fifth week) up to the maintenance dose as determined by your physician. A maximum dose of 150 mg losartan (60 ml of COZAAR suspension) once daily may be used.

In the treatment of heart failure, losartan is usually combined with a diuretic (medicine that increases the amount of water that you pass out through your kidneys) and/or digitalis (medicine that helps to make the heart stronger and more efficient) and/or a beta-blocker.

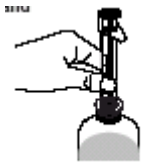
Dosage in special patient groups

The doctor may advise a lower dose, especially when starting treatment in certain patients such as those treated with diuretics in high doses, in patients with liver impairment, or in patients over the age of 75 years. The use of losartan is not recommended in patients with severe hepatic impairment (see section "Do not take COZAAR").

How to measure and give a dose of oral suspension

Always shake COZAAR oral suspension well before use!

1. Shake the bottle well before use.
2. Push the plunger of the syringe completely down.
3. Insert the syringe into the adaptor on the medicine bottle until a tight seal is made.



4. With the syringe, adaptor, and bottle attached, turn the entire assembly upside down.
5. Pull out the plunger to withdraw the medicine into the syringe.

6. Turn the whole thing to an upright position.
7. Remove the syringe and take the medicine.
8. Replace the screw cap onto the bottle.

If you take more COZAAR than you should
If you accidentally take too much COZAAR oral suspension, contact your doctor immediately. Symptoms of overdose are low blood pressure, increased heartbeat, possibly decreased heartbeat.

If you forget to take COZAAR
If you accidentally miss a daily dose, just take the next dose as normal. Do not take a double dose to make up for a forgotten dose. If you have any further questions on the use of this medicine, ask your doctor, pharmacist, or nurse.

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 losartan and tell your doctor immediately or go to the casualty department of your nearest hospital:

A severe allergic reaction (rash, itching, swelling of the face, lips, mouth or throat that may cause difficulty in swallowing or breathing).

This is a serious but rare side effect, which affects more than 1 out of 10,000 patients but fewer than 1 out of 1,000 patients. You may need urgent medical attention or hospitalisation.

The following side effects have been reported with COZAAR:

Common (may affect up to 1 in 10 people):
- dizziness,
- low blood pressure (especially after excessive loss of water from the body within blood vessels e.g. in patients with severe heart failure or under treatment with high dose diuretics),

- dose-related orthostatic effects such as lowering of blood pressure appearing when rising from a lying or sitting position,
- debility,
- fatigue,
- too little sugar in the blood (hypoglycaemia),
- too much potassium in the blood (hyperkalaemia),
- changes in kidney function including kidney failure,
- reduced number of red blood cells (anaemia),
- increase in blood urea, serum creatinine and serum potassium in patients with heart failure.

Uncommon (may affect up to 1 in 100 people):
- somnolence,
- headache,
- sleep disorders,
- feeling of increased heart rate (palpitations),
- severe chest pain (angina pectoris),
- shortness of breath (dyspnoea),
- abdominal pain,
- obstipation,
- diarrhoea,
- nausea,
- vomiting,
- hives (urticaria),
- itching (pruritus),
- rash,
- localised swelling (oedema),
- cough.

Rare (may affect up to 1 in 1,000 people):
- hypersensitivity,
- angiooedema,
- inflammation of blood vessels (vasculitis including Henoch-Schönlein purpura),
- numbness or tingling sensation (paraesthesia),
- fainting (syncope),
- very rapid and irregular heartbeat (atrial fibrillation)
- brain attack (stroke),
- inflammation of the liver (hepatitis),
- elevated blood alanine aminotransferase (ALT) levels, usually resolved upon discontinuation of treatment.

Not known (frequency cannot be estimated from the available data):
- reduced number of thrombocytes,
- migraine,
- liver function abnormalities,
- muscle and joint pain,
- flu-like symptoms,
- back pain and urinary tract infection,
- increased sensitivity to the sun (photosensitivity),
- unexplained muscle pain with dark (tea-colored) urine (rhabdomyolysis),
- impotence,
- inflammation of the pancreas (pancreatitis),
- low levels of sodium in the blood (hyponatraemia),
- depression,
- generally feeling unwell (malaise),

- ringing, buzzing, roaring, or clicking in the ears (tinnitus),
- disturbed taste (dysgeusia).

