Austell Pharmaceuticals (Pty) Ltd, 491087-9, Acenten, Renlin, Enalapril HCTZ Austell, 20/12,5 mg, Tablets

Approved Patient Information Leaflet for Medicines for Human Use:

[PRODUCT NAME]

Please note: This application for registration is submitted as a triplicate and hence [PRODUCT NAME] is used in 1.3 to indicate the registered names as on the registration certificates:

Master (Proposed proprietary name)	**Duplicate 1 (Proposed proprietary name)**	**Duplicate 2 (Proposed proprietary name)**
ACENTEN 20/12,5	**RENLIN 20/12,5**	**ENALAPRIL HCTZ 20/12,5 AUSTELL**

SCHEDULING STATUS: S3

[PRODUCT NAME]

Enalapril Maleate 20 mg and Hydrochlorothiazide 12,5 mg Tablets

Contains sugar.

Each tablet contains lactose monohydrate 130,10 mg.

Read all of this leaflet carefully before you start taking [PRODUCT NAME].

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- [PRODUCT NAME] 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 [PRODUCT NAME] is and what it is used for

2. What you need to know before you take [PRODUCT NAME]

3. How to take [PRODUCT NAME]

4. Possible side effects

5. How to store [PRODUCT NAME]

6. Contents of the pack and other information

1. WHAT [PRODUCT NAME] is and what it is used for:

[PRODUCT NAME] contains a combination of enalapril maleate and hydrochlorothiazide:

• enalapril belongs to a group of medicines called angiotensin converting enzyme inhibitors (ACE inhibitors), which work by widening your blood vessels

• hydrochlorothiazide belongs to a group of medicines known as water tablets (diuretics), which increase the volume of urine you produce.

The effect of these medicines is to lower your blood pressure. [PRODUCT NAME] is used to treat high blood pressure (hypertension). Taking both medicines that [PRODUCT NAME] contains can increase their effect compared to taking just one.

2. What you need to know before you take [PRODUCT NAME]

Do not take [PRODUCT NAME]

- if you are allergic to enalapril maleate, hydrochlorothiazide or any of the other ingredients of this medicine (listed in section 6)
- if you have previously been treated with a medication in the same group of medicines as this medicine (ACE inhibitors) and have had allergic reactions with swelling of the face, lips, tongue and/or throat with difficulty in swallowing or breathing. You should not take this medicine if you have had these types of reactions without a known cause, or if you have been diagnosed with hereditary or idiopathic angioedema
- if you are allergic to any sulfonamide-derived medicines. (Ask your doctor if you are not sure what sulfonamide-derived medicines are.)

- if you are not passing urine
- if you have severe kidney problems
- if you have a condition known as renal artery stenosis (narrowing of the arteries that supply the blood to your kidneys)
- if you have a condition known as aortic stenosis (narrowing of the valve in the large artery in the heart)
- if you are taking other diuretics such as spironolactone, triamterene, amiloride
- if you have a condition known as porphyria (disorders resulting from an accumulation of certain chemicals associated with red blood cell proteins.)
- if you are on lithium therapy
- if you are pregnant or breastfeeding
- if you have diabetes or impaired kidney function and you are treated with a blood pressure lowering medicine containing aliskiren
- if you have severe liver problems
- if you are being treated with sacubitril/valsartan, a medicine for heart failure
- if you are being treated with fluoroquinolones (medicines used to treat infections).
- if you have previously had or currently have cancer of the skin and/or lip

Do not take this medicine if any of the above apply to you. If you are not sure, talk to your doctor or pharmacist before taking this medicine.

Warnings and precautions

Tell your doctor or health care provider before being given [PRODUCT NAME]:

- if you have kidney problems, have had a recent kidney transplantation, are a dialysis patient, or are taking water tablets (diuretics)
- if you have blood disorders or liver problems

- if you are on a salt restricted diet, or have suffered from excessive vomiting or diarrhoea recently
- if you have a heart condition called ‘aortic stenosis’, ‘hypertrophic cardiomyopathy’ or ‘outflow obstruction’
- if you have collagen vascular disease, are taking immunosuppressant therapy (used for the treatment of autoimmune disorders such as 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 you have a history of ‘angioedema’ while taking other medicines. The signs may have been itching, nettle rash, wheezing or swelling of your hands, throat, mouth or eyelids
- if you have diabetes and are taking antidiabetic medicines, including insulin to control your diabetes (you should monitor your blood for low blood glucose levels, especially during the first month of treatment)
- if you are taking potassium supplements, potassium containing salt substitutes, or other medicines that may increase potassium in your blood (e.g., heparin [a medicine used to prevent blood clots], trimethoprim-containing products such as cotrimoxazole [medicines used to treat infections])
- if you are taking lithium, used for the treatment of some psychiatric illnesses
- if you have been told by your doctor that you have an intolerance to some sugars
- if you think you are (or might become) pregnant (see pregnancy section)
- if you have 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 types of skin and lip cancer (non-melanoma skin cancer). Protect your skin from sun exposure and UV rays while taking [PRODUCT NAME]

