Approved Professional Information for Medicines for Human Use:

[PRODUCT NAME]

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

[PRODUCT NAME] 25 25 mg TABLETS

[PRODUCT NAME] 50 50 mg TABLETS

[PRODUCT NAME] 100 100 mg TABLETS

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

[PRODUCT NAME] 25: Each film-coated tablet contains losartan potassium 25 mg.

[PRODUCT NAME] 50: Each film-coated tablet contains losartan potassium 50 mg.

[PRODUCT NAME] 100: Each film-coated tablet contains losartan potassium 100 mg.

Sugar free

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablets

[PRODUCT NAME] 25: White to off white, oval, biconvex film-coated tablets with “25” debossing on one side and “BL” on the other side.

[PRODUCT NAME] 50: White to off white, oval, biconvex film-coated tablets with “50” debossing on one side and “BL” on the other side.

[PRODUCT NAME] 100: White to off white, almond shaped, biconvex film-coated tablets with “100” debossing on one side and “BL” on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

[PRODUCT NAME] is indicated for:

- The treatment of hypertension
- Renal protection in type 2 diabetic patients with hypertension and proteinuria

4.2 Posology and method of administration

Posology

Hypertension

The usual starting and maintenance dose is 50 mg once daily for most patients. The maximum antihypertensive effect is achieved 3-6 weeks after initiation of therapy. The dose may be increased to 100 mg once daily.

Renal protection in type 2 diabetic patients with hypertension and proteinuria

The usual starting dose is 50 mg once daily. The dose may be increased to 100 mg once daily based on blood pressure response.

Special populations

Patients with intravascular volume-depletion

For patients with intravascular volume-depletion (e.g. those treated with high-dose diuretics), a starting dose of 25 mg once daily should be considered (see section 4.4).

Renal impairment

No initial dosage adjustment is necessary for patients with renal impairment, including patients on dialysis.

Hepatic impairment

A lower dose should be considered for patients with a history of hepatic impairment (see section 4.4).

Elderly population

No initial dosage adjustment is necessary for the elderly patients.

Paediatric population

The safety and efficacy of [PRODUCT NAME] in children have not yet been established.

Method of administration

[PRODUCT NAME] is indicated for oral administration.

[PRODUCT NAME] may be administered with or without food.

[PRODUCT NAME] may be administered with other antihypertensive medicines of a different class.

4.3 Contraindications

- Hypersensitivity to the losartan potassium or to any of the excipients listed in section 6.1
- In patients with a history of angio-oedema related to ACE-inhibitors or angiotensin receptor antagonists such as [PRODUCT NAME]
- Hypertrophic obstructive cardiomyopathy
- [PRODUCT NAME] is not recommended for patients with severe renal impairment or for patients with hepatic impairment

- Aortic stenosis, left ventricular outflow track obstruction
- Bilateral renal artery stenosis
- Renal artery stenosis in patients with a single kidney
- Concomitant therapy with potassium sparing diuretics such as spironolactone, triamterene and amiloride
- Pregnancy and lactation (see section 4.6)
- Concomitant use of fluoroquinolones in patients with moderate to severe renal impairment.

4.4 Special warnings and precautions for use

Pregnancy

Women of childbearing age should ensure adequate contraception (see sections 4.3 and 4.6).

Renal function impairment

[PRODUCT NAME] should be used with caution in patients with bilateral renal artery stenosis or stenosis of an artery to a single kidney, aortic valve stenosis or hypertrophic obstructive cardiomyopathy.

When impaired renal function is present, changes in renal function as a consequence of inhibiting the renin-angiotensin system including renal failure have been reported in susceptible individuals. These changes in renal function may be reversible upon discontinuation of [PRODUCT NAME] therapy, in some patients.

In patients whose renal function may depend on the activity of the renin-angiotensin-aldosterone system (e.g. patients with severe congestive heart failure), treatment with angiotensin converting enzyme inhibitors has been associated with oliguria and/or

progressive azotemia and (less frequently) with acute renal failure and/or death. Similar outcomes are likely with [PRODUCT NAME] therapy.

Medicines affecting the renin-angiotensin system may increase blood urea and serum creatinine in patients with bilateral renal artery stenosis or stenosis of the artery to a solitary kidney. These changes in renal function may be reversible upon discontinuation of [PRODUCT NAME] therapy.

Symptomatic hypotension

Symptomatic hypotension may occur after initiation of [PRODUCT NAME].

Hepatic impairment

Reduced doses must be considered in patients with hepatic impairment.

