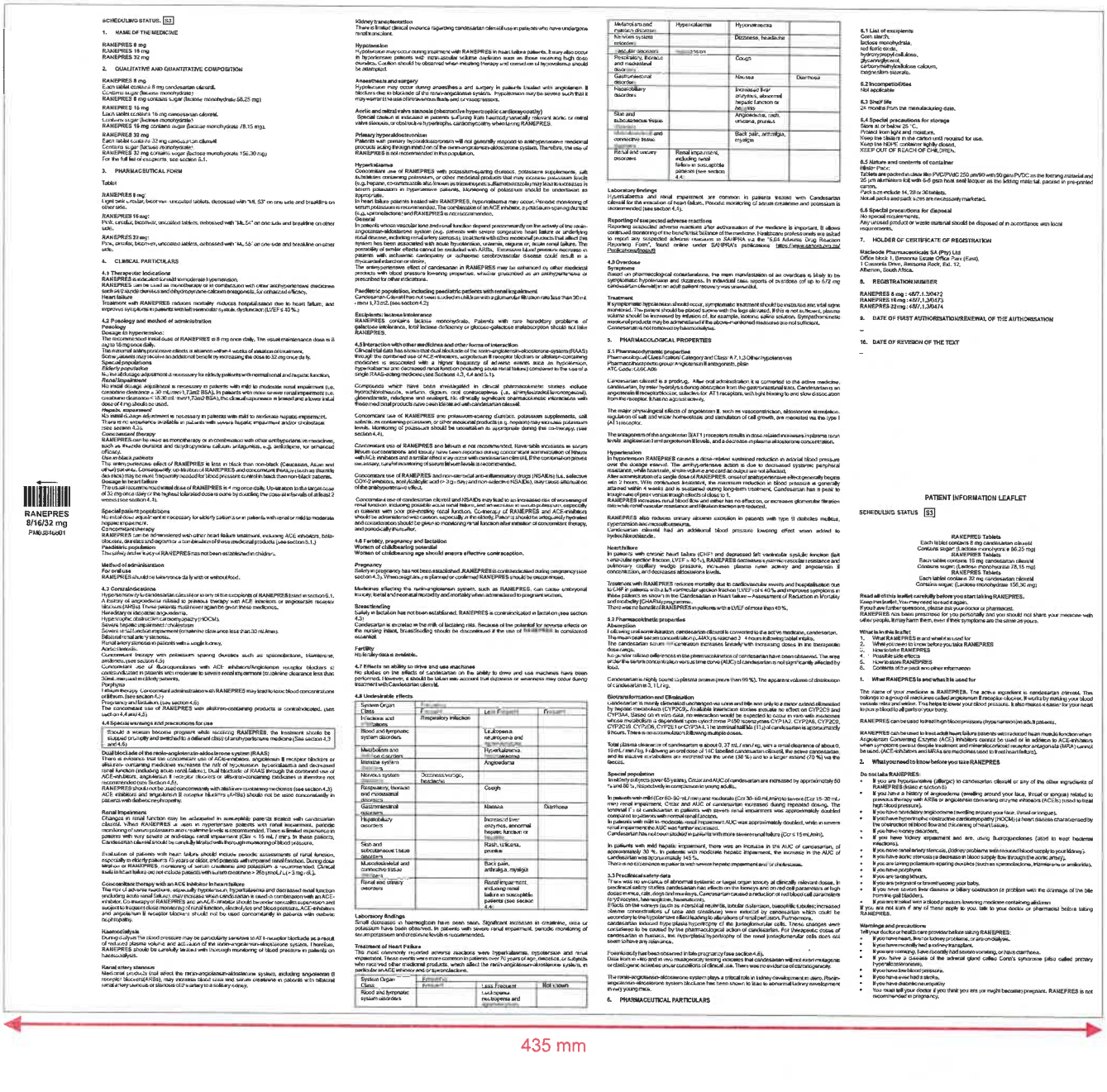
Front Side



SCHEDULING STATUS: S3

1. NAME OF THE MEDICINE

RANEPRES 8 mg
RANEPRES 16 mg
RANEPRES 32 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

RANEPRES 8 mg
Each tablet contains 8 mg candesartan cilexetil.
Contains sugar (lactose monohydrate)
RANEPRES 8 mg contains sugar (lactose monohydrate 68.25 mg)

RANEPRES 16 mg
Each tablet contains 16 mg candesartan cilexetil.
Contains sugar (lactose monohydrate)
RANEPRES 16 mg contains sugar (lactose monohydrate 78.15 mg).

RANEPRES 32 mg
Each tablet contains 32 mg candesartan cilexetil
Contains sugar (lactose monohydrate)
RANEPRES 32 mg contains sugar (lactose monohydrate 156.30 mg)
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet

RANEPRES 8 mg:
Light pink, circular, biconvex, uncoated tablets, debossed with "ML 53" on one side and breakline on other side.

RANEPRES 16 mg:
Pink, circular, biconvex, uncoated tablets, debossed with "ML 54" on one side and breakline on other side.

RANEPRES 32 mg:
Pink, circular, biconvex, uncoated tablets, debossed with "ML 55" on one side and breakline on other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications
Posology
Dosage in hypertension:
The recommended initial dose of RANEPRES is 8 mg once daily. The usual maintenance dose is 8 mg to 16 mg once daily.
The maximal antihypertensive effects is attained within 4 weeks of initiation of treatment.
Some patients may receive an additional benefit by increasing the dose to 32 mg once daily.
Special populations
Elderly population
No the dosage adjustment is necessary for elderly patients with normal renal and hepatic function.
Renal Impairment
No initial dosage adjustment is necessary in patients with mild to moderate renal impairment (i.e. creatinine clearance > 30 mL/min/1.73m2 BSA). In patients with more severe renal impairment (i.e. creatinine clearance < 30 mL/ min/1.73m2 BSA), the clinical experience is limited and a lower initial dose of 4 mg should be used.
Hepatic impairment
No initial dosage adjustment is necessary in patients with mild to moderate hepatic impairment. There is no experience available in patients with severe hepatic impairment and/or cholestasis (see section 4.3.).
Concomitant therapy
RANEPRES can be used as monotherapy or in combination with other antihypertensive medicines, such as thiazide diuretics and dihydropyridine calcium antagonists, e.g. amlodipine, for enhanced efficacy.
Use in black patients
The antihypertensive effect of RANEPRES is less in black than non-black (Caucasian, Asian and other) patients. Consequently, titration of RANEPRES and concomitant therapy (such as thiazide diuretics) may more frequently needed for blood pressure control in black than non-black patients.
Dosage in heart failure
The usual recommended initial dose of RANEPRES is 4 mg once daily. Up-titration to the target dose of 32 mg once daily or the highest tolerated dose is done by doubling the dose at intervals of at least 2 weeks (see section 4.4).

Special patient populations
No initial dose adjustment is necessary for elderly patients or patients with renal or mild to moderate hepatic impairment.
Concomitant therapy
RANEPRES can be administered with other heart failure treatment, including ACE inhibitors, beta-blockers, diuretics and digoxin or a combination of these medicinal products (see section 5.1.)
Paediatric population
The safety and efficacy of RANEPRES has not been established in children.

Method of administration
For oral use.
RANEPRES should be taken once daily with or without food.

