LOSI-25

LOSARTAN POTASSIUM TABLETS BP 25 MG

COMPOSITION:
Each film coated tablet contains:
Losartan Potassium BP 25mg
Excipients q.s.
Colour: Titanium Dioxide BP

DESCRIPTION:
Losartan Tablets contains Losartan Potassium BP 25 mg indicated for the treatment of essential hypertension in adults and in children, renal disease in adult patients with hypertension and type 2 diabetes mellitus with proteinuria ≥0.5g/day as part of an antihypertensive treatment.
It is also used in treatment of chronic heart failure in adult patients.

INDICATION:
- 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 ≥0.5g/day as part of an antihypertensive treatment.
- Treatment of chronic heart failure in adult patients, when treatment with 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. The patients should have a left ventricular ejection fraction ≤40% and should be stabilised under the treatment of the chronic heart failure.
- Reduction in the risk of stroke in adult hypertensive patients with left ventricular hypertrophy documented by ECG

PHARMACOKINETICS:

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 potassium is approx. 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.
Biotransformation
About 14% of an intravenously or orally administered dose of Losartan is converted to its active metabolite. Following oral and intravenous administration of 14 C-labelled Losartan, circulating plasma radioactivity primarily is attributed to Losartan and its active metabolite.
Elimination
Plasma clearance of Losartan and its active metabolite is about 600 ml/minute and 50 ml/minute, respectively. Renal clearance of Losartan and its active metabolite is about 74 ml/minute and 26 ml/minute, 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. The pharmacokinetics of Losartan and its active metabolite are linear with oral Losartan potassium doses up to 200 mg.
Characteristics in patients
In patients with mild to moderate alcohol-induced hepatic cirrhosis, the plasma levels of Losartan and its active metabolite after oral administration were respectively 5 and 1.7 times higher than in young male volunteers.
Plasma concentrations of Losartan are not altered in patients with creatinine clearance above 10 ml/minute. Compared to patients with normal renal function, the AUC for Losartan is about two times higher in haemodialysis patients.
The plasma concentrations of the active metabolite are not altered in patients with renal impairment or in haemodialysis patients.
Neither Losartan nor the active metabolite can be removed by haemodialysis.
Pharmacokinetics in paediatric patients
The pharmacokinetics of Losartan have been investigated in 50 hypertensive paediatric patients > 1 month to < 16 years of age following once daily oral administration of approximately 0.54 to 0.77 mg/ kg of Losartan (mean doses).

PHARMACODYNAMICS:
Pharmacotherapeutic group: Angiotensin II antagonists, plain
ATC code: C09CA01
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. Losartan selectively blocks the AT1 receptor. In vitro and in vivo, both Losartan and its pharmacologically active carboxylic acid metabolite E-3174 block all physiologically relevant actions of angiotensin II, regardless of its source or route of synthesis.

DOSAGE AND ADMINISTRATION:
Posology
Hypertension
The usual starting and maintenance dose is 50 mg once daily for most patients. 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).
Hypertensive-type II diabetic patients with proteinuria ≤0.5g/day
The usual starting dose is 50 mg once daily. The dose may be increased to 100 mg once daily based on blood pressure response from one month onwards after initiation of therapy. Losartan may be administered with other antihypertensive agents (e.g. diuretics, calcium channel blockers, alpha- or beta-blockers, and centrally acting agents) as well as with insulin and other commonly used hypoglycaemic agents (e.g. Sulfonylureas, Glitazones and Glucosidase inhibitors).
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.
Reduction in the risk of stroke in hypertensive patients with left ventricular hypertrophy documented by ECG.
The usual starting dose is 50mg of Losartan once daily. A low dose of hydrochlorothiazide should be added and/or the dose of Losartan should be increased to 100mg once daily based on blood pressure response.
Special Populations
Use in patients with renal impairment and haemodialysis patients
No initial dosage adjustment is necessary in patients with renal impairment and in haemodialysis patients.
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.
Paediatric populations
6 months – less than 6 years
The safety and efficacy of children aged 6 months to less than 6 years has not been established.
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.
Losartan is also not recommended in children with hepatic impairment.
Use in the 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.

CONTRAINDICATION:
- Hypersensitivity to the active substance or to any of the excipients
- Second and third trimesters of pregnancy
- Severe hepatic impairment
- The concomitant use of Losartan with Aliskiren-containing products is contraindicated in patients with diabetes mellitus or renal impairment.

