Package leaflet: Information for the patient

Co-Prenessa 2 mg/0.625 mg tablets
Co-Prenessa 4 mg/1.25 mg tablets
Co-Prenessa 8 mg/2.5 mg tablets
perindopril tert-butylamine/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 Co-Prenessa is and what it is used for

What are Co-Prenessa tablets?
Co-Prenessa is a combination of two active ingredients, perindopril and indapamide. Co-Prenessa is an anti-hypertensive medicine used in the treatment of high blood pressure (hypertension).

What Co-Prenessa tablets are used for?
Perindopril belongs to a class of medicines called angiotensin-converting enzyme inhibitors (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.

Co-Prenessa 8 mg/2.5 mg tablets
Co-Prenessa is indicated in patients already receiving separate tablets of 8 mg perindopril and indapamide 2.5 mg. These patients may instead take one tablet of Co-Prenessa which contains two active ingredients.

2. What you need to know before you take Co-Prenessa

Do not take Co-Prenessa:
- if you are allergic to perindopril or any other ACE inhibitor; or to indapamide or any other sulphonamides 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 severe liver disease or suffer from a condition called hepatic encephalopathy (a degenerative disease of the brain),

- if you have a severe kidney disease or 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, Co-Prenessa may not be suitable for you.
- if you have low or high blood potassium,
- if you are suspected of having untreated decompensated heart failure (symptoms can include severe water retention, difficulty in breathing),
- if you are more than 3 months pregnant. (It is also better to avoid Co-Prenessa in early pregnancy – see pregnancy section.),
- if you have diabetes or impaired kidney function and you are treated with a blood pressure lowering medicine containing aliskiren.
- if you have taken or are currently taking sacubitril/valsartan, a medicine used to treat a type of long-term (chronic) heart failure in adults, as the risk of angioedema (rapid swelling under the skin in an area such as the throat) is increased.

Only Co-Prenessa 8 mg/2.5 mg tablets
- if you have a moderate kidney disease.

Warnings and precautions
Talk to your doctor or pharmacist before taking Co-Prenessa tablets:
- 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 kidneys problems, or if you are receiving dialysis,
- 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 diuretics (spironolactone, triamterene) as their use with Co-Prenessa tablets should be avoided (see "Other medicines and Co-Prenessa"),
- 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 Co-Prenessa".
- if you are of black origin since you may have a higher risk of angioedema and this medicine 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 (rapid swelling under the skin in area such as the throat) is increased:

- racecadotril (used to treat diarrhea)
- sirolimus, everolimus, temsirolimus and other drugs belonging to the class of so-called mTor inhibitors (used to avoid rejection of transplanted organs and for cancer)
- linagliptin, saxagliptin, sitagliptin, vildagliptin and other drugs belonging to the class of the also called gliptins (used to treat diabetes).

Angioedema
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 Co-Prenessa. This may occur at any time during treatment. If you develop such symptoms, you should stop taking Co-Prenessa and see a doctor immediately. See also section 4.

A higher incidence of angioedema has been reported in black patients treated with ACE inhibitors than in non-black patients.

You must tell your doctor if you think that you are (or might become) pregnant. Co-Prenessa 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 and breast-feeding").

When you are taking Co-Prenessa tablets, 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 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 Co-Prenessa. 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. You should discontinue Co-Prenessa treatment and seek medical attention.

Athletes should be aware that Co-Prenessa tablets contain an active ingredient (indapamide), which may give a positive reaction in drug tests.

Children and adolescents
Co-Prenessa tablets should not be given to children and adolescents.

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

You should avoid taking Co-Prenessa tablets with:
- lithium (used to treat depression),
- aliskiren (medicine used to treat hypertension) if you have no diabetes mellitus or kidney problems,
- potassium supplements (including salt substitutes), potassium-sparing diuretics (spironolactone, triamterene), potassium salts, other drugs which can increase the amount of potassium in your body (such as heparin, a medicine used to thin blood to prevent clots; trimethoprim and co-trimoxazole also known as trimethoprim/sulfamethoxazole for infections caused by bacteria; ciclosporin, an immunosuppressant medicine used to prevent organ transplant rejection),
- estramustine (used in cancer therapy),
- other medicines used to treat high blood pressure: angiotensin-converting-enzyme inhibitors and

angiotensin receptor blockers.

Treatment with Co-Prenessa can be affected by other medicines. Make sure to tell your doctor if you are taking any of the following medicines as special care may be required:
- other medicines for treating high blood pressure including angiotensin II receptor blocker (ARB) or aliskiren (see also information under the headings “Do not take Co-Prenessa 2.5mg/0.625mg” 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,
- sacubitril/valsartan (used to treat long-term heart failure). See sections “Do not take Co-Prenessa” and “Warnings and precautions”.
- anaesthetic medicines,
- procainamide (for the treatment of an irregular heart beat),
- allopurinol (for the treatment of gout),
- terfenadine or astemizole, mizolastine (antihistamines for hay fever or allergies),
- 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),
- medicines for the treatment of cancer,
- erythromycin by injection, moxifloxacin, sparfloxacin (antibiotics),
- halofantrine (used to treat certain types of malaria),
- pentamidine (used to treat pneumonia),
- 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, 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),
- amphotericin B by injection (to treat severe fungal disease),
- medicines 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),
- vasodilators including nitrates (products that make the blood vessels become wider),
- injectable gold (used to treat rheumatoid polyarthritis),
- medicine, which is most often used to treat diarrhea (racecadotril),
- medicines, which are most often used to 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”,
- medicines used for the treatment of low blood pressure, shock or asthma (e.g. ephedrine, noradrenaline or adrenaline).