4.3 Contraindications
Hypersensitivity to candesartan cilexetil or any of the excipients of RANEPRES listed in section 6.1.
A history of angioedema related to previous therapy with ACE inhibitors or angiotensin receptor blockers (ARBs). These potentially may occur regardless of the class medicines.
Hereditary or idiopathic angioedema.
Hypertrophic obstructive cardiomyopathy (HOCM).
Severe hepatic impairment/ cholestasis.
Severe renal function impairment (creatinine clearance less than 30 mL/min).
Bilateral renal artery stenosis.
Renal artery stenosis in patients with a single kidney.
Aortic stenosis.
Concomitant therapy with potassium sparing diuretics such as spironolactone, triamterene, amiloride, (see section 4.5).
Concomitant use of Sacubitril/valsartan with ACE inhibitors/Angiotensin receptor blockers or diabetes-containing medicines increases the risk of hypotension, hyperkalaemia and decreased renal function (including acute renal failure). Dual blockade of RAAS through the combined use of ACE-inhibitors, angiotensin II receptor blockers or diabetes-containing medicines is therefore not recommended (see Section 4.5).
RANEPRES should not be used concomitantly with diabetes-containing medicines (see section 4.3).
ACE inhibitors and angiotensin II receptor blockers (ARBs) should not be used concomitantly in patients with diabetic nephropathy.

Renal Impairment
Changes in renal function may be enhanced in susceptible patients treated with candesartan cilexetil. When RANEPRES is used in hypertensive patients with renal impairment, periodic monitoring of serum potassium and creatinine levels is recommended. There is limited experience in patients with very severe or end-stage renal impairment (Clcr < 15 mL / min). In these patients, Candesartan cilexetil should be carefully titrated with thorough monitoring of blood pressure.

Evaluation of patients with heart failure should include periodic assessments of renal function, especially in elderly patients 75 years or older, and patients with impaired renal function. During dose titration of RANEPRES, monitoring of serum creatinine and potassium is recommended. Clinical trials in heart failure did not include patients with serum creatinine > 265 µmol/L (> 3 mg /dL).

Concomitant therapy with an ACE inhibitor in heart failure
The risk of adverse reactions, especially hypotension, hyperkalaemia and decreased renal function (including acute renal failure) may increase when candesartan is used in combination with an ACE-inhibitor. Co-therapy of RANEPRES and an ACE-inhibitor should be under specialists supervision and subjected to frequent clinical monitoring of renal function, electrolytes and blood pressure. ACE-inhibitors and angiotensin II receptor blockers should not be used concomitantly in patients with diabetic nephropathy.

Haemodialysis
During dialysis the blood pressure may be particularly sensitive to AT-1 receptor blockade as a result of reduced plasma volume and activation of the renin-angiotensin-aldosterone system. Therefore, RANEPRES should be carefully titrated with thorough monitoring of blood pressure in patients on haemodialysis.

Renal artery stenosis
Medicinal products that affect the renin-angiotensin-aldosterone system, including angiotensin II receptor blocker(ARBs), may increase blood urea and serum creatinine in patients with bilateral renal artery stenosis or stenosis of the artery to a solitary kidney.

Kidney transplantation
There is limited clinical evidence regarding candesartan cilexetil use in patients who have undergone renal transplant.

Hypotension
Hypotension may occur during treatment with RANEPRES in heart failure patients. It may also occur in hypertensive patients with intravascular volume depletion such as those receiving high dose diuretics. Caution should be observed when initiating therapy and correction of hypovolaemia should be attempted.

Anaesthesia and surgery
Hypotension may occur during anaesthesia and surgery in patients treated with angiotensin II blockers due to blockade of the renin-angiotensin system. Hypotension may be severe such that it may warrant the use of intravenous fluids and/or vasopressors.

Aortic and mitral valve stenosis (obstructive hypertrophic cardiomyopathy)
Special caution is indicated in patients suffering from haemodynamically relevant aortic or mitral valve stenosis, or obstructive hypertrophic cardiomyopathy when taking RANEPRES.

Primary hyperaldosteronism
Patients with primary hyperaldosteronism will not generally respond to antihypertensive medicinal products acting through inhibition of the renin-angiotensin-aldosterone system. Therefore, the use of RANEPRES is not recommended in this population.

Hyperkalaemia
Concomitant use of RANEPRES with potassium-sparing diuretics, potassium supplements, salt substitutes containing potassium, or other medicinal products that may increase potassium levels (e.g. heparin, co-trimoxazole also known as trimethoprim/sulfamethoxazole) may lead to increases in serum potassium in hypertensive patients. Monitoring of potassium should be undertaken as appropriate.
In heart failure patients treated with RANEPRES, hyperkalaemia may occur. Periodic monitoring of serum potassium is recommended. The combination of an ACE inhibitor, a potassium-sparing diuretic (e.g., spironolactone) and RANEPRES is not recommended.
General
In patients whose vascular tone and renal function depend predominantly on the activity of the renin-angiotensin-aldosterone system (e.g., patients with severe congestive heart failure or underlying renal disease, including renal artery stenosis), treatment with other medicinal products that affect this system has been associated with acute hypotension, uraemia, oliguria or, acute renal failure. The possibility of similar effects cannot be excluded with ARBs. Excessive blood pressure decrease in patients with ischaemic cardiopathy or ischaemic cerebrovascular disease could result in a thromboembolic event or stroke.
The antihypertensive effect of candesartan in RANEPRES may be enhanced by other medicinal products with blood pressure-lowering properties, whether prescribed as an antihypertensive or prescribed for other indications.

Paediatric population, including paediatric patients with renal impairment
Candesartan cilexetil has not been studied in children with a glomerular filtration rate less than 30 mL / min / 1.73 m2. (see section 4.2)

Excipients: lactose intolerance
RANEPRES contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take RANEPRES.

4.5 Interaction with other medicines and other forms of interaction
Clinical trial data has shown that dual blockade of the renin-angiotensin-aldosterone-system (RAAS) through the combined use of ACE-inhibitors, angiotensin II receptor blockers or aliskiren-containing medicines is associated with a higher frequency of adverse events such as hypotension, hyperkalaemia and decreased renal function (including acute renal failure) compared to the use of a single RAAS-acting medicines (see Subclause 4.3, 4.4 and 5.1).

Compounds which have been investigated in clinical pharmacokinetic studies include hydrochlorothiazide, warfarin, digoxin, oral contraceptives (i.e., ethinylestradiol/levonorgestrel), glibenclamide, nifedipine and enalapril. No clinically significant pharmacokinetic interactions with these medicinal products have been observed and with candesartan cilexetil.

Concomitant use of RANEPRES and potassium-sparing diuretics, potassium supplements, salt substitutes containing potassium, or other medicinal products (e.g., heparin) may increase potassium levels. Monitoring of potassium should be undertaken as appropriate during this co-therapy. (see section 4.4).

Concomitant use of RANEPRES and lithium is not recommended. Reversible increases in serum lithium concentrations and toxicity have been reported during concomitant administration of lithium with ACE inhibitors and a similar effect may occur with candesartan cilexetil. If the combination proves necessary, careful monitoring of serum lithium levels is recommended.

Concomitant use of RANEPRES and non-steroidal anti-inflammatory drugs (NSAIDs) (i.e., selective COX-2 inhibitors, acetylsalicylic acid (> 3 g / day) and non-selective NSAIDs), may cause attenuation of the antihypertensive effect.

