LOSARTAN POTASSIUM
LORSA

For use by a registered medical practitioner or laboratory only.

Composition:
LORSA 50
Each film coated tablet contains :Losartan Potassium U.S.P 50 mg .
Each Lorsa 50 mg tablet contains 37.5mg Anhydrous lactose.
LORSA 100
Each film coated tablet contains :Losartan Potassium U.S.P 100mg.
Each Lorsa 100mg contains 157 mg Anhydrous lactose.

Pharmacodynamic properties.
Pharmacotherapeutic group:
Anti-hypertensive (Angiotensin II Antagonist)
Mechanism of action
Losartan is a synthetic oral angiotensin-II receptor (type AT1) antagonist. Angiotensin II, a potent vasoconstrictor, is the primary active hormone of the renin/angiotensin system and an important determinant of the pathophysiology of hypertension. Angiotensin II binds to the AT1 receptor found in many tissues (e.g. vascular smooth muscle, adrenal gland, kidneys and the heart) and elicits several important biological actions, including vasoconstriction and the release of aldosterone. Angiotensin II also stimulates smooth muscle cell proliferation.

Pharmacokinetic properties
Absorption:
Following oral administration, losartan is well absorbed and undergoes first-pass metabolism, forming an active carboxylic acid metabolite and other inactive metabolites. The systemic bioavailability of losartan tablets is approximately 33%. Mean peak concentrations of losartan and its active metabolite are reached in 1 hour and in 3-4 hours, respectively.
Distribution:
Both losartan and its active metabolite are ≥ 99% bound to plasma proteins, primarily albumin. The volume of distribution of losartan is 34 litres.
Metabolism:
About 14% of an orally-administered dose of losartan is converted to its active metabolite.
Excretion:
Plasma clearance of losartan and its active metabolite is about 600 ml/min and 50 ml/min, respectively. Renal clearance of losartan and its active metabolite is about 74 ml/min and 26 ml/min, respectively. When losartan is administered orally, about 4% of the dose is excreted unchanged in the urine, and about 6% of the dose is excreted in the urine as active metabolite.

Therapeutic indications
- Treatment of essential hypertension in adults and in children and adolescents 6-18 years of age.
- Treatment of renal disease in adult patients with hypertension and type 2 diabetes mellitus with proteinuria ≥ 0.5 g/day as part of an antihypertensive treatment.
- Treatment of chronic heart failure in adult patients when treatment with Angiotensin converting enzyme (ACE) inhibitors is not considered suitable due to incompatibility, especially cough, or contraindication. Patients with heart failure who have been stabilised with an ACE inhibitor should not be switched to Losartan.
- Reduction in the risk of stroke in adult hypertensive patients with left ventricular hypertrophy documented by ECG.

Posology and method of administration
Hypertension
The usual starting and maintenance dose is 50 mg once daily. The maximal antihypertensive effect is attained 3-6 weeks after initiation of therapy. Some patients may receive an additional benefit by increasing the dose to 100 mg once daily (in the morning). Losartan may be administered with other antihypertensive agents, such as diuretics (e.g. hydrochlorothiazide).
Heart Failure
The usual initial dose of losartan in patients with heart failure is 12.5 mg once daily. The dose should generally be titrated at weekly intervals (i.e. 12.5 mg daily, 25 mg daily, 50 mg daily, 100 mg daily, up to a maximum dose of 150 mg once daily) as tolerated by the patient.
Use in patients with hepatic impairment
A lower dose should be considered for patients with a history of hepatic impairment. There is no therapeutic experience in patients with severe hepatic impairment. Therefore, losartan is contraindicated in patients with severe hepatic impairment.
Patients between 6 months to less than 6 years
The safety and efficacy in children aged 6 months to less than 6 years has not been established.
Patients between 6 years to 18 years
For patients who can swallow tablets, the recommended dose is 25 mg once daily in patients >20 to <50 kg. (In exceptional cases the dose can be increased to a maximum of 50 mg once daily). Dosage should be adjusted according to blood pressure response.
In patients >50 kg, the usual dose is 50 mg once daily. In exceptional cases the dose can be adjusted to a maximum of 100 mg once daily. Doses above 1.4 mg/kg (or in excess of 100 mg) daily have not been studied in paediatric patients.
Losartan is not recommended for use in children under 6 years old, as limited data are available in these patient groups. It is not recommended in children with glomerular filtration rate < 30 ml/min/1.73 m^2, as no data are available. Losartan is also not recommended in children with hepatic impairment.
Use in Elderly
Although consideration should be given to initiating therapy with 25 mg in patients over 75 years of age, dosage adjustment is not usually necessary for the elderly.
Method of administration
Losartan tablets should be swallowed with a glass of water. Losartan tablets may be administered with or without food.
Contraindications
- Hypersensitivity to the active substance or to lactose.
- 2nd and 3rd trimester of pregnancy.
- Severe hepatic impairment.
- Losartan should not be administered with Aliskiren in patients with diabetes mellitus or renal impairment (GFR < 60 ml/min/1.73 m^2).