Based on reported pharmacokinetic data which demonstrate significantly increased plasma concentrations of losartan in cirrhotic patients, a dose of 25 mg should be considered for patients with a history of hepatic impairment (see section 4.2).

Volume-depletion

Patients with volume-depletion (e.g. those treated with high-dose diuretics) may experience hypotension, which may be minimised by initiating treatment with a low dose of [PRODUCT NAME]. Halving of the dose should also be considered for patients with a history of hepatic impairment (see section 4.2).

Electrolyte imbalance

Since hyperkalaemia may occur, serum-potassium concentrations should be monitored, especially in the elderly and patients with renal impairment and the concomitant use of potassium-sparing diuretics should generally be avoided (see section 4.5).

Fluoroquinolones

Concomitant use of fluoroquinolones with ACE inhibitors, such as [PRODUCT NAME], may precipitate acute kidney injury in patients, especially those with moderate to severe renal impairment and elderly patients (see section 4.3 and 4.5). Renal function should be assessed before initiating treatment and monitored during treatment with [PRODUCT NAME].

4.5 Interaction with other medicines and other forms of interaction

Combinations containing any of the following medications, depending on the amount present, may also interact with [PRODUCT NAME]:

Non-steroidal anti-inflammatory drugs (NSAIDs)

NSAIDs may antagonise the antihypertensive effect of [PRODUCT NAME].

Sympathomimetic medicines

Concurrent use with sympathomimetics may reduce the antihypertensive effects of [PRODUCT NAME].

Potassium

Potassium-sparing diuretics, potassium containing medication or potassium supplements used concurrently with [PRODUCT NAME] may result in hyperkalaemia since reduction of aldosterone production induced by [PRODUCT NAME] may lead to elevation of serum potassium.

Fluoroquinolones

Concomitant use of fluoroquinolones and ACE inhibitors, such as [PRODUCT NAME], may precipitate acute kidney injury (see sections 4.3 and 4.4).

Lithium

As with other medicines which affect the elimination of sodium, lithium excretion may be reduced. Therefore, serum lithium levels should be monitored carefully if lithium salts are to be co-administered with angiotensin II receptor antagonists.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential / Contraception in males and females

Women of childbearing age should ensure adequate contraception.

Pregnancy

[PRODUCT NAME] is contraindicated for use during pregnancy (see section 4.3)

When pregnancy is detected, [PRODUCT NAME] should be discontinued as soon as possible. Not to be used in pregnancy as teratogenicity has been shown in experimental animals (see section 4.3).

Breastfeeding

Safety has not been established.

Fertility

There are no fertility data.

4.7 Effects on ability to drive and use machines

Dizziness or hypotension may occur when taking [PRODUCT NAME], in particular during initiation of treatment or when the dose is increased. Patients should see how [PRODUCT NAME] affects them before driving or operating machinery.

4.8 Undesirable effects

b) Tabulated list of adverse reactions

The table below shows all adverse drug reactions (ADRs) observed during clinical trials and postmarket spontaneous reports with losartan.

System Organ Class	**Frequency**		
	Frequent	**Less Frequent**	**Not known**
Infections and infestations	Upper respiratory infection		
Blood and lymphatic system disorders		Thrombocytopenia	Symptomatic anaemia, decreased haemoglobin concentrations, neutropenia, anaemia
Immune system disorders		Angioedema (involving swelling of the face, lips, and/or tongue) has been reported in patients treated with [PRODUCT NAME].	
Psychiatric disorders	Insomnia		
Nervous system disorders	Headache, dizziness, vertigo		Migraine
Cardiac disorders	Palpitations, tachycardia,		Hypotension, chest pain

Vascular disorders		Orthostatic hypotension	Oedema /swelling, vasculitis, including Henoch-Schönlein purpura
Respiratory, thoracic and mediastinal disorders	Cough, nasal congestion, pharyngitis, sinus disorder		
Gastrointestinal disorders		Diarrhoea, dyspepsia, nausea, abdominal pain	taste disturbances, complete taste loss, vomiting
Hepatobiliary disorders			Severe acute hepatotoxicity, cholestasis, acute pancreatitis, hepatitis
Skin and subcutaneous tissue disorders		Urticaria, rash	Atypical cutaneous lymphoid infiltrates, pruritus, erythroderma, photosensitivity