Concomitant use of candesartan cilexetil and NSAIDs may lead to an increased risk of worsening of renal function, including possible acute renal failure, and an increase in serum potassium, especially in patients with poor (pre-existing) renal function. Co-therapy of RANEPRES and ACE-inhibitors should be administered with caution, especially in the elderly. Patients should be adequately hydrated and consideration should be given to monitoring renal function after initiation of concomitant therapy, and periodically thereafter.

4.6 Fertility, pregnancy and lactation
Women of childbearing potential
Women of childbearing age should ensure effective contraception.

Pregnancy
Safety in pregnancy has not been established. RANEPRES is contraindicated during pregnancy (see section 4.3). When pregnancy is planned or confirmed RANEPRES should be discontinued.

Medicines affecting the renin-angiotensin system, such as RANEPRES, can cause embryonal toxicity (renal and neonatal mortality and mortality when administered to pregnant women.

Breastfeeding
Safety in lactation has not been established. RANEPRES is contraindicated in lactation (see section 4.3)
Candesartan is excreted in the milk of lactating rats. Because of the potential for adverse effects on the nursing infant, breastfeeding should be discontinued if the use of RANEPRES is considered essential.

Fertility
No fertility data is available.

4.7 Effects on ability to drive and use machines
No studies on the effects of candesartan on the ability to drive and use machines have been performed. However, it should be taken into account that dizziness or weariness may occur during treatment with candesartan cilexetil.

4.8 Undesirable effects

System Organ Class	Frequency		
	Less Frequent	Less Frequent	Frequent
Infections and infestations	Respiratory infection		
Blood and lymphatic system disorders		Leukopenia, neutropenia and agranulocytosis	
Metabolism and nutrition disorders		Hyperkalaemia, hyponatraemia	
Immune system disorders		Angioedema	
Nervous system disorders	Dizziness, vertigo, headache		
Respiratory, thoracic and mediastinal disorders		Cough	
Gastrointestinal disorders		Nausea	Diarrhoea
Hepatobiliary disorders		Increased liver enzymes, abnormal hepatic function or hepatitis	
Skin and subcutaneous tissue disorders		Rash, urticaria, pruritus	
Musculoskeletal and connective tissue disorders		Back pain, arthralgia, myalgia	
Renal and urinary disorders		Renal impairment, including renal failure in susceptible patients (see section 4.4)	

Laboratory findings
Small decreases in haemoglobin have been seen. Significant increases in creatinine, urea or potassium have been observed in patients with severe renal impairment. Periodic monitoring of serum potassium and creatinine levels is recommended.

Treatment of Heart Failure
The most commonly reported adverse reactions were hyperkalaemia, hypotension and renal impairment. These events were more common in patients over 70 years of age, females, or subjects who received other medicinal products, which affect the renin-angiotensin-aldosterone system, in particular an ACE inhibitor and or spironolactone.

System Organ Class	Frequency		
	Frequent	Less Frequent	Not known
Blood and lymphatic system disorders		Leukopenia, neutropenia and agranulocytosis	
Metabolism and nutrition disorders	Hyperkalaemia	Hyponatraemia	
Nervous system disorders		Dizziness, headache	
Vascular disorders	Hypotension		
Respiratory, thoracic and mediastinal disorders		Cough	
Gastrointestinal disorders		Nausea	Diarrhoea
Hepatobiliary disorders		Increased liver enzymes, abnormal hepatic function or hepatitis	
Skin and subcutaneous tissue disorders		Angioedema, rash, erythema, pruritus	
Musculoskeletal and connective tissue disorders		Back pain, arthralgia, myalgia	
Renal and urinary disorders	Renal impairment, including renal failure in susceptible patients (see section 4.4)		

Laboratory findings
Hyperkalaemia and renal impairment are common in patients treated with Candesartan cilexetil for the indication of heart failure. Periodic monitoring of serum creatinine and potassium is recommended (see section 4.4).

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions at SAHPRA via the "Side Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose
Symptoms
Based on pharmacological considerations, the main manifestation of an overdose is likely to be symptomatic hypotension and dizziness. In individual case reports of an intake of up to 672 mg candesartan cilexetil in an adult patient recovery was uneventful.

Treatment
If symptomatic hypotension should occur, symptomatic treatment should be instituted and vital signs monitored. The patient should be placed supine with the legs elevated. If this is not sufficient, plasma volume should be increased by infusion of, for example, isotonic saline solution. Sympathomimetic medicinal products may be administered if the above-mentioned measures are not sufficient.
Candesartan is not removed by haemodialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Pharmacotherapeutic Group: Cardiac Therapy
Pharmacotherapeutic group: Angiotensin II antagonists, plain
ATC Code: C09CA06

Candesartan cilexetil is a prodrug. After oral administration it is converted to the active medicine, candesartan, by ester hydrolysis during absorption from the gastrointestinal tract. Candesartan an angiotensin II receptor blocker, selective for AT1 receptors, with high binding to and slow dissociation from the receptor. It has no agonist activity.

The major physiological effects of angiotensin II, such as vasoconstriction, aldosterone stimulation, regulation of salt and water homeostasis and stimulation of cell growth, are mediated via the type I (AT1) receptor.

The antagonism of the angiotensin (AT1) receptors results in dose-related increases in plasma renin levels, angiotensin I and angiotensin II levels, and a decrease in plasma aldosterone concentration.

Hypertension
In hypertension RANEPRES causes a dose-related sustained reduction in arterial blood pressure over the dosage interval. The antihypertensive action is due to decreased systemic peripheral resistance, while total renal, stroke volume and cardiac output are not affected.
After administration of a single dose of RANEPRES onset of antihypertensive effect generally begins within 2 hours. With continued treatment, the maximum reduction in blood pressure is generally attained within 4 weeks and is sustained during long-term treatment. Candesartan has a peak to trough ratio of peak versus trough effects of close to 1.
RANEPRES increases renal blood flow and either has no effect on, or increases glomerular filtration rate while renal vascular resistance and filtration fraction are reduced.

RANEPRES also reduces urinary albumin excretion in patients with type II diabetes mellitus, hypertension and microalbuminuria.
Candesartan cilexetil had an additional blood pressure lowering effect when added to hydrochlorothiazide.

Heart failure
In patients with chronic heart failure (CHF) and depressed left ventricular systolic function (left ventricular ejection fraction, LVEF ≤ 40 %), RANEPRES decreases systemic vascular resistance and pulmonary capillary wedge pressure, increases plasma renin activity and angiotensin II concentration, and decreases aldosterone levels.

Treatment with RANEPRES reduces mortality due to cardiovascular events and hospitalisation due to CHF in patients with a left ventricular ejection fraction (LVEF) of ≤ 40 % and improved symptoms in these patients as shown in the Candesartan in Heart failure – Assessment of Reduction in Mortality and morbidity (CHARM) programme.
Three trials have been performed in patients with a LVEF of more than 40 %.

5.2 Pharmacokinetic properties
Absorption
Following oral administration, candesartan cilexetil is converted to the active medicine, candesartan. The mean peak serum concentration (CMAX) is reached 3 - 4 hours following tablet intake. The candesartan serum concentration increases linearly with increasing doses in the therapeutic dose range.
No gender related differences in the pharmacokinetics of candesartan have been observed. The area under the serum concentration versus time curve (AUC) of candesartan is not significantly affected by food.

