Professional Information for Medicines for Human Use:

AUSTELL LOSARTAN

SCHEDULING STATUS

S3

PROPRIETARY NAME AND DOSAGE FORM

AUSTELL LOSARTAN 25 TABLETS

AUSTELL LOSARTAN 50 TABLETS

AUSTELL LOSARTAN 100 TABLETS

COMPOSITION

AUSTELL LOSARTAN 25:

Each film-coated tablet contains losartan potassium 25 mg.

AUSTELL LOSARTAN 50:

Each film-coated tablet contains losartan potassium 50 mg.

AUSTELL LOSARTAN 100:

Each film-coated tablet contains losartan potassium 100 mg.

Excipients

Colloidal anhydrous silica (Aerosil 200), magnesium stearate, maize starch (dried), microcrystalline cellulose (Avicel PH 200), purified talc and sodium starch glycollate (Type A).

Film coating: hypromellose (15 cps), macrogol 600, purified talc and titanium dioxide (C.I No 77891).

THE CATEGORY AND CLASS

A7.1.3 Other hypotensives

PHARMACOLOGICAL ACTION

Pharmacodynamic properties

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 feed back 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.

Pharmacokinetic properties

Following oral administration, bioavailability is approximately 33%. 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.

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

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.

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.

INDICATIONS

AUSTELL LOSARTAN is indicated for the treatment of hypertension.

CONTRAINDICATIONS

Patients who are hypersensitive to any component of this product.

The use of AUSTELL LOSARTAN during pregnancy is contraindicated

(see PREGNANCY AND LACTATION). AUSTELL LOSARTAN should be discontinued as soon as possible, when pregnancy is suspected.

Safety and efficacy have not been established in children.

Concomitant use of fluoroquinolones in patients with moderate to severe renal impairment.

WARNINGS AND SPECIAL PRECAUTIONS

Women of childbearing age should ensure adequate contraception.

AUSTELL LOSARTAN is contra-indicated in pregnancy and should be used with care, if at all, during breast-feeding.

AUSTELL LOSARTAN 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.

Symptomatic hypotension may occur after initiation of **AUSTELL LOSARTAN**.

Reduced doses must be considered in patients with hepatic impairment.

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 **AUSTELL LOSARTAN**. Halving of the dose should also be considered for patients with a history of hepatic impairment (see **"Dosage and Directions for use"**).

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 **"Interactions"**).

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 **AUSTELL LOSARTAN** 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 **AUSTELL LOSARTAN** therapy.

Agents 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 **AUSTELL LOSARTAN** therapy.

Concomitant use of fluoroquinolones with ACE inhibitors, such as **AUSTELL LOSARTAN**, may precipitate acute kidney injury in patients, especially those with moderate to severe renal impairment and elderly patients (see **CONTRAINDICATIONS**). Renal function should be assessed before initiating treatment, and monitored during treatment with **AUSTELL LOSARTAN**.

INTERACTIONS

Combinations containing any of the following medications, depending on the amount present, may also interact with **AUSTELL LOSARTAN**:

Non-steroidal anti-inflammatory drugs (NSAIDs) may antagonise the antihypertensive effect of **AUSTELL LOSARTAN**.

Concurrent use with sympathomimetics may reduce the antihypertensive effects of **AUSTELL LOSARTAN**.

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

Fluoroquinolones

Concomitant use of fluoroquinolones and ACE inhibitors, such as **AUSTELL LOSARTAN**, may precipitate acute kidney injury (see **CONTRAINDICATIONS**).

HUMAN REPRODUCTION

Pregnancy (see CONTRA-INDICATIONS):

- **AUSTELL LOSARTAN** should be discontinued as soon as possible, when pregnancy is suspected.
- **AUSTELL LOSARTAN** should not to be used in pregnancy as teratogenicity has been shown in experimental animals.

Lactation:

- Safety has not been established.

DOSAGE AND DIRECTIONS FOR USE

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.

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 “SPECIAL PRECAUTIONS”).

No initial dosage adjustment is necessary for the elderly patients or for patients with renal impairment, including patients on dialysis. A lower dose should be considered for patients with a history of hepatic impairment (see “SPECIAL PRECAUTIONS”).

AUSTELL LOSARTAN may be administered with other antihypertensive agents of a different class.

AUSTELL LOSARTAN may be administered with or without food.

SIDE EFFECTS

Hypersensitivity

Rare: Angioedema (involving swelling of the face, lips, and/or tongue) has been reported in patients treated with **AUSTELL LOSARTAN**.

Gastro-intestinal

Less frequent: Diarrhoea.

The following side effects have been reported and frequencies are unknown:

Dyspepsia, nausea.

Buccal

The following side effects have been reported and frequencies are unknown: Taste disturbances, complete taste loss.

Skin

Rare: Urticaria, rash.

The following side effects have been reported and frequencies are unknown:

Atypical cutaneous lymphoid infiltrates.

Cardiovascular

The following side effects have been reported and frequencies are unknown:

Hypotension, palpitations, tachycardia.

Musculoskeletal

Less frequent: Back pain.

Rare: Muscle cramps, leg pain, Myalgia.

Nervous/Psychiatric

More frequent: Headache.

Less frequent: Dizziness.

Rare: Insomnia.

The following side effects have been reported and frequencies are unknown:

Migraine.

Respiratory

Less frequent: Cough, nasal congestion, upper respiratory infection, pharyngitis.

Rare: Sinus disorder.

Hepatic

Rare: Raised liver enzymes values.

The following side effects have been reported and frequencies are unknown:

Severe acute hepatotoxicity, cholestasis.

Haematological

The following side effects have been reported and frequencies are unknown:

Symptomatic anaemia, decreased haemoglobin concentrations, neutropenia.

Pancreatic

The following side effects have been reported and frequencies are unknown:

Acute pancreatitis.

Body as a Whole

Less frequent: Asthenia/fatigue.

The following side effects have been reported and frequencies are unknown:

Abdominal pain, chest pain and oedema/swelling.

Renal

The following side effects have been reported and frequencies are unknown:

Impaired renal function.

KNOWN SYMPTOMS OF OVER-DOSAGE AND PARTICULARS OF ITS TREATMENTS

The symptoms of an over-dosage of **AUSTELL LOSARTAN** would be hypotension and tachycardia. Bradycardia could occur from parasympathetic (vagal) stimulation. If symptomatic hypotension should occur, supportive treatment should be instituted. Neither **AUSTELL LOSARTAN** nor the active metabolite can be removed by haemodialysis.

IDENTIFICATION

AUSTELL LOSARTAN 25:

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

AUSTELL LOSARTAN 50:

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

AUSTELL LOSARTAN 100:

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

PRESENTATION

AUSTELL LOSARTAN 25:

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

AUSTELL LOSARTAN 50:

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

AUSTELL LOSARTAN 100:

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

STORAGE INSTRUCTIONS

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

REGISTRATION NUMBER

AUSTELL LOSARTAN 25: 41/7.1.3/0496

AUSTELL LOSARTAN 50: 41/7.1.3/0497

AUSTELL LOSARTAN 100: 41/7.1.3/0498

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

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