LOZILON-H

COMPOSITION

LOZILON-H Tablets
Each film-coated tablet contains:
Losartan Potassium 50 mg
Hydrochlorothiazide IP 12.5 mg

DOSAGE FORM

Tablet

DESCRIPTION

LOZILON-H is a fixed-dose combination containing losartan, an angiotensin II receptor (type AT1) antagonist, and hydrochlorothiazide, a thiazide diuretic. This combination provides synergistic blood pressure reduction in hypertension patients.

INDICATIONS

→**Hypertension**: LOZILON-H is indicated for the treatment of hypertension. This fixed-dose combination is not indicated for initial therapy of hypertension, except when the hypertension is severe enough that the value of achieving prompt blood pressure control exceeds the risk of initiating combination therapy in these patients.

→**Hypertensive patients with left ventricular hypertrophy :** LOZILON-H is indicated to reduce the risk of stroke in patients with hypertension and left ventricular hypertrophy.

DOSAGE AND ADMINISTRATION

→**Hypertension:** The usual initial dosage is one tablet of LOZILON-H daily. It may be increased, if necessary, to two tablets of LOZILON-H once daily. The dosage however should be individualized. 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. It may be administered with or without food.

→**Use in Patients with Renal Impairment :** The usual regimens of therapy with LOZILON-H may be followed as long as the patient's creatinine clearance is >30 mL/min. LOZILON-H is not recommended in patients with more severe renal impairment.

→**Patients with Hepatic Impairment :** LOZILON-H is not recommended for titration in patients with hepatic impairment because the appropriate 25 mg starting dose of losartan cannot be given.

→**Hypertensive Patients with Left Ventricular Hypertrophy :** Treatment should be initiated with losartan 50 mg once daily. If the blood pressure reduction is inadequate, LOZILON-H should be substituted. If additional blood pressure reduction is

needed, the dose may be increased to two tablets of LOZILON-H daily. For further blood pressure reduction, other antihypertensives should be added.

CONTRAINDICATIONS

- Hypersensitivity to either component
- Hypersensitivity to other sulfonamide-derived drugs
- Anuria

WARNINGS AND PRECAUTIONS

Drug Interactions

Rifampin: Rifampin, an inducer of drug metabolism, decreased the concentrations of losartan and its active metabolite.

Fluconazole: Fluconazole, an inhibitor of P450 2C9, decreased active metabolite concentration and increased losartan concentration.Agents That Increase Serum Potassium: As with other drugs that block angiotensin II or its effects, concomitant use of potassium-sparing diuretics (e.g.,spironolactone, triamterene, amiloride), potassium supplements or salt substitutes containing potassium may lead to increases in serum potassium. 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 cholestyramine and colestipol 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 (eg, norepinephrine): Possible decreased response to pressor amines but not sufficient to preclude their use.

Non-Depolarizing Skeletal Muscle Relaxants (e.g., tubocurarine): 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. Lithium should not generally be given with LOZILON-H.

Non-Steroidal Anti-Inflammatory Agents (NSAIDs) including Selective Cyclooxygenase-2 Inhibitors: In some patients with compromised renal function who are being treated with NSAIDs, including those that selectively inhibit cyclooxygenase-2 inhibitors (COX-2 inhibitors), the co-administration of losartan may result in a further deterioration of renal function. These effects are usually reversible. Reports suggest that NSAIDs, including selective COX-2 inhibitors, can reduce the diuretic, natriuretic effects of thiazide diuretics and may diminish the antihypertensive effects of thiazide diuretics and losartan. Therefore, when LOZILON-H and non-steroidal anti-inflammatory agents including selective cyclooxygenase-2 inhibitors are used concomitantly, the patient should be observed closely to determine if the desired effect of the diuretic is obtained.

Symptomatic Hypotension: Inadequate fluid intake, excessive perspiration, diarrhea, 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 (eg, those treated with diuretics), symptomatic hypotension may occur after initiation of therapy with LOZILON-H. This condition should be corrected prior to administration of LOZILON-H.

Systemic Lupus Erythematosus:Thiazide diuretics have been reported to cause exacerbation or activation of systemic lupus erythematosus.

General

Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. Hydrochlorothiazide therapy is associated with electrolyte imbalance, namely, hyponatremia, hypochloremic alkalosis, and hypokalemia. Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Warning signs or symptoms of fluid and electrolyte imbalance, irrespective of cause, include dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, confusion, seizures, muscle pains or cramps, muscular faigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbances such as nausea and vomiting. Hypokalemia may develop, especially with brisk diuresis, when severe cirrhosis is present or after prolonged therapy. Interference with adequate oral electrolye intake will also contribute to hypokalemia. Hypokalemia may cause cardiac arrhythmia and may also sensitize or exaggerate the response of the heart to the toxic effects of digitalis (e.g., increased ventricular irritability). Chloride replacement may be required in the treatment of metabolic alkalosis. Dilutional hyponatremia may occur in edematous patients in hot weather. Hyperuricemia may occur or acute gout may be recipitated in certain patients receiving thiazides. Hyperglycemia may occur with thiazide diuretics. Hydrochlorothiazide has been shown to increase the urinary excretion of magnesium; this may result in hypomagnesemia. Hydrochlorothiazide may decrease urinary calcium excretion. Hydrochlorothiazide may cause intermittent and slight elevation of serum calcium in the absence of known disorders of calcium metabolism. Hydrochlorothiazide should be discontinued before carrying out tests for parathyroid function. Increases in cholesterol and triglyceride levels may be associated with hydrochlorothiazide therapy.

Renal Impairment

As a consequence of inhibiting the renin-angiotensin-aldosterone system, changes in renal function have been reported in susceptible individuals treated with losartan; in some patients, these changes in renal function were reversible upon discontinuation of therapy. Losartan treatment in patients whose renal function may depend on the activity of the renin angiotensin aldosterone system (eg, patients with severe congestive heart failure) has been associated with oliguria and/or progressive azotemia and, rarely, with acute renal failure and/or death. Also, losartan treatment in patients with unilateral or bilateral renal artery stenosis was associated with increases in serum creatinine or blood urea nitrogen (BUN). In some patients, these effects were reversible upon discontinuation of therapy. 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

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

Pregnancy

Drugs that act directly on the renin angiotensin aldosterone system can cause fetal and neonatal morbidity and death when administered to pregnant women. Hence, the combination is contraindicated in pregnancy.

Lactation

It is not known whether losartan is excreted 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.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

UNDESIRABLE 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, and occasional increases in liver enzymes, blood urea or serum creatinine. Angioedema has been reported rarely.

OVERDOSAGE

Losartan

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 hemodialysis.

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.

PACKAGING INFORMATION

LOZILON-H Alu-Alu pack of 10 tablets