Candesartan is highly bound to plasma protein (more than 99 %). The apparent volume of distribution of candesartan is 0.1 L/ kg.

Biotransformation and Elimination
Candesartan is mainly eliminated unchanged via urine and bile and only to a minor extent eliminated by hepatic metabolism (CYP2C9). Available interaction studies include no effect on CYP2C9 and CYP3A4. Based on in vitro data, no interaction would be expected to occur in vivo with medicinal active metabolites dependent upon cytochrome P450 isoenzymes CYP1A2, CYP2A6, CYP2C9, CYP2C19, CYP2D6, CYP2E1 or CYP3A4. The terminal half-life (T1/2) of candesartan is approximately 9 hours. There is no accumulation following multiple doses.

Total plasma clearance of candesartan is about 0.37 mL / min / kg, with a renal clearance of about 0.19 mL / min / kg. Following an oral dose of 14C labelled candesartan cilexetil, the active candesartan, and its inactive metabolites are excreted via the urine (26 %) and to a larger extent (70 %) via the faeces.

Special populations
In elderly patients (over 65 years), Cmax and AUC of candesartan are increased by approximately 50 % and 80 %, respectively in comparison to young adults.

In patients with mild (Ccr 60–90 mL/min) and moderate (Ccr 30–60 mL/min) to severe (Ccr 15–30 mL/ min) renal impairment, Cmax and AUC of candesartan increased during repeated dosing. The terminal T1/2 of candesartan in patients with severe renal impairment was approximately doubled compared to patients with normal renal function.
In patients with mild to moderate renal impairment AUC was approximately doubled, while in severe renal impairment the AUC was further increased.
Candesartan has not been studied in patients with more severe renal failure (Ccr ≤ 15 mL/min).

In patients with mild hepatic impairment, there was an increase in the AUC of candesartan, of approximately 30 %. In patients with moderate hepatic impairment, the increase in the AUC of candesartan was approximately 145 %.
There is no experience in patients with severe hepatic impairment and/or cholestasis.

5.3 Preclinical safety data
There was no evidence of abnormal systemic or target organ toxicity at clinically relevant dose. In preclinical safety studies candesartan has effects on the kidneys and on red cell parameters at high doses in mice, rats, dogs and marmosets. Candesartan caused a reduction of red blood cell parameters (erythrocytes, haemoglobin, haematocrit).
Effects on the kidneys (such as interstitial nephritis, tubular dilatation, basophilic tubules; increased plasma concentrations of urea and creatinine) were induced by candesartan which could be secondary to the hypotensive effect leading to alterations of renal perfusion. Furthermore, candesartan induced hypertrophy of the juxtaglomerular cells. These changes were considered to be caused by the pharmacological action of candesartan. For therapeutic doses of candesartan in humans, the hypertrophy/hyperplasia of the renal juxtaglomerular cells does not seem to have any relevance.

Foetotoxicity has been observed in late pregnancy (see section 4.6).
Data from in vitro and in vivo mutagenicity testing indicates that candesartan will not exert mutagenic or clastogenic activities under conditions of clinical use. There was no evidence of carcinogenicity.

The renin-angiotensin-aldosterone system plays a critical role in kidney development in utero. Renin-angiotensin-aldosterone system blockade has been shown to lead to abnormal kidney development in early young mice.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Corn starch,
lactose monohydrate,
red ferric oxide,
hydroxypropylcellulose,
glyceryldibehenate,
carboxymethylcellulose calcium,
magnesium stearate.

6.2 Incompatibilities
Not applicable

6.3 Shelf life
24 months from the manufacturing date.

6.4 Special precautions for storage
Store at or below 25 °C.
Protect from light and moisture.
Keep the blisters in the carton until required for use.
Keep the HDPE container tightly closed.
KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container
Blister Pack:
Tablets are packed in clear film PVC/PVdC 250 µm/90 with 90 gsm PVDC on the forming material and 95 µm aluminium foil with 6-9 gsm heat seal lacquer as the lidding material, packed in pre-printed cartons.
Pack size include 14, 28 or 30 tablets.
Not all packs and pack sizes are necessarily marketed.

6.6 Special precautions for disposal
No special requirements.
Any unused product or waste material should be disposed of in accordance with local requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Racleode Pharmaceuticals SA (Pty) Ltd
Office block 1, Bessemia Estate Office Park (East),
1 Cassinia Drive, Bessemia Rock, Ext. 12,
Atherton, South Africa.

8. REGISTRATION NUMBER

RANEPRES 8 mg : 48/7.1/30472
RANEPRES 16 mg : 48/7.1/30473
RANEPRES 32 mg : 48/7.1/30474

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

–

10. DATE OF REVISION OF THE TEXT

–

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S3

RANEPRES Tablets
Each tablet contains 8 mg candesartan cilexetil
Contains sugar (Lactose monohydrate 68.25 mg)
RANEPRES Tablets
Each tablet contains 16 mg candesartan cilexetil
Contains sugar (Lactose monohydrate 78.15 mg)
RANEPRES Tablets
Each tablet contains 32 mg candesartan cilexetil
Contains sugar (Lactose monohydrate 156.30 mg)

Read all of this leaflet carefully before you start taking RANEPRES.
Keep this leaflet. You may need to read it again.
If you still have further questions, please ask your doctor or pharmacist.
RANEPRES 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 RANEPRES is and what it is used for
2. What you need to know before you take RANEPRES
3. How to take RANEPRES
4. Possible side effects
5. How to store RANEPRES
6. Contents of the pack and other information

1. **What RANEPRES is and what it is used for**

The name of your medicine is RANEPRES. The active ingredient is candesartan cilexetil. This belongs to a group of medicines called angiotensin II receptor blocker. It works by making your blood vessels relax and widen. This helps to lower your blood pressure. It also makes it easier for your heart to pump blood to all parts of your body.

RANEPRES can be used to treat high blood pressure (hypertension) in adult patients.

RANEPRES can be used to treat adult heart failure patients with reduced heart muscle function when Angiotensin Converting Enzyme (ACE) inhibitors cannot be used or in addition to ACE-inhibitors when symptoms persist despite treatment and mineralocorticoid receptor antagonists (MRA) cannot be used. (ACE-inhibitors and MRAs are medicines used to treat heart failure).

2. **What you need to know before you take RANEPRES**

Do not take RANEPRES:
- If you are hypersensitive (allergic) to candesartan cilexetil or any of the other ingredients of RANEPRES (listed in section 6)
- If you have a history of angioedema (swelling around your face, throat or tongue) related to previous therapy with ARBs or angiotensin converting enzyme inhibitors (ACEIs) (used to treat high blood pressure).
- If you have hereditary angioedema (swelling around your face, throat or tongue).
- If you have hypertrophic obstructive cardiomyopathy (HOCM) (a heart disease characterized by the obstruction of blood flow and thickening of heart tissue).
- If you have kidney disorders.
- If you have kidney impairment and are using fluoropyrimidines (used to treat bacterial infections).
- If you have renal artery stenosis, (kidney problems with reduced blood supply to your kidney).
- If you have aortic stenosis (a decrease in blood supply flow through the aortic artery).
- If you are taking potassium-sparing diuretics (such as spironolactone, triamterene or amiloride).
- If you have polyphyria.
- If you are taking lithium.
- If you are pregnant or breastfeeding your baby.
- If you have severe liver disease or biliary obstruction (a problem with the drainage of the bile from the gall bladder).
- If you are treated with a blood pressure lowering medicine containing aliskiren
- If you are not sure if any of these apply to you, talk to your doctor or pharmacist before taking RANEPRES.

