℞

Losartan Tablets IP

ZARGO® - 25/50 ज़ारगो– 25/50

COMPOSITION
ZARGO® -25
Each film coated tablet contains
Losartan potassium IP 25mg

ZARGO® -50
Each film coated tablet contains
Losartan potassium IP 50mg

DESCRIPTION
Losartan potassium, the first of a new class of antihypertensives, is an angiotensin II receptor (type AT1) antagonist. Chemically it is described as 2-Buty 4-choro-1 [(IH tetrazol-5) (1,1'-biphenyl)-4yl] methyl)-1H-imdazole-5 methanol. Losartan and its Principal active metabolite block the vasoconstrictor and aldosterone-secreting effects of angiotensin II by selectively blocking the binding of angiotensin II to the AT1receptor found in many tissues (e.g. vascular smooth muscle, adrenal gland). In vitro binding studies indicate that Losartan is a reversible, competitive inhibitor of the AT1receptor. The active metabolite is 10 to 40 times more potent by weight than losartan and appears to be a reversible non-competitive inhibitor of the AT1 receptor.

PHARMACOKINETICS
Following oral administration, losartan is well absorbed and undergoes substantial first-passs metabolism. The systemic bioavailability of losartan is approximately 33%, About 14% of an orally administered dose of losartan is converted to the active metabolite. Mean peak plasma concentrations of losartan and its active metabolite are reached in 1 hour and 3-4 hours respectively. While maximum plasma concentrations of Losartan and its active metabolite are approximately equal, the AUC of the metabolite is about 4 times as great as that of Losartan. A meal slows absorption of losartan and decreases its Cmax-but has only minor effects on losartan AUC or on the AUC of the metabolite (about 10% decrease). Both Losartan and its active metabolite are highly bound to plasma proteins, primarily albumin, with plasma free fractions of 1.3% and 0.2% respectively. Studies in rats indicate that Losartan crosses the blood-brain barrier poorly, if at all about 4% of the dose is excreted unchanged in urine and about 6% is excreted unchanged in urine as active metabolite. Biliary excretion contributes to the elimination of Losartan and its metabolites.

Losartan pharmacokinetics have not been investigated in patients <18 years of age Losartan pharmacokinetics have been investigated in the elderly(65-75 years) and in both genders. Plasma concentrations of losartan and its active metabolite are similar in elderly and young hypertensives. Plasma concentrations of losartan are about twice as high in female hypertensives as in male hypertensives. But concentrations of the active metabolite are similar in males and females. No dosage adjustment is necessary.

INDICATIONS
Losartan potassium is indicated for the treatment of mild to moderate hypertension. It may be used alone or in combination with other antihypertensive agents.

CONTRAINDICATIONS AND PRECAUTIONS
Losartan potassium is contraindicated in patients who are hypersensitive to it.

A lower dose of losartan potassium should be considered for patients with impaired liver function. As a consequence of inhibiting the renin-angiotensin-aldosterone system, changes in renal function have been reported in susceptible individuals treated with losartan potassium. In some patients these changes in renal function were reversible upon discontinuation of therapy.

In patients whose renal function may depend on the activity of the renin-angiotensin aldosterone system (e.g. patients with severe congestive heart failure). treatment with losartan potassium has been associated with oliguria and /or death. In patients with unilateral or bilateral renal artery stenosis increases in serum creatinine or BUN have been reported with oral adminstration of losartan potassium in some patients these effects with reversible upon discontinuation of therapy.

In patients who are intravascularly volume-depleted (e.g. those treated with diuretics) symptomatic hypotension may occur after initiation of therapy with losartan potassium.

These conditions should be corrected prior to administration of losartan potassium or a lower starting dose should be used.

℞

Losartan Tablets IP

ZARGO® - 25/50 ज़ारगो– 25/50

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

Safety and effectiveness in paediatric patients has not been established.

No overall differences in effectiveness or safety were observed between elder and younger patients but greater sensitivity of some older individuals cannot be ruled out.

USE IN PREGNANCY
When used in pregnancy during the second and third trimester drugs that act directly on the renin angiotensin system can cause injury and even death to developing fetus. When pregnancy is detected, losartan should be discontinued as soon as possible.

ADVERSE EFFECTS
Losartan potassium is well tolerated. Adverse effects are generally rare but those seen most often are dizziness or light-headedness and rash. Angioedema (involving swelling of face, lips and/or tongue) have been rarely reported in patients treated with losartan potassium. Drug related adverse events experienced most frequently with losartan potassium were headache (4.2%), asthenia, fatigue (2%) and also dizziness, which was the only drug related adverse event reported more frequently with losartan potassium than with placebo (5.7 VS 2.9%) Clinically important changes in standard laboratory parameters were rarely associated with losartan potassium therapy. All this data is as obtained from various clinical trial reports.

DRUG INTERACTIONS
Losartan potassium does not affect the pharmacokinetics or pharmacodynamics of a single dose of warfarin and also of intravenous or oral digoxin. Coadministration of losartan potassium and cimetidine leads to an increase of about 18% in AUC of losartan potassium but does not affect the pharmacokinetics of its active metabolite. There is no pharmacokinetic interaction between losartan potassium and hydrochlorothiazide.

DOASGE AND ADMINISTRATION
The usual starting dose of Zargo is 50 mg once daily with 25 mg used in patients with possible depletion of intravascular volume (e.g. patients treated with diuretics) and patients with a history of hepatic impairment. Zargo can be administered once or twice daily with total daily doses ranging from 25 mg to 100 mg. No dosage adjustment is necessary for elderly patients or for patients with renal impairment, including patients on dialysis Zargo may be administered with other antihypertensive agents. Zargo may be administered with or without food.

OVERDOSAGE
Significant lethality was observed on mice and rats, after oral administration of 1000 mg/Kg and 2000 mg/kg respectively. The most likely manifestation of overdosage would be hypotension and tachycardia.Bradycardia could occur from parasympathetic (vagal) stimulation.

If symptomatic hypotension occurs, supportive treatment should be instituted.

STORAGE
Store protected from light and moisture

PRESENTATION
ZARGO® -25 : Alu-Alu Foil Strip of 10 tablets
ZARGO® -50 : Alu-AluFoil Strip of 10 tablets

Manufactured by:
Swiss Garnier Life Sciences,
21 to 23, Industrial Area,
Mehatpur, Dist. UNA,
Himachal Pradesh - 174 315

Marketed by:
Biocon Limited
20th KM, Hosur Road,
Electronics City,
Bangalore – 560100

BF/LL/008/1.00