Musculoskeletal and connective tissue disorders		Back pain, muscle cramps, leg pain, myalgia	Arthralgia
Renal and urinary disorders			Impaired renal function
Reproductive system and breast disorders			Erectile dysfunction/ impotence
General disorders and administration site conditions		Asthenia/fatigue	Malaise
Investigations		Hyperkalaemia, elevations of ALT	Liver function abnormalities

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 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

4.9 Overdose

The symptoms of an overdosage of [PRODUCT NAME] would be hypotension and tachycardia. Bradycardia could occur from parasympathetic (vagal) stimulation. If symptomatic hypotension should occur, supportive treatment should be instituted. Neither [PRODUCT NAME] nor the active metabolite can be removed by haemodialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and Class: A7.1.3 Other hypotensives

Pharmacotherapeutic group: Angiotensin II antagonists, plain, ATC code: C09CA01

Losartan is a nonpeptide angiotensin II receptor antagonist with high affinity and selectivity for the AT1 receptor, without binding to or blocking other hormone receptors or ion channels important in cardiovascular regulation. Angiotensin II is a potent vasoconstrictor, a primary active hormone of the renin-angiotensin system, and a major determinant of the pathophysiology of hypertension. Losartan blocks the vasoconstrictor and aldosterone-secreting effects of angiotensin II by inhibiting the binding of angiotensin II to the AT1 receptor.

Losartan is a specific antagonist of the angiotensin II receptor type AT1; it does not inhibit ACE (kininase II), the enzyme that degrades bradykinin. Removal of angiotensin II negative feedback on renin secretion leads to increased plasma renin activity during losartan administration. A 2-3-fold increase in angiotensin II in plasma, comes as a result of increases in plasma renin activity. However, antihypertensive activity and suppression of plasma aldosterone concentration are apparent, indicating effective angiotensin II receptor blockade. After discontinuation of losartan, plasma renin activity and angiotensin levels declined.

5.2 Pharmacokinetic properties

Absorption

Following oral administration, bioavailability is approximately 33 %.

The mean peak concentrations of losartan and its active metabolite are reached in 1 hour and 3-4 hours, respectively.

Distribution

Both losartan and the carboxylic acid metabolite are greater than, or equal to 99 % bound to plasma proteins. The distribution volume of losartan is 34 litres.

Biotransformation

It undergoes first-pass metabolism to form an active carboxylic acid metabolite, (which has greater pharmacological activity than losartan) and some inactive metabolites. About 14 % of an intravenously or orally administered dose is converted to its active metabolite.

Elimination

The terminal half-life of losartan is 2 hours and of its active metabolite is 6-9 hours.

Losartan is excreted in the urine, and in the faeces, as unchanged drug and metabolites. Following oral dosing, about 35 % of the dose is excreted in the urine and about 60 % in the faeces. Neither losartan nor the active metabolite can be removed by haemodialysis.

Plasma concentrations of losartan are not altered in patients with impaired renal function and a creatinine clearance above 10 mL/min. Compared to patients with normal renal function, the AUC for losartan is approximately 2-fold greater in patients on haemodialysis.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core

Colloidal anhydrous silica (Aerosil 200),

magnesium stearate,

maize starch (dried),

microcrystalline cellulose (Avicel PH 200),

purified talc,

sodium starch glycollate (Type A).

Film coating

hypromellose (15 cps),

macrogol 600,

purified talc,

titanium dioxide (C.I No 77891).

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store in a dry place at or below 25 °C. Protect from light, heat and moisture.

Keep blister packs in carton until required for use.

KEEP OUT OF THE REACH OF CHILDREN

6.5 Nature and contents of container

[PRODUCT NAME] 25:

Blister pack (White Opaque PVC film and Aluminium foil) of 2 x 14 and 3 x 10 tablets.

[PRODUCT NAME] 50:

Blister pack (White Opaque PVC film and Aluminium foil) of 2 x 14 and 3 x 10 tablets.

[PRODUCT NAME] 100:

Blister pack (White Opaque PVC film and Aluminium foil) of 2 x 14 and 3 x 10 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Austell Pharmaceuticals (Pty) Ltd

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8. REGISTRATION NUMBER(S)

AUSTELL LOSARTAN 25 mg: 41/7.1.3/0496

AUSTELL LOSARTAN 50 mg: 41/7.1.3/0497

AUSTELL LOSARTAN 100 mg: 41/7.1.3/0498

LORTELL 25 mg: 41/7.1.3/0502

LORTELL 50 mg: 41/7.1.3/0503

LORTELL 100 mg: 41/7.1.3/0517

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

04 December 2009

10. DATE OF REVISION OF THE TEXT

09 November 2022