Warnings and precautions
Tell your doctor or health care provider before taking RANEPRES:
- If you have heart, liver or kidney problems, or are on dialysis.
- If you have recently had a kidney transplant.
- If you are vomiting, have recently had severe vomiting, or have diarrhoea.
- If you have a disease of the adrenal gland called Conn's syndrome (also called primary hyperaldosteronism).
- If you have low blood pressure.
- If you have ever had a stroke.
- If you have diabetes mellitus nephropathy
- You must tell your doctor if you think you are (or might become) pregnant. RANEPRES is not recommended in pregnancy.

RANEPRES
8/16/32 mg
PM0318e001

400 mm

435 mm

Back Side

- 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
- If you are taking an ACE-inhibitor together with a medicine, which belongs to the class of medicines, known as mineralocorticoid receptors antagonists (MRA). These medicines are for the treatment of heart failure (see "Other medicines and RANEPRES").

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 RANEPRES"
Your doctor may want to see you more often and do some tests if you have any of these conditions.

If you are going to have an operation, tell your doctor or dentist that you are taking **RANEPRES**. This is because **RANEPRES**, when combined with some anaesthetics, may cause an excessive drop in blood pressure.

Children and adolescents
RANEPRES must not be given to children.

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

Tell your doctor if you are using any of the following medicines:
- Other medicines to help lower your blood pressure, including beta-blockers, Diazoxide and ACE-inhibitors such as enalapril, captopril, lisinopril or ramipril.
- Non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen, naproxen, diclofenac, celecoxib or etoricoxib (medicines to relieve pain and inflammation).
- Acetylsalicylic acid (if you are taking more than 3 g each day) (medicine to relieve pain and inflammation).
- Potassium supplements or salt substitutes containing potassium (medicines that increase the amount of potassium in your blood).
- Heparin (a medicine for thinning the blood).
- Co-trimoxazole (an antibiotic medicine) also known as trimethoprim/sulfamethoxazole
- Water tablets (diuretics).
- Lithium (a medicine for mental health problems)
- If you are taking an ACE-inhibitor or aliskiren-containing medicines (see also information under the headings "Do not take **RANEPRES**" and "Warnings and precautions")
- If you are being treated with an ACE-inhibitor together with certain other medicines to treat your heart failure, which are known as mineralocorticoid receptor antagonists (MRA) (for example: spironolactone, eplerenone).

RANEPRES with food, drink and alcohol
You can take **RANEPRES** with or without food.

Pregnancy and breastfeeding
You must use effective contraceptives, if you are a woman of childbearing age.
Pregnancy
If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional for advice before taking [RANEPRES].
You should not take RANEPRES if you are pregnant, as it may cause serious harm to your baby.

Breastfeeding
Tell your doctor if you are breastfeeding or about to start breastfeeding. **RANEPRES** is not recommended for mothers who are breastfeeding, and your doctor may choose another treatment for you if you wish to breastfeed your baby.

Driving and using machines
Some people may feel tired or dizzy when taking **RANEPRES**. If this happens to you, do not drive or use any tools or machines.
It is not always possible to predict to what extent **RANEPRES** 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 **RANEPRES** affects them.

RANEPRES contains lactose
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

3. How to take RANEPRES

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

Always take **RANEPRES** exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.
The usual starting dose is one 8 mg tablet once a day.
Your doctor may increase the dose depending on your response to treatment.
RANEPRES can be taken together with other medicines and your doctor will decide which treatment is suitable for you.

Your doctor will tell you how long your treatment with **RANEPRES** will last. Do not stop early treatment. If you have the impression that the effect of **RANEPRES** is too strong or too weak, tell your doctor or pharmacist.

You can take **RANEPRES** with or without food.
Swallow the tablet with a drink of water.
Try to take the tablet at the same time each day. This will help you to remember to take it.

Use in children and adolescents with high blood pressure
RANEPRES must not be given to children.

If you take more RANEPRES than you should
In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.

If you forget to take RANEPRES
Do not take a double dose to make up for a forgotten tablet.

If you stop taking RANEPRES
If you stop taking **RANEPRES**, your blood pressure may increase again. Therefore, do not stop taking **RANEPRES** without first talking to your doctor.
If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

RANEPRES can have side effects.
Not all side effects reported for **RANEPRES** are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking **RANEPRES**, please consult your health care provider for advice.

If any of the following happens, stop taking **RANEPRES** and tell your doctor immediately or go to the casualty department at your nearest hospital:
- Difficulties in breathing, with or without swelling of the face, lips, tongue and/or throat.
- Swelling of the face, lips, tongue and/or throat, which may cause difficulties in swallowing.
- Severe itching of the skin (with raised lumps).

These are very serious side effects. If you have them, you may have had a serious reaction to **RANEPRES**. 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:
- Tiredness, an infection or fever.
- Difficulty breathing.
- Yellowing of the skin and eyes, dark urine, and tiredness, which may be symptoms of liver problems.

RANEPRES may cause a reduction in number of white blood cells. Your resistance to infection may be decreased and you may notice tiredness, an infection or a fever. If this happens, contact your doctor. Your doctor may occasionally do blood tests to check whether **RANEPRES** has had any effect on your blood (agranulocytosis).

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:
- Changes in blood test results:
  - A reduced amount of sodium in your blood. If this is severe then you may notice weakness, lack of energy, or muscle cramps.
  - An increased or reduced amount of potassium in your blood, especially if you already have kidney problems or heart failure. If this is severe, you may notice tiredness, weakness, irregular heartbeat or pins and needles.
  - An increased amount of cholesterol, sugar or uric acid in your blood.
- Sugar in your urine.
- Feeling dizzy or spinning sensation or weak.
- Headache.
- Respiratory infection.

Less frequent side effects:
- Skin rash, lumpy rash (hives), itching.
- Fever, tiredness, an infection.
- Back pain, pain in joints and muscles.
- Changes in how your liver is working, including inflammation of the liver (hepatitis). You may notice tiredness, yellowing of your skin and the whites of your eyes and flu like symptoms.
- Nausea.
- Changes in blood test results:
  - A reduced amount of sodium in your blood. If this is severe then you may notice weakness, lack of energy, or muscle cramps.
- Cough

Unknown frequency side effects:
- Diarrhoea

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 **RANEPRES** 8/16/32mg.

5. How to store RANEPRES

Store at or below 25 °C.
Store in the original package.
Keep the blisters in the carton until required for use.
Store all medicines out of reach of children.
Protect from light and moisture.
Do not store in a bathroom.
Do not use after the expiry date stated on the blister / label / 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

RANEPRES 8 mg tablets
The active substance is Candesartan cilexetil 8 mg
RANEPRES 16 mg tablets
The active substance is Candesartan cilexetil 16 mg
RANEPRES 32 mg tablets
The active substance is Candesartan cilexetil 32 mg
The other ingredients are corn starch, lactose monohydrate, red ferric oxide, hydroxypropyl cellulose, glycerol/glycerol, carboxymethylcellulose calcium, magnesium stearate.