- tell your doctor if you are taking an 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) or a medicine containing a neprilysin inhibitor such as sacubitril (available as fixed-dose combination with valsartan), used in patients with heart failure, and racecadotril, used in patients with acute diarrhoea. You may be at increased risk for an allergic reaction called angioedema
- tell your doctor 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
  - fluoroquinolone (medicine used to treat infections)
  - aliskiren.

Your doctor may check your kidney function, blood pressure, and the amount of electrolytes (e.g., potassium) in your blood at regular intervals.

See also information under the heading "Do not take [PRODUCT NAME]."

If you are about to have any of the following procedures, you should tell your doctor who is treating you that you are taking [PRODUCT NAME]:

- any surgery or receive anaesthetics (even at the dentist)
- a treatment called LDL apheresis, to remove cholesterol from your blood using a machine
- desensitisation treatment, to reduce the effect of an allergy to bee or wasp stings.

Routine tests

When you first start to take [PRODUCT NAME], 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.

Tell your doctor if you have taken or will need to take an anti-doping test, as this medicine can produce a positive result.

Children

[PRODUCT NAME] is not recommended for use in children.

Other medicines and [PRODUCT NAME]

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

This applies in particular if you are also taking:

- an angiotensin II-receptor blocker (ARB) or aliskiren (see also information under the headings “Do not take [PRODUCT NAME]” and “Warnings and precautions”)
- potassium sparing water tablets (diuretics) such as spironolactone, eplerenone, triamterene or amiloride, potassium supplements, potassium-containing salt substitutes or other medicines that may increase potassium in your blood (e.g., heparin [a medicine used to prevent blood clots], trimethoprim-containing products such as cotrimoxazole or fluoroquinolones [medicines used to treat infections]) [PRODUCT NAME] may increase the levels of potassium in your blood leading to high potassium levels. This causes few signs and is usually seen by a test

- water tablets (diuretics) such as thiazides, furosemide, bumetanide
- other medicines that lower blood pressure, such as nitroglycerin, nitrates, and vasodilators
- lithium, used for the treatment of some psychiatric illnesses. [PRODUCT NAME] should not be taken with this medicine
- barbiturates (sedatives used for sleeplessness or epilepsy)
- tricyclic antidepressants such as amitriptyline, used for depression, antipsychotics such as phenothiazines, used for severe anxiety
- pain killers such as morphine or anaesthetics, because your blood pressure may become too low
- cholestyramine or colestipol (used to help control cholesterol levels)
- medicines used for, stiffness and inflammation associated with painful conditions, particularly those affecting your muscles, bones and joints:

  -including gold therapy which can lead to flushing of your face, feeling sick (nausea), vomiting and low blood pressure, when taken with [PRODUCT NAME], and

  -non-steroidal anti-inflammatory drugs (NSAIDs), for example diflunisal or diclofenac. They may prevent your blood pressure from being well controlled and may increase the level of potassium in your blood
- medicines such as ephedrine, used in some cough and cold remedies, or norepinephrine (noradrenaline) and epinephrine (adrenaline) used for low blood pressure, shock, cardiac failure, asthma or allergies. If used with [PRODUCT NAME] these medicines may keep your blood pressure high
- ACTH (to test whether your adrenal glands are working properly)
- corticosteroids (used to treat certain conditions such as rheumatism, arthritis, allergic conditions, asthma or certain blood disorders)
- allopurinol (used to treat gout)

- ciclosporins (immunosuppressive agents used for autoimmune disorders)
- medicines for the treatment of cancer
- procainamide, amiodarone or sotalol (used to treat abnormal heart rhythms)
- digitalis (used to treat heart rhythm problems)
- carbenoxalone (used to treat stomach ulcers)
- excessive use of laxatives
- antidiabetic medicines such as insulin. [PRODUCT NAME] may cause your blood sugar levels to drop even further if you take it with antidiabetics
- a 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). See also information under the heading "Warnings and precautions"
- 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. See also information under the headings "Do not take [PRODUCT NAME]" and "Warnings and precautions".

If you are not sure if any of the above apply to you, talk to your doctor or pharmacist before taking [PRODUCT NAME].

[PRODUCT NAME] with food, drink and alcohol

Take [PRODUCT NAME] with a drink of water.

