Tablets

LARSEN

Angiotensin II Receptor Antagonist
Losartan potassium BP

Tablets

LARSEN-T

Angiotensin II Receptor Antagonist-Diuretic
Losartan potassium-Hydrochlorothiazide

Action and Clinical Pharmacology: Larsen-T combines the actions of losartan potassium, an angiotensin II receptor antagonist, and that of a thiazide diuretic, hydrochlorothiazide.

Losartan: Losartan antagonizes angiotensin II by blocking the angiotensin type I (AT1) receptor. Angiotensin II is the primary vasoactive hormone of the renin-angiotensin system. Its effects include vasoconstriction and the stimulation of secretion by the adrenal cortex. Losartan, and its active metabolite, block the vasconstrictor and aldosterone-secreting effects of angiotensin II by selective blocking the binding of angiotensin II to AT1 receptor found in many tissues, including vascular smooth muscle. A second type of angiotensin II receptor has been identified as the AT2 receptor, but it plays no known role in cardiovascular homeostasis to date. Both losartan and its active metabolite do not exhibit any agonist activity at the AT1 receptor, and have much greater affinity, in the order of 1 000- fold, for the AT1 receptor than for the AT2 receptor. In vitro binding studies indicate that losartan itself is a reversibile competitive antogonist at the AT1 receptor, while the active metabolite is 10 to 40 times more potent than losartan, and is a reversible, non-competitive antagonist of the AT1 receptor.

Hydrochlorothiazide: Hydrochlorothiazide is a diuretic and antihypertensive which interferes with the renal tubular mechanism of electrolyte reabsorption. It increase excretion of sodium and chloride in approximately equivalent amounts. Natriuresis may be accompanied by some loss of potassium and bicarbonate. While this compound is predominantly a saluretic agent, in vitro studies have shown that it has a carbonic anhydrase inhibitory action which seems to be relatively specific for the renal tublar mechanism. It does not appear to be concentrated in erythrocytes or the brain in sufficient amounts to influence the activity of carbonic anhydrase in those tissues.

Pharmacokinetics: Losartan is an orally active agent that undergoes substantial first-pass metabolism by cytochrome P450 enzymes. It is converted, in part, to an active carboxylic acid metabolite, that is responsible for most of the angiotensin II receptor antagonism that follows oral losartan administration. Mean peak concentration of losartan occur at about 1 hour, and that of its active metabolite at about 3 to 4 hours. Although maximum plasma concentrations of losartan and its active metabolite are approximately equal, the AUC of the metabolite is about 4 times greater than that of losartan.

Hydrochlorothiazide: Hydrochlorothiazide is not metabolized but is eliminated rapidly by the kidney. The plasma half-life is 5.6 to 14.8 hours when the plasma levels can be followed for at least 24hours. At least 61% of the oral dose is eliminated unchanged within 24 hours. Hydrochlorothiazide crosses the placental barrier but not the blood-brain barrier and is excreted in breast milk.

Pharmacodynamics: Losartan inhibit the pressor effect of angiotensin II. A dose of 100mg inhibit this effect by about 85% at peak, with 25 to 40% inhibition persisting for 24 hours. Removal of the negative feedback of angiotensin II cause a 2- to 3- fold rise in plasma renin activity, and a consequent rise in angiotensin II plasma concentration, in hypertensive patients.

Losartan - Hydrochlorothiazide: The components of losartan potassium have been shown to have an additive effect on blood pressure reduction, reducing blood pressure to a greater degree than either component alone.

Indication and Clinical Uses: For the treatment of essential hypertension in patients for whom combination therapy is appropriate. Losartan should normally be used in those patients in whom treartment with diuretic or beta-blocker was found ineffective or has been associated with unacceptable adverse effects.

Contra-Indications: In patients who are hypersensitive to any component of this product. Because of the hydrochlorothiazide component, it is also contraindicated in patients with anuria, and in patients who are hypersensitive to other sulfonamide-derived drugs.

Warnings In Clinical States: Drug that act directly on the second and third trimesters of pregnancy has been associated with fetal and neonatal injury, including hypotension, neonatal skull hypoplasia, anuria, reversible or irreversible renal failure, and death. Oligohydramnios has also been reported, presumably resulting from desreased fetal renal function, oligohydramnios in this setting has been associated with fetal limb contractures, craniofacial deformation and hypoplastic lung development. Prematurity, intrauterine growth retardation, and patent ductus arteriosus have also been reported, although it is not clear whether these occurrences were due to exposure to the drug. These adverse effects do not appear to have resulted from intrauterine drug exposure that has been limited to the first trimester. If oligohydramnios is observed, losartan should be discontinued unless it is considered life-saving for the mother. Contraction stress testing (CST), a nonstress test (NST), or biophysical profiling (BPP) may be appropriate, depending upon the week of pregnancy. Patients and physicians should be aware, however that oligohydramnios may not appear until after the fetus has sustained irreversible injury. Thiazide cross the placental barrier and appear in cord blood. The routine use of diuretics in otherwise healthy pregnant women in not recommended and exposes mother and fetus to unnecessary hazard including fetal or neonatal jaundice, thrombocytopenia and possibly other adverse experiences which have occurred in the adult. Diuretics do not prevent development of toxemia of pregnancy and there is no satisfactory evidence that they are useful in the treatment of toxemia.

Azotemia: Azotemia may be precipitated or increased by hydrochlorothiazide. Cumulative effects of the drug my develop in patients with impaired renal function. If increasing azotemia and oliguria occur during treatment of severe progressive renal disease the diuretic should be discontinued.

Hypersensitivity Reactions: Sensitivity reactions to hydrochlorothiazide may occur in patients with or without a history of allergy or bronchial asthma.