What RANEPRES looks like and contents of the pack
RANEPRES 8 mg tablets:
Light pink circular, biconvex, uncoated tablets, debossed with "ML 53" on one side and breakline on other side.
RANEPRES 16 mg tablets.
Pink, circular, biconvex, uncoated tablets, debossed with "ML 54" on one side and breakline on other side.
RANEPRES 32 mg tablets:
Pink, circular, biconvex, uncoated tablets, debossed with "ML 55" on one side and breakline on other side.

Blister Pack:
Tablets are packed in clear film PVC/PVdC 250 µm/90 with 90 gsm PVdC as the forming material and 25 µm aluminium foil with 6-8 gsm heat seal lacquer as the lidding material, packed in pre-printed carton.
Pack size include 14, 28 or 30 tablets.
Not all packs and pack sizes are necessarily marketed

Holder of Certificate of Registration
MACLEODS PHARMACEUTICALS SA (PTY) LTD
Office block 1, Bassonia Estate Office Park (East),
1 Cussonia Drive, Bassonia Rock, Ext. 12,
Alberton, South Africa.

This leaflet was last revised in
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Registration Number
RANEPRES 8 mg : 48/7.1.3/0472
RANEPRES 16 mg : 48/7.1.3/0473
RANEPRES 32 mg : 48/7.1.3/0474

PASIËNTINLIGTINGSTUK

SKEDULERINGSTATUS: S3

RANEPRES 8 mg Tablette
Elke tablet bevat 8 mg kandesartan sileksetil
Bevat suiker: (86,25 mg Laktosemonohidraat)

RANEPRES 16 mg Tablette
Elke tablet bevat 16 mg kandesartan sileksetil
Bevat suiker: (78,15 mg Laktosemonohidraat)

RANEPRES 32 mg Tablette
Elke tablet bevat 32 mg kandesartan sileksetil
Bevat suiker: (156,30 mg Laktosemonohidraat)

Lees hierdie hele inligtingstuk sorgvuldig deur voordat jy RANEPRES begin neem
- Hou hierdie inligtingstuk. Dit mag nodig wees dat jy dit weer moet lees.
- Vra asseblief jou dokter of apteker indien jy verdere vrae het.
- **RANEPRES** is vir jou persoonlik voorgeskryf, en jy moet nie jou medisyne met ander persone deel nie. Dit mag skadelik vir hulle wees, selfs al is hul simptome dieselfde as joune.

Wat in hierdie inligtingstuk is
1. Wat RANEPRES is en waarvoor dit gebruik word
2. Wat jy behoort te weet voordat jy RANEPRES neem
3. Hoe om RANEPRES te neem
4. Moontlike newe-effekte
5. Hoe om RANEPRES te bewaar
6. Inhoud van die pak en ander inligting

1. Wat RANEPRES is en waarvoor dit gebruik word

Die naam van jou medisyne is **RANEPRES**. Die aktiewe bestanddeel is kandesartan sileksetil. Dit behoort aan 'n groep medisyne naamlik angiotensien II reseptor blokkeerders. Dit werk deurdat dit jou bloedvate laat ontspan en verwyd. Dit help om jou hoë bloeddruk te verlaag. Dit maak dit ook makliker vir jou hart om bloed na al die dele van jou liggaam te pomp.

RANEPRES kan gebruik word om hoë bloeddruk (hipertensie) in volwasse pasiënte te behandel.

RANEPRES kan gebruik word om volwasse hartversakingpasiënte met verminderde hartspierfunksie te behandel wanneer Angiotensien Omskakelende Ensiem (AOE) inhibeerders nie gebruik kan word nie, of bykomend tot AOE inhibeerders wanneer simptome voortduur ten spyte van behandeling en mineralokortikoied reseptor antagoniste (MRA) nie gebruik kan word nie. (AOE inhibeerders en MRA's is medisyne wat gebruik word om hartversaking te behandel).

2. Wat jy behoort te weet voordat jy RANEPRES neem

Moet nie RANEPRES neem nie:
- Indien jy hipersensitief (allergies) vir kandesartan sileksetil of enige van die ander bestanddele van **RANEPRES** is (gelys in afdeling 6).
- Indien jy 'n geskiedenis van angioëdeem het (swelling van jou gesig, tong of keel) wat verband hou met vorige behandeling met ARB's of angiotensien omskakelende ensiem inhibeerders (AOE'e) (wat gebruik word om hoë bloeddruk te behandel).
- Indien jy oorerflike angioedeem het (swelling van jou gesig, keel of tong).
- Indien jy hipertrofiese obstruktiewe kardiomiopatie het (HOKM) ('n hartsiekte wat gekarakteriseer word deur die obstruksie van bloedvloei en verdikking van hartweefsel).
- Indien jy nier of/en lewer siektes het.
- Indien jy nierversaking het en fluorokinolone gebruik (wat gebruik word om bakteriële infeksies te behandel).
- Indien jy renale slagaar stenose het (nierprobleme met verminderde bloedtoevoer na jou niere).
- Indien jy aortiese stenose het ('n verminderde bloedtoevoer vloei deur die aortiese arterie).
- Indien jy kaliumbesparende diuretika neem (soos bv. spironolaktoon, triamtereen of amiloried).
- Indien jy porfirie het.
- Indien jy litium gebruik.
- Indien jy swanger is of jou baba borsvoed
- Indien jy ernstige lewersiekte of biliêre obstruksie het ('n probleem met die dreinering van die gal vanaf die galblaas).
- Indien jy met 'n bloeddruk verlagende middel behandel word wat aliskiren bevat.

Indien jy nie seker is of enige van die op jou van toepassing is nie, praat met jou dokter of apteker voordat jy RANEPRES gebruik.

Waarskuwings en voorsorgmaatreëls
Vertel jou dokter of gesondheidsorgverskaffer voordat jy **RANEPRES** neem:
- Indien jy hart-, lewer- of nierprobleme het, of op dialise is.
- Indien jy onlangs 'n nieroorplanting gehad het.
- Indien jy braak, onlangs erge braking gehad het, of diaree het.
- Indien jy 'n siekte van die bynier het wat Conn se sindroom genoem word (ook genoem primêre hiperaldosteronisme).
- Indien jy lae bloeddruk het.
- Indien jy al ooit 'n beroerte gehad het.
- Indien jy diabetiese neuropatie het.
- Jy moet jou dokter vertel as jy vermoed dat jy swanger is (of kan word). **RANEPRES** word nie tydens swangerskap aanbeveel nie.
- Indien jy enige van die volgende medisyne neem wat gebruik word om hoë bloeddruk te behandel.
  - 'n AOE inhibeerder (byvoorbeeld enalapril, lisinopril, ramipril), veral as jy diabetes-verwante nierprobleme het.
  - aliskiren
- Indien jy 'n AOE inhibeerder neem saam met 'n middel wat aan die klas medisyne behoort wat bekend staan as mineralokortikoied resepore antagoniste (MRA). Hierdie medisyne is vir die behandeling van hartversaking (sien "Ander medisyne en RANEPRES").