Special warnings and precautions for use
Hypersensitivity - Patients with a history of angioedema (swelling of the face, lips, throat,etc) should be closely monitored.
Hypotension and Electrolyte/Fluid Imbalance - Symptomatic hypotension, especially after the first dose and after increasing of the dose, may occur in patients who are volume- and/or sodium-depleted by vigorous diuretic therapy, dietary salt restriction, diarrhea or vomiting. These conditions should be corrected prior to administration of losartan, or a lower starting dose should be used.
Electrolyte imbalances - Electrolyte imbalances are common in patients with renal impairment, with or without diabetes, and should be addressed.
Hepatic impairment - Based on pharmacokinetic data which demonstrate significantly increased plasma concentrations of losartan in cirrhotic patients, a lower dose should be considered for patients with a history of hepatic impairment.
Renal impairment - As a consequence of inhibiting the renin-angiotensin system, changes in renal function including renal failure have been reported (in particular, in patients whose renal function is dependent on the renin- angiotensin-aldosterone system such as those with severe cardiac insufficiency or pre-existing renal dysfunction). As with other medicinal products that affect the renin-angiotensin-aldosterone system, increases in blood urea and serum creatinine have also been reported 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 therapy.
Excipients - This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Overdose
Symptoms of intoxication:
Limited data are available with regard to overdose in humans. The most likely manifestation of overdose would be hypotension and tachycardia. Bradycardia could occur from parasympathetic (vagal) stimulation.
Treatment of intoxication:
If symptomatic hypotension should occur, supportive treatment should be instituted.
Stabilisation of the cardiovascular system should be given priority. After oral intake, the administration of a sufficient dose of activated charcoal is indicated. Afterwards, close monitoring of the vital parameters should be performed. Vital parameters should be corrected if necessary. Neither losartan nor the active metabolite can be removed by haemodialysis.

Interaction with other medicinal products and other forms of interaction
- Other antihypertensive agents may increase the hypotensive action of losartan. Concomitant use with other substances which may induce hypotension as an adverse reaction (like tricyclic antidepressants, antipsychotics, baclofen and amifostine) may increase the risk of hypotension.
- As with other medicinal products that block angiotensin II or its effects, concomitant use of other medicinal products which retain potassium (e.g. potassium-sparing diuretics: amiloride, triamterene, spironolactone) or may increase potassium levels (e.g. heparin), potassium supplements or salt substitutes containing potassium may lead to increases in serum potassium. Co-medication is not advisable.
- Reversible increases in serum lithium concentrations and toxicity have been reported during concomitant administration of lithium with ACE inhibitors. Co-administration of lithium and losartan should be undertaken with caution. If this combination proves essential, serum lithium level monitoring is recommended during concomitant use
- When angiotensin II antagonists are administered simultaneously with NSAIDs (i.e. selective COX-2 inhibitors, acetylsalicylic acid at anti-inflammatory doses and non-selective NSAIDs), attenuation of the antihypertensive effect may occur. Concomitant use of angiotensin II antagonists or diuretics 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.
- Dual blockade (e.g., by adding an ACE-inhibitor or aliskiren to an angiotensin II receptor antagonist) should be limited to individually defined cases with close monitoring of blood pressure, renal function, and electrolytes. Do not co-administer aliskiren with losartan in patients with diabetes or in patients with renal impairment (GFR < 60 ml/min.)

Use in pregnancy and lactation.
The use of losartan is not recommended during the first trimester of pregnancy. The use of losartan is contra-indicated during the 2nd and 3rd trimester of pregnancy.
Should exposure to losartan have occurred from the second trimester of pregnancy, ultrasound check of renal function and skull is recommended.
Infants whose mothers have taken losartan should be closely observed for hypotension.

Presentation
Lorsa 50mg: Available in blister packs of 3x10's packed in unit boxes.
Lorsa 100mg: Available in blister packs of 3x10's packed in unit boxes.

Storage:
Do not store above 30°C. Store in the original package in order to protect from moisture. Store in a dry place. Protect from direct sunlight. Keep out of reach of children.

Legal category:
Prescription only medicines.

Manufactured by:

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