PATIENT INFORMATION LEAFLET

ENAP CO

SCHEDULING STATUS

S3

ENAP-CO 20,0/12,5 mg tablets

Enalapril maleate and hydrochlorothiazide

ENAP-CO contains sugar (lactose monohydrate 122,16 mg)

Essentially 'sodium free'.

Read all of this leaflet carefully before you start taking ENAP-CO

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.
- ENAP-CO has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

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

1. What ENAP-CO is and what it is used for

ENAP-CO contains two active substances: enalapril maleate and hydrochlorothiazide and belongs to a group of medicines called antihypertensives (medicines that lower your blood pressure).

ENAP-CO is used to treat hypertension (high blood pressure). Your doctor will usually prescribe

ENAP-CO when your blood pressure has already been controlled after taking both the individual active ingredients of this medicine separately.

2. What you need to know before you take ENAP-CO

Do not take ENAP-CO:

- if you are hypersensitive (allergic) to enalapril, hydrochlorothiazide, or to any of the ingredients of ENAP-CO (see section 6)
- if you have previously been treated with medicines of the same type as ENAP-CO and have experienced allergic reactions with difficulties in breathing or swallowing, swelling of hands, feet or ankles, or if you or your family have had this reaction due to other reasons. You must never take these medicines, including ENAP-CO, again
- if you have hereditary angioedema (a condition that makes you more prone to the swelling described above)
- if you have an increase in the thickness of the heart muscle (known as hypertrophic cardiomyopathy)
- if you have severe kidney problems (e.g. you are not passing urine)
- if you have a narrowing of the blood vessels to both kidneys or to a single kidney
- if you have aortic stenosis, a narrowing of the aortic valve opening between the left ventricle (large pumping chamber of the heart) and the aorta (the main artery leading away from the heart)
- if you have liver problems or disease
- if you are already taking potassium sparing water tablets which contain eplerenone, spironolactone, triamterene or amiloride (used to treat fluid retention in patients with high blood pressure, heart, liver or kidney problems)
- if you have Addison’s disease (a disorder in which the adrenal glands situated on top of your kidney do not produce enough hormones)
- if you are taking lithium (used to treat depression or mood disorders)
- if you are taking aliskiren-containing products (to treat high blood pressure)

- if you have kidney problems and/or are elderly, and you are taking fluoroquinolones (type of antibiotic) such as ciprofloxacin or levofloxacin with ENAP-CO, contact your doctor to re-evaluate your treatment
- if you are being treated with sacubitril/valsartan, a medicine for heart failure
- if you have previously had or currently have cancer of the skin and/or lip
- if you are pregnant, think you may be pregnant, plan to become pregnant or are breastfeeding. A different medicine should be taken if you are planning a pregnancy
- if you suffer from porphyria (a rare blood disorder).

Warnings and precautions

Take special care with ENAP-CO:

Before you take ENAP-CO you must inform your pharmacist or doctor:

- if you are pregnant or think you may be pregnant. You must not take ENAP-CO (see Pregnancy and breastfeeding)
- if you have a history of angioedema (a severe allergic reaction) to medicines. The signs may be itching, rash, wheezing or swelling of your hands, throat, mouth or eyelids
- if you are taking either of the following medicines used to treat high blood pressure:
    - an angiotensin II receptor blocker (ARB) (also known as sartans – for example valsartan, telmisartan, irbesartan etc), in particular if you have diabetes-related kidney problems
    - aliskiren
- if you are about to undergo desensitization therapy due to allergy against bee or wasp stings
- if you are about to receive a treatment called low-density lipoprotein (LDL) apheresis, which removes cholesterol from your blood using a machine
- tell your doctor if you are taking an mammalian target of rapamycin (mTOR) inhibitor (e.g. temsirolimus, sirolimus, everolimus: medicines used to treat certain types of cancer or to

prevent the body's immune system from rejecting a transplanted organ), you may be at increased risk for an allergic reaction called angioedema