Jou dokter kan jou nierfunksie, bloeddruk en die hoeveelheid elektroliete (bv. kalium) in jou bloed met gereelde tussenposes nagaan.
Sien ook inligting onder die opskrif "Moet nie **RANEPRES** neem nie"
Jou dokter sal jou moontlik meer gereeld wil sien en 'n paar toetse doen indien jy enige van hierdie toestande het.

Indien jy 'n operasie gaan ondergaan, vertel jou dokter of tandarts dat jy **RANEPRES** neem. Dit is omdat **RANEPRES**, wanneer dit gekombineer word met sommige narkosemiddels, 'n oormatige daling in bloeddruk kan veroorsaak.

Kinders en adolessente
RANEPRES moet nie aan kinders gegee word nie.

Ander medisyne en RANEPRES
Vertel altyd vir jou gesondheidsorgverskaffer indien jy enige ander medisyne neem. (Dit sluit alle komplementêre of tradisionele medisyne in.)

Vertel jou dokter indien jy enige van die volgende medisyne gebruik:
- Ander medisyne om jou bloeddruk te help verlaag, insluitend betablokkeerders, Diasoksied en AOE inhibeerders soos enalapril, kaptopril, lisinopril of ramipril.
- Nie-steroïed anti-inflammatoriese middels (NSAIM's) soos ibuprofen, naproksen, diklofenak, selekoksib of etorikoksib (medisyne om pyn en inflammasie te verlig).
- Asetielsalisielsuur (indien jy meer as 3 g elke dag neem) (medisyne om pyn en inflammasie te verlig).
- Kaliumaanvullings of kaliumbevattende soutvervangers (medisyne wat die hoeveelheid kalium in jou bloed verhoog).
- Heparien ('n medisyne om die bloed te verdun).
- Ko-trimoksasool ('n antibiotiese middel) ook bekend as trimetoprim/sulfametoksasool.
- Watertablette (diuretika).
- Litium ('n medisyne vir geestesgesondheidsprobleme).
- Indien jy 'n AOE inhibeerder of medisyne wat aliskiren bevat gebruik (sien ook inligting onder die opskrifte "Moet nie **RANEPRES** neem nie" en "Waarskuwings en voorsorgmaatreëls").
- Indien jy vir jou hartversaking behandel word met 'n AOE inhibeerder saam met sekere ander medisyne wat bekend staan as mineralokortikoied reseptor antagoniste (MRA) (byvoorbeeld: spironolaktoon, eplerenoon).

RANEPRES met voedsel, drank en alkohol
Jy kan **RANEPRES** met of sonder kos neem.

Swangerskap en borsvoeding
Jy moet effektiewe voorbehoedmiddels gebruik as jy 'n vrou van kinderbarende ouderdom is.
Swangerskap
Indien jy swanger is of jou baba borsvoed, raadpleeg asseblief jou dokter, apteker of ander professionele gesondheidsorgwerker vir advies voordat jy RANEPRESS gebruik.
Jy moet nie RANEPRES neem as jy swanger is nie, aangesien dit ernstige skade aan jou baba kan veroorsaak.

Borsvoeding
Vertel jou dokter indien jy borsvoed of binnekort gaan begin borsvoed. **RANEPRES** word nie aanbeveel vir moeders wat borsvoed nie, en jou dokter kan moontlik 'n ander behandeling vir jou kies indien jy graag jou baba wil borsvoed.

Bestuur en gebruik van masjinerie
Sommige mense kan moeg en duiselig voel wanneer hulle **RANEPRES** gebruik. Indien dit met jou gebeur, moet jy nie bestuur of enige gereedskap of masjiene gebruik nie.
Dit is nie altyd moontlik om te voorspel tot watter mate **RANEPRES** met die daaglikse aktiwiteite van 'n pasiënt kan inmeng nie. Pasiënte moet seker maak dat hulle nie in die bogenoemde aktiwiteite betrokke raak nie, totdat hulle bewus is van die mate waartoe **RANEPRES** hulle affekteer.

RANEPRES bevat laktose
Raadpleeg jou dokter voordat jy hierdie medisyne neem, indien jou dokter vir jou gesê het dat jy 'n onverdraagsaamheid teenoor sommige suikers het.

3. Hoe om RANEPRES te neem

Moet nie medisyne wat vir jou voorgeskryf is met enige ander persoon deel nie.

Neem altyd **RANEPRES** presies soos jou dokter of apteker jou beveel het. Vra jou dokter of apteker indien jy nie seker is nie.
Die gewone aanvangsdosis is een 8 mg tablet een keer per dag.
Jou dokter kan die dosis verhoog, afhangende van jou reaksie op die behandeling.
RANEPRES kan saam met ander medisyne geneem word en jou dokter sal besluit watter behandeling vir jou geskik is.

Jou dokter sal vir jou sê hoe lank jou behandeling met **RANEPRES** sal duur. Moet nie met die behandeling vroeër ophou nie. Indien jy onder die indruk is dat die effek van **RANEPRES** te [illegible] te swak is, praat met jou dokter of apteker.

Jy kan **RANEPRES** met of sonder kos neem.
Sluk die tablet met 'n glas water.
Probeer om die tablet elke dag op dieselfde tyd te neem. Dit sal jou help om te onthou om dit te neem.

Gebruik in kinders en adolessente met hoë bloeddruk
RANEPRES moet nie aan kinders gegee word nie.

Indien jy meer RANEPRES neem as wat jy behoort te neem
In die geval van 'n oordosering, raadpleeg jou dokter of apteker. Indien nie een beskikbaar is nie, kontak die naaste hospitaal of gifbeheersentrum.

Indien jy vergeet om RANEPRES te neem
Moet nie 'n dubbele dosis neem om vir 'n vergete tablet op te maak nie.

Indien jy ophou om RANEPRES te neem
Indien jy ophou om **RANEPRES** te neem, kan jou bloeddruk weer styg. Moet dus nie ophou om **RANEPRES** te neem, sonder om dit eers met jou dokter te bespreek nie.
Indien jy enige verdere vrae oor die gebruik van hierdie medisyne het, vra jou dokter of apteker.

4. Moontlike newe-effekte

RANEPRES kan newe-effekte hê.
Nie alle newe-effekte wat vir **RANEPRES** aangemeld is, is in hierdie inligtingstuk ingesluit nie. Sou jou algemene gesondheid versleg of indien jy enige ongewenste effekte ervaar terwyl jy **RANEPRES** gebruik, raadpleeg asseblief jou gesondheidsorgverskaffer vir advies.

Indien enige van die volgende gebeur, hou op om **RANEPRES** te gebruik en vertel onmiddellik jou dokter daarvan of gaan na die ongevalle afdeling van jou naaste hospitaal:
- Asemhalingsprobleme, met of sonder swelling van die gesig, lippe, tong en/of keel.
- Swelling van die gesig, lippe, tong en/of keel, wat dit moeilik kan maak om te sluk.
- Erge jeuk van die vel (met opgehewe knoppe).

Al hierdie newe-effekte is baie ernstig. Indien jy dit ervaar, het jy moontlik 'n ernstige reaksie op **RANEPRES** gehad. Jy mag dringende mediese aandag of hospitalisasie benodig.

Vertel onmiddellik jou dokter of gaan na die ongevalle afdeling van jou naaste hospitaal indien jy enige van die volgende waarneem:
- Moegheid, 'n infeksie of koors.
- Sukkel om asem te haal.
- Vergeling van die vel en oë, donker urine en moegheid, wat simptome van lewerprobleme kan wees.