Precautions: As a consequence of inhibiting the renin-angiotensin-aldosterone system, changes in renal functions have seen in susceptible individuals. In patients whose renal function may depend on the activity of the renin-angiotensin-aldosterone system, such as patients with bilateral renal artery stenosis, unilateral renal artery stenosis to a solitary kidney, or severe congestive heart failure, treatment with agents that inhibit this system has been associated with oliguria, progressive azotemia, and rarely, acute renal failure and/or death. In susceptible patients, concomitant diuretic use may further increase risk. Thiazides should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alteration of fluid and electrolyte balance may precipitate hepatic coma. Thiazides may decrease urinary calcium excretion. Thiazide may cause intermittent and slight elevation of serum calcium in the absence of known disorders of calcium metabolism. Marked hypercalcemia may be evidence of hidden hyperparathyroidism. Thiazide should be discontinued before carrying out tests for parathyroid function.

Valvular Stenosis: There is concern on theoretical grounds that patients with aortic stenosis might be at particular risk of decreased coronary perfusion when treated with vasodilators because they do not develop as much afterload reduction.

Lactation: It is not known whether losartan or its active metabolite are excreted in human milk, however significant levels of both of these compounds have been shown to be present in the milk of lactating rats. Thiazide appear in human milk. A decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

Children: Losartan potassium has not been studied in children, therefore use in this age group is not recommended.

Geriatrics: No overall differences in safety were observed between elderly patients and younger patients, but appropriate caution should nevertheless be used when prescribing to the elderly, as increased vulnerability to drug effect is possible in this patients population.

Drug Interactions: Patients on diuretic, and especially those in whom diuretic therapy was recently instituted, may occasionally experience an excessive reduction of blood pressure after inhibition of therapy with losartan. The possibility of symptomatic hypotension with losartan can be minimized by discontinuing the diuretic or increasing the salt intake prior to initiation of treatment with losartan potassium.

Lithium Salt: As with other drug which eliminate sodium, lithium clearance may be reduced in the presence of losartan. Therefore, serum lithium levels should be monitored carefully if lithium salts are to be administered with losartan.

Digitalis: In 9 healthy volunteers, when a single oral dose of 0.5 mg digoxin was administered to patients receiving losartan for 11 days, digoxin AUC and digoxin Cmax ratios, relative to placebo, were found to be 1.06(90% C.I. 0.98 to 1.14) and 1.12 (90% C.I. 0.97 to 1.28), respectively. The effect of losartan on steady-state pharmacokinetics of cardiac glycosides is not known.

Warfarin: Losartan administration for 7 days did not affect the pharmacokinetics or pharmacodynamic activity of a single dose of warfarin. The effects of losartan on steady-state pharmacokinetics of warfarin is not known.

Alcohol, Barbiturates or Narcotics: Diuretic potentiation of orthostatic hypotension may occur.

Corticosteroids, ACTH: Intensified electrolyte depletion, particularly hypokalemia, may occur when given concomitantly with diuretics.

Adverse Reactions: Losartan potassium has been evaluated for safety in 2 498 patients treated for essential hypertension. Of these, 1 088 were treated with Losartan potassium monotherapy in controlled clinical trials. In open studies, 926 patients were treated with losartan potassium for a year or more. Thrombocytopenia and Adult Respiratory Distress Syndrome have been reported rarely in postmarketing experience. In double-blind, controlled clinical trials with losartan alone, the following adverse experience were reported at an occurrence rate of less than 1% regardless of drug relationship: orthostatic effects, somnolence, vertigo, epistaxis, tinnitus, constipation, malaise, rash.

Symptoms And Treatment Of Overdose: No specific information is available on the treatment of overdosage with losartan potassium treatment is symptomatic and supportive.

Losartan: Limited data are available in regard to overdosage in humans. The most likely manifestation of overdosage would be hypotension and tachycardia. If symptomatic hypotension should occur, supportive treatment should be instituted. Neither losartan nor its active metabolite can be removed by hemodialysis.

Hydrochlorothiazide: The most common signs and symptoms observed are caused by electrolyte depletion (hypokalemia, hypochloremia, hyponatremia) and dehydration resulting from excessive diuresis. If digitalis has also been administered, hypokalemia may accentuate cardiac arrhythmias. The degree to which hydrochlorothiazide is removed by hemodialysis has not been established.

Dosage And Administration: Dosage must be individualized. The fixed combination is not for initial therapy. The dose should be determined by the titration of the individual components. Once the patient has been stabilized on the individual components, either one 50/12.5mg tablet or 2 tablets once daily may be substituted if the doses on which the patient was stabilized are the same as those in the fixed combination. Losartan potassium may be administered with or without food, however it should be taken consistently with respect to food intake.

Availability And Storage:

LARSEN-T TABLETS
Each tablet contains:
Losartan potassium 50mg, hydrochlorothiazide 12.5mg. Pack of 20 tablets in blisters.
Store in a cool, dry place. Protect from direct sunlight. Keep out of the reach of children.

LARSEN TABLETS
Each film coated tablet Contains:
Losartan potassium 50mg(BP). Pack of 20 tablets in blisters.
Store in a cool, dry place. Protect from direct sunlight. Keep out of the reach of children.

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لوسارٹن پوٹاشیم بی پی لوسارٹن پوٹاشیم + ہائیڈروکلوروتھائیزائیڈ

دھوپ، گرمی اور نمی سے محفوظ رکھیں۔
تمام ادویات بچوں کی پہنچ سے دور رکھیں۔
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Manufactured by :
Pharmedic Laboratories (Pvt) Limited.
16 Km. Multan Road, Lahore - Pakistan