- if you suffer from low blood pressure. You may notice this as feeling dizzy or light-headed, especially when standing up
- if your body lacks salt due to a low salt diet, or you have recently lost a lot of body fluids through taking strong water tablets (diuretics), or due to vomiting or diarrhoea
- if you have heart problems
- if you have kidney problems, have recently had a kidney transplant or you are having kidney dialysis
- if you have fluid or electrolyte imbalances. The electrolyte imbalance must be corrected before you start treatment with ENAP-CO. Warning signs of fluid or electrolyte imbalance are dry mouth, thirst, weakness, tiredness, sleepiness, restlessness, muscle pain or cramps, muscle tiredness, low blood pressure, reduced frequency of urination, fast heartbeat, nausea and vomiting. Your doctor may want to monitor the different levels of salt or electrolytes in your blood, especially if you have kidney problems
- if you are taking fluoroquinolones (type of antibiotic) such as ciprofloxacin or levofloxacin with ENAP-CO, contact your doctor to re-evaluate your treatment
- if you are taking potassium supplements, potassium containing salt substitutes, or other medicines that may increase potassium in your blood (e.g. medicines used to prevent blood clots such as heparin, medicines used to treat infections such as trimethoprim, water tablets called potassium-sparing diuretics such as spironolactone, eplerenone, triamterene or amiloride)
- if you have liver problems
- if you are going to have surgery or be given an anaesthetic. You must tell your doctor before surgery that you take ENAP-CO since you may experience a sudden drop in blood pressure
- if you have diabetes or if you have gout, your need for insulin and other treatment against diabetes may be altered. You should monitor your blood for low blood glucose levels,

especially during the first month of treatment

- if you experience coughing
- if you have collagen vascular disease (a disease which affects the connective tissue which forms the support system for your body)
- if you are taking immunosuppressant therapy (used to treat rheumatoid arthritis or following transplant surgery)
- if you are taking allopurinol (used for the treatment of gout), or procainamide (used to treat abnormal heart rhythms)
- if you develop an infection (symptoms may be high temperature or fever), you should let your doctor know immediately. Your doctor may take a blood sample from time to time to check your white blood cell count
- if your ethnic group is black, as you may be at an increased risk of having an allergic reaction to ENAP-CO, this medicine may not work as well for you as for other ethnic groups
- if you have had skin cancer or if you develop an unexpected skin lesion (unusual growth of skin) during the treatment. Treatment with hydrochlorothiazide, particularly long-term use with high doses, may increase the risk of some types of skin and lip cancer (non-melanoma skin cancer). Protect your skin from sun exposure and UV rays while taking ENAP-CO
- if you are taking lithium, used for the treatment of some psychiatric illnesses
- 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 ENAP-CO. This can lead to permanent vision loss, if not treated. If you have had a penicillin or sulfonamide allergy, you can be at higher risk of developing this.

Routine tests

When you first start to take ENAP-CO, your doctor will monitor your blood pressure frequently to ensure you have been given the correct dose. In addition, for some patients the doctor may want to

do some tests to measure your potassium, sodium, magnesium, creatinine and liver enzyme levels. Your doctor may also check your kidney function.

Tell your doctor if you have or will take an anti-doping test since this medication can produce a positive result.

Children and adolescents

DO NOT give ENAP-CO to adolescents and children younger than 18 years as safety and efficacy have not been established.

Other medicines and ENAP-CO

Always tell your healthcare provider if you are taking any other medicine. (This includes complementary or traditional medicines.)