SPECIAL WARNING AND PRECAUTION FOR USE:
Hypersensitivity:
Angiooedema
Patients with a history of angiooedema (swelling of the face, lips, throat, and/or tongue) should be closely monitored. 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. There is no therapeutic experience with Losartan in patients with severe hepatic impairment. Therefore Losartan must not be administered in patients with severe hepatic impairment.
Losartan is not recommended in children with 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).
Primary hyperaldosteronism
Patients with primary aldosteronism generally will not respond to antihypertensive medicinal products acting through inhibition of the renin-angiotensin system. Therefore, the use of Losartan is not recommended.
Heart failure
In patients with heart failure, with or without renal impairment, there is - as with other medicinal products acting on the renin-angiotensin system - a risk of severe arterial hypotension, and (often acute) renal impairment.
Pregnancy
AIIRAs should not be initiated during pregnancy. Unless continued AIIRA therapy is considered essential, patients planning pregnancy should be changed to alternative antihypertensive treatments which have an established safety profile for use in pregnancy. When pregnancy is diagnosed, treatment with AIIRAs should be stopped immediately, and, if appropriate, alternative therapy should be started.

INTERACTION WITH OTHER MEDICINE AND CONCOMITANT
Other antihypertensive agents may increase the hypotensive effects of Losartan. Concomitant use with other substances inducing hypotension (like tricyclic antidepressants, antipsychotics, Baclofen, and Amifostine), may increase the risk of hypotension. As with other drugs that block angiotensin II or its effects, concomitant use of other drugs which retain Potassium (e.g. Potassium-sparing diuretics: Amiloride, Triamteren, 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. Very rare cases have also been reported with angiotensin II receptor antagonists. 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 simultaniously 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. The combination should be administered with caution, especially in the elderly.

PREGNACY AND LACTATION:
Pregnancy
The use of AIIRAs is not recommended during the first trimester of pregnancy. The use of AIIRAs is contra-indicated during the second and third trimesters of pregnancy.
Epidemiological evidence regarding the risk of teratogenicity following exposure to ACE inhibitors during the first trimester of pregnancy has not been conclusive; however a small increase in risk cannot be excluded.
When pregnancy is diagnosed, treatment with AIIRAs should be stopped immediately, and, if appropriate, alternative therapy should be started.
Exposure to AIIRA therapy during the second and third trimesters is known to induce human fetotoxicity (decreased renal function, oligohydramnios, skull ossification retardation) and neonatal toxicity (renal failure, hypotension, hyperkalaemia).
Infants whose mothers have taken AIIRAs should be closely observed for hypotension .
Breast-feeding
Because no information is available regarding the use of Losartan during breastfeeding, Losartan is not recommended and alternative treatments with better established safety profiles during breast-feeding are preferable, especially while nursing a newborn or preterm infant.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:
No studies on the effects on the ability to drive and use machines have been performed. However, when driving vehicles or operating machinery it must be borne in mind that dizziness or drowsiness may occasionally occur when taking antihypertensive therapy, in particular during initiation of treatment or when the dose is increased.

UNDESIRABLE EFFECT:
The frequencies assigned to all other undesirable reactions (i.e. those occurring at < 1/1000) were mainly determined using post-marketing data and refer to a reporting rate rather than a true frequency.
The following convention has been used for the classification of frequency:
Common ≤1/100 to <1/10
Uncommon ≤ 1/1000 to < 1/100
Hypertension
Nervous system disorders
Common: dizziness
Uncommon: somnolence, headache, sleep disorders
Cardiac disorder
Uncommon: palpitations, angina pectoris
Gastrointestinal disorders
Uncommon: abdominal pain, obstipation
Ear and Labyrith disorder
Common: vertigo
Skin and subcutaneous disorders
Uncommon: Rash
Hypertension and type 2 diabetes with renal disease
Nervous system disorders
Common: dizziness
Vascular disorders
Common: (orthostatic) hypotension (including doserelated orthostatic effects)
General disorders and administration site conditions
Common: asthenia/fatigue

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. Measures are depending on the time of drug intake and kind and severity of symptoms. 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 by removed by haemodialysis.

INCOMPATIBILITY:
Not Applicable

SHELF LIFE:
3 Years

PACKAGING:
10 tablets are packed in Alu-Alu blister and such 10 blisters are packed in a carton along with pack insert.

STORAGE CONDITION:
Store in dry place below 30°C.
Keep out of reach of children.

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