Side effects in children are similar to those seen in adults.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist, or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly (see details below). By reporting side effects you can help provide more information on the safety of this medicine.
United Kingdom: Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store
Ireland: HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; e-mail: medsafety@hpra.ie

5. How to store COZAAR

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

Kit: Do not store above 25°C. Store in the original container.
After reconstitution, store the liquid suspension in a refrigerator (at 2°C - 8°C) for up to 4 weeks.

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 COZAAR contains

The active substance is losartan potassium.
Each sachet contains 500 mg of losartan potassium powder. A medical or healthcare professional/pharmacist mixes each sachet with 200 ml of solvent to create a suspension. One ml of suspension contains 2.5 mg of losartan potassium.

The other ingredients are*:*

Powder
Microcrystalline cellulose (E460), Lactose monohydrate, Pregelatinized maize starch, Magnesium stearate (E572), Hydroxypropyl cellulose (E463), Hypromellose (E464) and titanium dioxide (E171)

Solvent
Microcrystalline cellulose (E460), carboxymethylcellulose sodium, citric acid anhydrous, purified water, xantham gum (E415), methylhydroxybenzoate (E218), sodium phosphate monobasic monohydrate, potassium sorbate, carrageenan calcium sulfate trisodium phosphate, flavor berry citrus sweet, glycerin, propylhydroxybenzoate (E216), sodium citrate anhydrous, saccharin sodium, sorbitol (E420)antifoam Af emulsion (contains water, polydimethylsiloxane, C-14-18, mono- and di-glycerides, polyethylene glycol stearate, and polyethylene glycol).

What COZAAR looks like and contents of the pack

COZAAR powder is a white to off-white powder. After suspension in solvent, COZAAR is an off-white liquid.

COZAAR powder and solvent for oral suspension is packaged in a kit containing:

- One foil sachet filled with powder equal to 500 mg losartan potassium
- One 473 ml bottle of solvent
- One 240 ml bottle with a child resistant closure for mixing the suspension
- One 10 ml oral dosing syringe
- One push-in bottle adaptor

Marketing Authorisation Holder and Manufacturer

MAH (UK): Merck Sharp & Dohme Limited, Hertford Road, Hoddesdon, Hertfordshire, EN11 9BU, UK.
MAH (Ireland): Merck Sharp & Dohme Ireland (Human Health) Ltd, Red Oak North, South County Business Park, Leopardstown, Dublin 18, Ireland.

Manufacturer: Merck Sharp & Dohme BV, Waarderweg 39, 2031 BN, Haarlem, Netherlands.

This medicinal product is authorized in the Member States of the EEA under the following names:

COZAAR	Belgium/Luxembourg, France, Iceland, Ireland, Netherlands, Norway, Portugal, United Kingdom
LORZAAR	Germany
LORTAAN 2,5 mg/ml polvere e solvente per sospensione orale	Italy

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The following information is intended for medical or healthcare professionals only:

Preparation of losartan potassium oral suspension [for 200 ml of a 2.5 mg/ml suspension]:
Add 200 ml of solvent to the 240 ml polyethylene terephthalate (PET) bottle provided. Before opening the sachet gently tap on the side of the sachet to facilitate transfer of the material. Carefully add the complete contents of the sachet into the PET container bottle containing the solvent, tapping the side of the sachet and inverting as necessary. It is normal to have a small amount of residual powder adhering to the interior surfaces of the sachet. The sachet should NOT be rinsed. Place the cap on the bottle and shake the contents well to disperse. After reconstitution, losartan suspension is an off-white liquid. Remove the cap, place the push-in bottle neck adaptor on the bottle, and re-cap the bottle. The suspension should be stored in a refrigerator at 2-8ºC for up to 4 weeks. Shake the suspension prior to each use and return promptly to the refrigerator.

Discard the excess solvent not used in the preparation of the suspension.