- other angiotensin-converting enzyme (ACE) inhibitors or aliskiren (used to treat high blood pressure) or angiotensin II receptor blockers (ARBs) also known as sartans e.g. valsartan, telmisartan, irbesartan, etc
- other medicines used to treat high blood pressure such as medicine containing aliskiren nitroglycerine, nitrates and vasodilators, as they may add to the blood pressure lowering effects of ENAP-CO and increase the frequency of side effects.
- lithium used to treat depression or mood disorders (see Do not take ENAP-CO)
- nonsteroidal anti-inflammatory drugs (NSAIDs) including aspirin (used to treat pain and inflammation)
- fluoroquinolones (type of antibiotic) such as ciprofloxacin or levofloxacin may lead to acute kidney injury, contact your doctor to re-evaluate your treatment
- potassium sparing water tablets (diuretics) such as eplerenone, spironolactone, triamterene or amiloride), potassium supplements or potassium-containing salt substitutes
- water tablets (diuretics) e.g. thiazides, furosemide, bumetanide
- tricyclic antidepressants used for depression, antipsychotics used for severe anxiety or

anaesthetics may further reduce your blood pressure

- medicines such as adrenaline (epinephrine), used in some cough and cold remedies or noradrenaline and adrenaline used for low blood pressure, shock, heart failure, asthma or allergies
- injectable gold (sodium aurothiomalate), an injectable medicine used to treat stiffness and inflammation in muscles, bones and joints
- medicines used to treat diabetes (e.g. insulin and metformin)
- allopurinol, probenecid or sulfinpyrazone (medicines used for the treatment of gout
- mammalian target of rapamycin inhibitors (e.g. temsirolimus, sirolimus, everolimus): medicine used to treat cancer or for the prevention of the rejection of an organ after an organ transplant. The risk of angioedema (swelling of the face, lips, tongue or throat with difficulty in swallowing or breathing) may be increased
- a medicine containing a neprilysin inhibitor such as sacubitril (available as fixed-dose combination with valsartan) and racecadotril. The risk of angioedema (swelling of the face, lips, tongue or throat, with difficulty in swallowing or breathing) may be increased
- co-trimoxazole, used to treat certain bacterial infections, such as pneumonia (a lung infection), bronchitis (infection of the tubes leading to the lungs), and infections of the urinary tract, ears, and intestines
- muscle relaxants (e.g. tubocurarine used to relax muscles during operations)
- barbiturates (sedatives used for sleepiness or epilepsy), alcohol or opioid analgesics (medicine used to treat pain e.g. tramadol, pethidine, codeine)
- cholestyramine and colestipol (used to help control cholesterol levels)
- quinidine, procainamide, amiodarone or sotalol (used to treat abnormal heart rhythms)
- digoxin (used to treat heart rhythm problems)
- corticosteroids (therapy for certain conditions such as rheumatism, arthritis, allergies, asthma or certain blood disorders)
- adrenocorticotropic hormone (ACTH) (to test whether your adrenal glands are working properly)

- carbenoxolone (used to treat stomach ulcers)
- excessive use of laxatives
- medicines for the treatment of cancer (e.g. methotrexate, cyclophosphamide)
- atropine (used during anaesthesia)
- biperiden (used alone or together with other medicines to treat Parkinson's disease)
- methyldopa (used to treat high blood pressure) due to the risk of a condition called haemolytic anaemia
- cyclosporin (used to prevent transplant rejection)
- carbamazepine (used to prevent and control seizures)
- medicines containing iodine that are given to patients to enhance the ability to see blood vessels and organs on medical images such as X-rays or computed tomography (CT) scans.

ENAP-CO with food and drink

ENAP-CO taken together with alcohol may cause dizziness or light-headedness.

ENAP-CO can be taken at any time of the day, with or without food.

Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding your baby, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare provider for advice before using ENAP-CO.

DO NOT take ENAP-CO if you are pregnant, plan to become pregnant, or think that you are pregnant. Contact your healthcare provider immediately.

DO NOT take ENAP-CO during breastfeeding.

Driving and using machines

Medicines which lower blood pressure may cause dizziness, drowsiness or blurred vision. Please make sure you know how ENAP-CO affects you before driving or using machinery.

It is not always possible to predict to what extent ENAP-CO may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which ENAP-CO affects them.

ENAP-CO contains lactose

ENAP-CO contains lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking ENAP-CO.