RANEPRES kan 'n vermindering in die aantal witbloedselle veroorsaak. Jou weerstand teen infeksie kan verminder word en jy kan moegheid, 'n infeksie of koors opmerk. Indien dit gebeur, kontak jou dokter. Jou dokter kan af en toe bloedtoetse doen om te bepaal of **RANEPRES** enige effek op jou bloed gehad het (agranulositose).

Al hierdie newe-effekte is ernstig. Jy mag dringende mediese aandag benodig.
Vertel jou dokter indien jy enige van die volgende opmerk:
Gereelde newe-effekte:
- Veranderinge in bloedtoets resultate:
  - 'n Verminderde hoeveelheid natrium in jou bloed. Indien dit ernstig is, kan jy swakheid, gebrek aan energie of spierkrampe ervaar.
  - 'n Verhoogde of verminderde hoeveelheid kalium in jou bloed, veral indien jy reeds nierprobleme of hartversaking het. Indien dit ernstig is, kan jy moegheid, swakheid, onreëlmatige hartklop of naalde en spelde ervaar.
  - 'n Verhoogde hoeveelheid van cholesterol, suiker of uriensuur in jou bloed.
- Suiker in jou urine.
- Voel duiselig, of spin sensasie, of swak.
- Hoofpyn.
- Respiratoriese infeksie.

Minder gereelde newe-effekte:
- Veluitslag, knobbelrige uitslag (galbulte), jeuk.
- Koors, moegheid, 'n infeksie.
- Rugpyn, pyn in gewrigte en spiere.
- Veranderinge in hoe jou lewer werk, insluitend ontsteking van die lewer (hepatitis). Jy mag dalk moegheid, vergeling van jou vel en die wit van jou oë en griepagtige simptome opmerk.
- Naarheid.
- Veranderinge in bloedtoets resultate:
  - 'n Verminderde hoeveelheid natrium in jou bloed. Indien dit ernstig is, kan jy swakheid, gebrek aan energie of spierkrampe opmerk.
- Hoes.

[illegible]:
- Diaree.

Indien jy enige newe-effekte waarneem wat nie in hierdie inligtingstuk genoem word nie, lig asseblief jou dokter of apteker in.

Aanmelding van newe-effekte
Indien jy newe-effekte kry, praat met jou dokter of apteker. Jy kan ook newe-effekte aan SAHPRA rapporteer via die "**6.04 Adverse Drug Reaction Reporting Form**", wat aanlyn gevind kan word onder SAHPRA se publikasies: [illegible]. Deur newe-effekte aan te meld, kan jy help om meer inligting beskikbaar te stel aangaande die veiligheid van **RANEPRES** 8/16/32 mg.

5. Hoe om RANEPRES te bewaar

Bewaar by of benede 25 °C.
Bewaar in die oorspronklike verpakking
Hou die stulpstroke in die buitenste karton totdat dit benodig word vir gebruik.
Bewaar alle medisyne buite bereik van kinders.
Beskerm teen lig en vog.
Moet nie in 'n badkamer bêre nie.
Moet nie gebruik na die vervaldatum wat op die stulpstrook/etiket/karton aangebring is nie.
Neem alle ongebruikte medisyne terug na jou apteker.
Moet nie ongebruikte medisyne in afvoerpype of rioolstelsels (bv. toilette) gooi nie.

6. Inhoud van die pak en ander inligting

RANEPRES 8 mg tablette
Die aktiewe bestanddeel is 8 mg Kandesartan sileksetil
RANEPRES 16 mg tablette
Die aktiewe bestanddeel is 16 mg Kandesartan sileksetil
RANEPRES 32 mg tablette
Die aktiewe bestanddeel is 32 mg Kandesartan sileksetil
Die ander bestanddele is mielиestysel, laktosemonohidraat, rooi ysteroksied, hidroksipropielsellulose, gliserien/gliserol, kalsiumkarboksimetielsellulose, magnesiumstearaat.

Hoe RANEPRES lyk en inhoud van die pak
RANEPRES 8 mg tablette:
Ligte pienk sirkelvormige, bikonvekse, onbedekte tablette, met "ML 53" ingeprent op die een kant en breeklyn op die ander kant.
RANEPRES 16 mg tablette.
Pienk sirkelvormige, bikonvekse, onbedekte tablette, met "ML 54" ingeprent op die een kant en breeklyn op die ander kant.
RANEPRES 32 mg tablette:
Pienk sirkelvormige, bikonvekse, onbedekte tablette, met "ML 55" ingeprent op die een kant en breeklyn op die ander kant.

Stulpverpakking:
Tablette word verpak in deursigtige film PVC/PVdC 250 µm/90 met 90 gsm PVdC as die vormingsmateriaal en 25 µm aluminiumfoelie met 6-8 gsm hitteseëllak as die dekmateriaal, verpak in voorafgedrukte karton.
Verpakkingsgroottes sluit 14, 28 of 30 tablette in.
Nie alle verpakkings en verpakkingsgroottes word noodwendig bemark nie.

Houer van die Registrasiesertifikaat
MACLEODS PHARMACEUTICALS SA (Edms) Bpk
Kantoorblok 1, Bassonia Estate Kantoorpark (Oos),
Cussonia Weg 1, Bassonia Rock, Uitbr. 12,
Alberton, Suid Afrika

Hierdie inligtingstuk was hersien in
–

Registrasienommer
RANEPRES 8 mg : 48/7.1.3/0472
RANEPRES 16 mg : 48/7.1.3/0473
RANEPRES 32 mg : 48/7.1.3/0474

400 mm

435 mm

PACKAGING RESEARCH & DEVELOPMENT

Restricted Circulation

(Front Page)

ARTWORK / PRINTPROOF APPROVAL FORM

1. Product: RANEPRES 8/16/32 MG (Candesartan tablets 8/16/32 mg)	
2. Country: South Africa	3. Packaging component: Patient Information
4. No. of Colours: 1 Colour	5. Pantone Shade No.: Black
6. Specification: 40 gsm bible paper	
7. Machine Layout No.: NA	8. Dimensions: 435 (L) x 400 (W) mm
9. Design / Style: NA	10. Item code No.: PM03846801
11. Artwork has been made: Actual Size	12. Pharma code No.: 31497 mini (1thin, 1thick, 1thin, 1thick, 4thins, 2thicks, 1thin, 3thicks)
13. Barcode/NDC No: NA	14. Supersedes Item code No: NA
15. Revision no: 00	16. A/W File name: Y:\Candesartan\SA Private Market\RANEPRES PI & PIL -PM03846801.cdr
Approved By:	17. Location: Daman

PRD	M.A. HOLDER	RAD	QC	PRODN	QA
14/11/22	Vanita Rajool	11/11/2022	12/11/22	12/11/22	Qyadav 14/11/22

Note: 1. To follow overleaf checklist for approval of Artwork / Print proof.

Instructions to Vendor :

1. Before processing, please ensure First pull out / Commercial supply should match with approved Artwork with respect to Design, Size, Fonts & Text.
2. Print proof to represent full printing area with Station Numbers.

FRM/CQA/021/04-01

Reason for revision :	Item code	Artwork Release Date	Artwork Implementation Date
1) New Artwork for South Africa	PM03846801		