[PRODUCT NAME] can be taken with or without food. However, if you drink alcohol while taking [PRODUCT NAME], it may cause your blood pressure to drop too much and you may experience dizziness, light-headedness or faintness. You should keep your alcohol intake to a minimum.

Pregnancy and breastfeeding

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other health care provider for advice before taking this medicine.

Your doctor will normally advise you to stop taking [PRODUCT NAME] before you become pregnant or as soon as you know you are pregnant and will advise you to take another medicine instead of [PRODUCT NAME]. This medicine is not recommended during pregnancy (see Do not take [PRODUCT NAME]), as it may cause serious harm to your baby.

Breastfeeding

Tell your doctor if you are breastfeeding or about to start breastfeeding. [PRODUCT NAME] is not recommended for mothers who are breastfeeding (see Do not take [PRODUCT NAME]).

Driving and using machines

Side effects of this medicine include blurred vision, feeling dizzy, feeling drowsy, or confused (see Possible side effects). If this happens do not drive or use any tools or machines.

[PRODUCT NAME] contains lactose

[PRODUCT NAME] contains lactose, which is a type of sugar. If you have been told by your doctor that you have intolerance to some sugars, contact your doctor before taking this medicine.

3. How to take [PRODUCT NAME]

Do not share medicines prescribed for you with any other person.

Always take [PRODUCT NAME] exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.

The usual dose is one tablet taken once a day.

Use in children

[PRODUCT NAME] is not recommended for use in children.

Method of administration

[PRODUCT NAME] can be used with or without food.

The tablets should be swallowed whole with a drink of water.

If you take more [PRODUCT NAME] than you should

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

The most common signs and symptoms of an overdose are a fall in blood pressure and stupor (a state of almost complete lack of consciousness). Other symptoms may include dizziness or light-headedness due to a fall in blood pressure, forceful and rapid heartbeat, rapid pulse, anxiety, cough, kidney failure, and rapid breathing.

If you forget to take [PRODUCT NAME]

• If you forget to take a tablet, skip the missed dose.

• Take the next dose as usual.

• Do not take a double dose to make up for a forgotten dose

If you stop taking [PRODUCT NAME]

Do not stop taking your medicine, unless your doctor tells you to. If you do your blood pressure may increase. If your blood pressure becomes too high, it may affect your heart and kidneys.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

[PRODUCT NAME] can have side effects.

Not all side effects reported for [PRODUCT NAME] are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking [PRODUCT NAME], please consult your health care provider for advice.

If you think you may have any of the following side effects, stop taking [PRODUCT NAME] and contact your doctor or go to your nearest hospital emergency room immediately:

- allergic reaction - you may get a rash, short of breath or wheezy and develop
- swelling of your hands, mouth, throat, face or eyes
- severe hypersensitivity reaction with high fever, skin rash that looks like targets (erythema multiforme); severe skin conditions with reddening, scaling and blistering of the skin (Stevens Johnson syndrome and toxic epidermal necrolysis)
- liver failure or hepatitis. This may cause yellowing of your skin (jaundice).

These are all very serious side effects. If you have them, you may have had a serious reaction to [PRODUCT NAME]. 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:

- severe dizziness, light-headedness, especially at the start of treatment or when your dose is increased or when you stand up.

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:

- blurred vision, cough, feeling sick (nausea), weakness
- low blood pressure (which may make you feel dizzy or light-headed, especially if you stand up quickly)
- headache, depression, fainting (syncope)
- chest pain, heart rhythm changes, angina or chest pain, fast heart beat, shortness of breath
- diarrhoea, pain around your stomach area (abdomen), changes in taste, fluid
- retention (oedema), feeling tired
- rash, allergic reactions with swelling of the face, extremities, lips, tongue, and/or
- throat has been reported
- increased blood potassium level, increases in serum creatinine (both are usually detected by a test); low levels of potassium in the blood, increased levels of cholesterol, increased levels of triglycerides, increased levels of uric acid in the blood
- muscle cramps.