ENAP-CO contains sodium

ENAP-CO contains less than 1 mmol (23 mg) sodium per tablet, that is to say essentially ‘sodium-free’.

3. How to take ENAP-CO

Do not share medicines prescribed for you with any other person. Always take ENAP-CO exactly as your doctor has told you. You should check with your doctor or pharmacist if you are unsure.

Adults:

The usual dose is one tablet taken once a day. Your doctor may increase the dose to two tablets taken once a day.

Children:

ENAP-CO should not be given to children or adolescents under the age of 18 years.

In any patient with kidney problems ENAP- CO must not be used as initial therapy.

Your doctor will tell you how long your treatment with ENAP-CO will last. Do not stop treatment early because your high blood pressure may return.

If you have the impression that the effect of ENAP-CO is too strong or too weak, tell your doctor or pharmacist.

If you take more ENAP-CO than you should

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre.

Symptoms of overdose may include:

- stupor (a state of almost complete lack of consciousness), light-headedness or dizziness, very slow, fast or irregular heartbeat and pulse, anxiety, kidney failure, cough and shortness of breath.

If you forget to take ENAP-CO

If you forget to take ENAP-CO, take as soon as you remember on the same day. If you do not take a tablet that same day, take your normal dose the next day. Do not take a double dose to make up for forgotten individual doses.

If you stop taking ENAP-CO

This medicine helps control high blood pressure. You may have to take high blood pressure medicine for the rest of your life. If high blood pressure is not treated, it can cause serious problems such as heart failure, blood vessel disease, stroke or kidney disease.

4. Possible side effects

ENAP-CO can have side effects.

Not all side effects reported for ENAP-CO are included in this leaflet. Should your general health worsen, or if you experience any untoward effects while using ENAP-CO, please consult your

healthcare provider for advice.

If any of the following happens, stop using ENAP-CO and tell your doctor immediately or go to the casualty department at your nearest hospital:

- swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing
- rash or itching
- fainting.

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to ENAP-CO. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- changes to your heart function, signs of which may include the following: chest pain, irregular or rapid heart rate, heart attack or stroke (in high risk patients)
- inflammation of the liver (hepatitis) including death of liver tissue or failure of the liver, blockage of flow of bile from the liver (cholestasis) with symptoms such as severe pain in the stomach and back, nausea, vomiting and yellow pigmentation of skin and eyes (jaundice)
- inflammation of the pancreas (pancreatitis)
- Stevens-Johnson syndrome and toxic epidermal necrolysis (severe skin conditions with reddening, scaling and blistering of the skin)
- eruption of lesions on the skin or mouth known as erythema multiforme that have a pink-red centre surrounded by a pale ring border and an outer pink-red ring. The lesions can sometimes be painful or itchy
- severe allergic reaction that has numerous symptoms including skin rash, fever, increased sensitivity to sunlight, swelling of glands, inflammation of blood vessels (vasculitis) and of the tissues lining the lungs, heart and stomach (with symptoms such as pain in the stomach,

chest, joints or muscles) and abnormal blood results. This type of allergic reaction is known as drug rash with eosinophilia and systemic symptoms (DRESS)

- kidney problems such as lower back pain and reduction in the amount of urine which you pass, kidney failure
- inflammation of the lungs (allergic alveolitis or eosinophilic pneumonia) due to an allergic reaction causing excessive fluid accumulation in lungs (pulmonary infiltrates) with symptoms such as breathlessness, wheezing, cough, chest tightness and difficulty in breathing
- pemphigus, a skin disease in which watery blisters form on the skin
- macular eruption or 'butterfly rash' (erythema and oedema of cheeks, sparing nasolabial folds) lasting hours to days, as well as erythematous papular rash on arms, sometimes forming large plaques and spreading widely. This may be cutaneous lupus erythematosus
- blood disorders which can make the skin pale and cause breathlessness, weakness, bruising, increase the risk of bleeding or make infections more likely
- electrolyte imbalances, including low blood levels of sodium (hyponatraemia) or low or high levels of potassium (hyperkalaemia) in the blood which can cause tiredness, confusion, and fits (convulsion)
- skin and lip cancer (non-melanoma skin cancer), with abnormal growth of skin, bump or sores on the lips that persist for a long period of time.