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 Co-Prenessa” and “Warnings and precautions”).

Co-Prenessa with food and drink
It is preferable to take Co-Prenessa tablets 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 you are (or might become) pregnant. Your doctor will normally advise you to stop taking Co-Prenessa before you become pregnant or as soon as you know you are pregnant and will advise you to take another medicine instead of Co-Prenessa. Co-Prenessa 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. Co-Prenessa is not recommended for mothers who are breast-feeding, and your doctor may choose another treatment for you if you wish to breast-feed.

Driving and using machines
Co-Prenessa tablets usually does not 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.

Co-Prenessa contains lactose and sodium
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.
This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

3. How to take Co-Prenessa

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 once a day.
Your doctor may decide to modify the dosage regimen if you suffer from renal impairment.
It is preferable to take your tablet in the morning and before a meal.
Swallow the tablet with a glass of water.

If you take more Co-Prenessa than you should
If you take too many tablets, contact your doctor or nearest hospital casualty department 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 the legs raised can help.

If you forget to take Co-Prenessa
It is important to take your medicine every day as regular treatment is more effective. However, if you forget to take a dose of Co-Prenessa tablets, 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 Co-Prenessa
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, toxic epidermal necrolysis) or other allergic reactions (Very rare) (may affect up to 1 in 10,000 people),
- Cardiovascular disorders (irregular heart beat, 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 heart 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).

The following side effects can include:

<u>Common (may affect up to 1 in 10 people):</u>

- hypersensitivity reactions, mainly 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, gastro-intestinal disorders (nausea, vomiting, abdominal pain, taste disturbances, dyspepsia or difficulty of digestion, diarrhoea, constipation, abnormally decreased appetite, dry mouth), allergic reactions (such as skin rashes, itching), muscle spasms, feeling of tiredness, low potassium in the blood.

<u>Uncommon (may affect up to 1 in 100 people):</u>

- mood swings, sleep disturbances, depression, purpura (red pinpoints on skin), blister cluster, kidney problems, impotence (inability to obtain or maintain an erection), erectile disfunction, 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 that may lead to dehydration and low blood pressure, somnolence, fainting, palpitations (awareness of your heartbeat), tachycardia (fast heartbeat), hypoglycaemia (very low blood sugar level) vasculitis (inflammation of blood vessels), photosensitivity reactions (increased sensitivity of the skin to sun), urticaria (hives), arthralgia (joint pain), myalgia (muscle pain), chest pain, malaise, oedema peripheral, fever, increased blood urea, increased blood creatinine, fall, hyperhidrosis,
- if you suffer from systemic lupus erythematosus (a type of collagen disease), this might get worse

Rare (may affect up to 1 in 1000 people)
- psoriasis worsening, changes in laboratory parameters: increased level of liver enzymes, high level of serum bilirubin, high level of calcium in the blood, low chloride in the blood, low magnesium in the blood, fatigue, decreased or absent urine output, flushing, 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), changes in blood values such as a lower number of white and red blood cells, lower haemoglobin and haematocrit, lower number of blood platelets, abnormal hepatic function.

Not known (frequency cannot be estimated from the available data):
– abnormal electrocardiogram values, 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).

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.
In cases of hepatic insufficiency (liver problems), there is a possibility of onset of hepatic encephalopathy (degenerative disease in the brain).

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

5. How to store Co-Prenessa

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 cardboard box and the blister. The expiry date refers to the last day of that month.

Co-Prenessa 2 mg/0.625 mg tablets
Co-Prenessa 4 mg/1.25 mg tablets
Do not store above 25 °C.
Store in the original package in order to protect from moisture.

Co-Prenessa 8 mg/2.5 mg tablets
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 Co-Prenessa contains
- The active substances are perindopril tert-butylamine and indapamide.

Co-Prenessa 2 mg/0.625 mg tablets
Each tablet contains 2 mg perindopril tert-butylamine equivalent to 1.67 mg perindopril and 0.625 mg indapamide.
Co-Prenessa 4 mg/1.25 mg tablets
Each tablet contains 4 mg perindopril tert-butylamine equivalent to 3.34 mg perindopril and 1.25 mg indapamide.
Co-Prenessa 8 mg/2.5 mg tablets
Each tablet contains 8 mg perindopril tert-butylamine equivalent to 6.68 mg perindopril and 2.5 mg indapamide.

- The other ingredients are calcium chloride hexahydrate, lactose monohydrate, crospovidone, microcrystalline cellulose, sodium hydrogen carbonate, colloidal hydrated silica, magnesium stearate. See section 2 “Co-Prenessa contains lactose and sodium”.

What Co-Prenessa looks like and contents of the pack
Co-Prenessa 2 mg/0.625 mg tablets
This medicinal product is presented as white to almost white, round, slightly biconvex tablets with bevelled edges, engraved with short line on one side.
Co-Prenessa 4 mg/1.25 mg tablets
This medicinal product is presented as white to almost white, round, slightly biconvex, one-side scored tablets with bevelled edges. The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.
Co-Prenessa 8 mg/2.5 mg tablets
This medicinal product is presented as white to almost white, round, slightly biconvex, one-side scored tablets. The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

These tablets are available in boxes of 14, 20, 28, 30, 50, 56, 60, 90, 100 tablets in blisters.

Not all pack sizes may be marketed.

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