Less frequent side effects:

- decreased number of red blood cells and low haemoglobin (anaemia) a sense of heightened awareness or a shaky feeling (caused by low blood sugar), confusion, feeling sleepy, difficulty sleeping, feeling nervous, tingling or numbness, feeling like you are spinning (vertigo)
- fast or uneven heart beats (palpitations), heart attack or stroke (in high risk patients)
- runny nose, sore throat and hoarseness, difficulty breathing or asthma

- slow movement of food through your intestine (ileus), inflammation of the pancreas (pancreatitis), being sick, indigestion, constipation, not feeling like eating properly (anorexia), stomach irritation, dry mouth, flatulence, gout
- burning, aching pain with an empty feeling and hunger, particularly when the stomach is empty (caused by a peptic ulcer), increased sweating, itching, hives
- (urticaria), hair loss, protein in your urine (usually detected by a test)
- impotence, decreased libido, flushing, ringing in your ears, feeling lethargic, high temperature
- increases in blood urea and decreases in blood sodium levels (usually detected by a test), feeling unwell (malaise)
- low level of magnesium in the blood (hypomagnesaemia)
- kidney problems
- joint pain
- strange dreams, sleep problems
- changes in blood test values such as a lower number of white and red blood cells, lower haemoglobin, lower number of blood platelets, and/or swollen glands in neck, armpit or groin
- autoimmune diseases, low blood flow to your fingers and toes causing redness and pain (Raynaud's), accumulation of fluid or other substances in the lungs (as seen on X-rays), runny or sore nose
- eosinophilic pneumonia (signs may be cough, high temperature and difficulty breathing)
- pain, swelling or ulcers in your mouth, infection or pain and swelling of your tongue, kidney problems such as lower back pain and reduction in the volume of urine you pass
- inflammation of the nose
- difficulty breathing, shortness of breath

- liver failure or hepatitis, this may cause yellowing of your skin (jaundice), gall bladder problems
- severe hypersensitivity reaction with high fever, skin rash that looks like targets (erythema multiforme), Stevens-Johnson syndrome and toxic epidermal necrolysis (severe skin conditions with reddening, scaling and blistering of the skin), severe skin rash with loss of skin and hair (exfoliative dermatitis), cutaneous lupus erythematosus (an immune disease), red rash with peeling of the skin spots on the skin (purpura)
- development of breasts in men
- increased liver enzymes or blood 'bilirubin' (usually detected by a blood test)
- increases in blood sugar
- muscle weakness, sometimes due to low potassium (paresis)
- swelling in your intestine (intestinal angioedema). Signs may include stomach pain, feeling sick and vomiting, elevated calcium level in blood

Side effects with frequency unknown:

- infection of salivary glands (sialadenitis) with symptoms such as pain, tenderness, redness, swelling of the gland, fever and chills
- a complex side effect has also been reported which may include some or all of the following signs:
    - fever, inflammation of your blood vessels, pain and inflammation of muscles or joints
    - blood disorders affecting the components of your blood (usually detected by a blood test)
    - rash, hypersensitivity to sunlight and other effects on your skin
    - overproduction of antidiuretic hormone, which causes fluid retention, resulting in weakness, tiredness or confusion

    - skin and lip cancer (non-melanoma skin cancer).
- mineral (electrolyte) imbalances, low blood levels of sodium which can cause tiredness and confusion
- restlessness
- yellow vision
- 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 or pharmacist. You can also report side effects to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of [PRODUCT NAME].

5. HOW TO STORE [PRODUCT NAME]

Store all medicines out of reach of children

Store at or below 25 °C. Store in the original container.

Do not put this medicine into another container as it might get mixed up.

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 the month.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What [PRODUCT NAME] contains

Active ingredients: Each tablet contains 20 mg of enalapril maleate and 12,5 mg of hydrochlorothiazide.

The other ingredients are:

lactose monohydrate

pregelatinized starch

maleic acid

iron oxide yellow (E172)

dried maize starch

sodium stearyl fumarate.

What [PRODUCT NAME] looks like and contents of the pack

[PRODUCT NAME] is pale yellow in colour, approximately 8,5 mm, circular, biconvex uncoated tablet with a break line on one side side and plain on the other side. The break line is not intended for division of the tablet. The tablet should be swallowed whole.

[PRODUCT NAME] is available in Aluminium/Aluminium blisters and HDPE bottle packs:

Aluminium/Aluminium blisters

[PRODUCT NAME] is packed in Aluminium/Aluminium blisters of 10 tablets; the blisters are then packed in an outer carton containing 30 tablets.

HDPE bottle pack

[PRODUCT NAME] is packed in white opaque HDPE (High Density Polyethylene) containers with cap and liner.

Pack size: 100 tablets.

Austell Pharmaceuticals (Pty) Ltd, 491087-9, Acenten, Renlin, Enalapril HCTZ Austell, 20/12,5 mg, Tablets

Not all pack sizes may be marketed.

HOLDER OF CERTIFICATE OF REGISTRATION

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RENLIN 20/12,5: 49/7.1.3/1088

ENALAPRIL HCTZ 20/12,5 AUSTELL: 49/7.1.3/1089

Access to the corresponding Professional Information

Professional Information for this medicine is available on the following URL:

https://austell.co.za/product-info/

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