LOSATRUST - H Tablets

Composition
Each film-coated tablet contains Losartan Potassium 50 mg and Hydrochlorothiazide IP 12.5 mg

Description
LOSATRUST-H is a fixed-dose combination containing Losartan and Hydrochlorothiazide.

Losartan is an orally active, nonpeptide angiotensin II (A II) receptor antagonist. It binds competitively and selectively to the A II subtype 1 (AT1) receptor thereby blocking A II induced effects. This leads to decreased vasopressor activity and aldosterone secretion. The active metabolite of losartan, a carboxylic acid derivative, contributes substantially to its antihypertensive effect which persists for 24 hours following once-daily administration.

Hydrochlorothiazide is a thiazide diuretic. It has a complex mechanism of action, including natriuresis and vasodilation.

Reduction in blood volume brought about by hydrochlorothiazide activates the renin angiotensin system (RAS). Hydrochlorothiazide also decreases serum potassium, as a result of its diuretic effects. Administration of losartan blocks the activation of the RAS and reverses the potassium loss associated with the diuretic. The combination of losartan and hydrochlorothiazide has an additive effect on blood pressure control which is sustained for at least 24 hours.

Indications
Hypertension not responding to monotherapy with Losartan or diuretics.

Dosage and Administration
The usual initial dosage is one tablet of **LOSATRUST - H** daily. It may be increased, if necessary, to two tablets of **LOSATRUST - H** daily. The dosage however should be individualised. The maximal antihypertensive effect is attained about 3 weeks after initiation of therapy. The combination is not meant for initial therapy. It may be substituted for the titrated individual components. It may be administered with other antihypertensive agents.

Contraindications
Hypersensitivity to either component, hypersensitivity to other sulfonamide-derived drugs, anuria, pregnancy

Warnings and Precautions

DRUG INTERACTIONS
Alcohol, barbiturates, or narcotics: Potentiation of orthostatic hypotension may occur.

Antidiabetic drugs (oral agents and insulin): Dosage adjustment of the antidiabetic drug may be required.

Cholestyramine and colestipol resins: Absorption of hydrochlorothiazide is impaired in the presence of anionic exchange resins. Single doses of either cholestyramine or colestipol resins bind the hydrochlorothiazide and reduce its absorption from the gastrointestinal tract by up to 85 and 43 percent, respectively.

Corticosteroids/ACTH: Intensified electrolyte depletion, particularly hypokalemia may occur.

Pressor amines (e.g. norepinephrine): Response to pressor amines may be increased.

Nondepolarizing skeletal muscle relaxants: Responsiveness to the muscle relaxant may be increased.

Lithium: Diuretic agents reduce the renal clearance of lithium and add a high risk of lithium toxicity.

Non-steroidal anti-inflammatory agents: In some patients, the administration of a non-steroidal anti-inflammatory agent can reduce the antihypertensive effects of **LOSATRUST - H**. Patients receiving these medications concomitantly should be observed closely to determine if the desired antihypertensive effect is obtained.

POTASSIUM SUPPLEMENTS
Patients receiving **LOSATRUST - H** should be told not to use potassium supplements or salt substitutes containing potassium without consulting the prescribing physician.

SYMPTOMATIC HYPOTENSION
Inadequate fluid intake, excessive perspiration, diarrhoea, or vomiting can lead to an excessive fall in blood pressure, with the consequences of lightheadedness and possible syncope.

HYPOTENSION - VOLUME DEPLETED PATIENTS
In patients who are intravascularly volume-depleted (e.g. those treated with diuretics), symptomatic hypotension may occur after initiation of therapy with **LOSATRUST - H**. This condition should be corrected prior to administration of **LOSATRUST - H**.

HYPERSENSITIVITY REACTION
Hypersensitivity reactions to hydrochlorothiazide may occur in patients with or without a history of allergy or bronchial asthma, but are more likely in patients with such a history.

SYSTEMIC LUPUS ERYTHEMATOSUS
Thiazide diuretics have been reported to cause exacerbation or activation of systemic lupus erythematosus.

PREGNANCY
When used in pregnancy during the second and third trimesters, ACE inhibitors can cause injury and death to the developing foetus. Hence the combination is contraindicated in pregnancy.

NURSING MOTHERS
It is not known whether losartan is excreted in human milk, but significant levels of losartan and its active metabolite were shown to be present in human milk. Thiazides appear in human milk. Because of the potential for adverse effects on the nursing infant, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

PAEDIATRIC USE
Safety and effectiveness in paediatric patients have not been established.

RENAL IMPAIRMENT
Effects similar to those occurring with ACE inhibitors should be anticipated since losartan also interferes with the RAS. In patients whose renal function may depend on the activity of the RAS (e.g. patients with severe congestive heart failure, patients with unilateral or bilateral renal stenosis), treatment with ACE inhibitors has been associated with oliguria, azotemia, increases in serum creatinine and blood urea nitrogen have been reported. Similar effects have been reported with losartan. Thiazides should be used with caution in severe renal disease. In patients with renal disease thiazides may precipitate azotemia. Cumulative effects of the drug may develop in patients with impaired renal function.

HEPATIC IMPAIRMENT
LOSATRUST - H is not recommended for titration in patients with hepatic impairment because the appropriate 25 mg starting dose of losartan cannot be given.

Side Effects
The combination of losartan and hydrochlorothiazide is well tolerated. The overall incidence of adverse experiences reported with the combination was comparable to placebo. The commonly observed side effects include headache, dizziness, abdominal pain, asthenia/fatigue, edema, occasional increases in liver enzymes, blood urea or serum creatinine. Angioedema has been reported rarely.

Overdosage
Losartan: Limited data is available regarding overdosage in humans. The most likely manifestation of overdosage would be hypotension and tachycardia; bradycardia could occur due to vagal stimulation. If symptomatic hypotension should occur, supportive treatment should be instituted. Neither losartan nor its active metabolite can be removed by dialysis.

Hydrochlorothiazide: The most common signs and symptoms observed are those 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.

Presentation

LOSATRUST - H (Strip of 10 tablets)