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

Frequent side effects:

- increase in cholesterol and triglycerides in the body (body fats)
- dizziness, insomnia, headache, depression, changes in taste, numbness, tingling, pins and needles, cold, warmth, tingling pressure of the skin (paraesthesia), feeling light-headed, low blood pressure (which may make you feel dizzy when you stand up)
- blurred vision

- cough
- feeling or being sick, diarrhoea, change in taste, vomiting, abdominal pain
- muscle cramps
- feeling extremely tired or weak.

Less frequent side effects:

- you may feel unwell due to changes to the content of your blood; your doctor will usually detect these changes in a blood test
- increased blood sugar levels (hyperglycaemia), or decrease in blood sugar levels (hypoglycaemia) which could include symptoms such as thirst, increased urination, blurred vision, confusion, anxiety and shakiness, increased levels of uric acid in the blood that causes attacks of gout in some patients
- gout (a type of arthritis, which often starts in the big toe)
- decreased sex drive, impotence
- problems sleeping, pins and needles, headache, nervousness, sleepiness, vertigo (spinning sensation), confusion, abnormal dreams, restlessness
- ringing in the ears (tinnitus)
- low blood flow to your fingers and toes causing redness and pain (Raynaud's phenomenon)
- shortness of breath, difficulty breathing or asthma, accumulation of fluid or other substances in the lungs (seen on X-rays), runny or sore throat and hoarseness
- dry mouth, wind, indigestion, pain around your stomach area, constipation, swollen and tender stomach, changes in taste, inflammation of the tongue, a blockage in the intestine, pain, swelling or ulcers in the mouth, anorexia
- rash, excessive sweating, excessive itchiness or redness of your skin with loss of skin and hair or baldness (alopecia) small fluid-filled bumps on the skin, sensitivity of the skin to sunlight
- muscle or joint pain

- autoimmune diseases (diseases in which the body's immune system attacks healthy cells)
- swelling of the breast tissue in males (gynaecomastia)
- general feeling of discomfort, illness, or unease, fever
- confusion
- flushing
- gout (a type of arthritis, which often starts in the big toe).

The following side effects have been reported but the frequency for them to occur is not known:

- overproduction of antidiuretic hormone, which causes fluid retention, resulting in weakness, tiredness or confusion called syndrome of inappropriate antidiuretic hormone secretion (SIADH)
- infection of salivary glands (sialadenitis) with symptoms such as pain, tenderness, redness and swelling in the affected area
- yellow vision (xanthopsia)
- 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)
- presence of glucose in the urine (glycosuria) after a urine test

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on the SAHPRA website.

An email can be sent directly to the company, pharmacovigilance@pharmadynamics.co.za, to ensure safety of the product.

By reporting side effects, you can help provide more information on the safety of ENAP-CO.

5. How to store ENAP-CO

Store all medicines out of reach of children.

Store at or below 30 °C in a dry place.

Protect from light and moisture.

Keep blisters in carton until required for use.

Do not use after the expiry date stated on the carton.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What ENAP-CO contains:

The active ingredients are enalapril maleate and hydrochlorothiazide.

ENAP-CO contains enalapril maleate 20,0 mg and hydrochlorothiazide 12,5 mg.

The other ingredients are:

Lactose monohydrate, magnesium stearate, maize starch, pregelatinised starch, sodium hydrogen carbonate, talc.

What ENAP-CO looks like and contents of the pack

Round, white, flat tablets scored on one side with beveled edges.

ENAP-CO tablets are available in cold formed OPA/Al/PVC film and aluminium foil blisters of 30 tablets, packed into a printed outer carton.

Holder of Certificate of Registration

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