Tansin®

(Losartan potassium 50mg)

ٹین سِن

Tansin-DS®

(Losartan potassium 100mg.)

ٹین سِن - ڈی ایس

COMPOSITION:

Each film-coated tablet of TANSIN® contains:
Losartan potassium ..... 50 mg.
Each film-coated tablet of TANSIN-DS® contains:
Losartan potassium .....100mg.

DESCRIPTION:

Losartan potassium, the first of a new class of antihypertensives, is an angiotensin II receptor (type AT1) antagonist. Losartan potassium, a non-peptide molecule, is chemically described as 2-buty-4-chloro-1-[p-1H-tetrazol-5-ylphenyl)-benzyl]imidazole-5-methanol monopotasium salt. Its empirical formula is $C_{22}H_{22}ClKN_6O$ having molecular weight of 461.01.

CLINICAL PHARMACOLOGY:

Mechanism of Action

Angiotensin II formed from angiotensin I in a reaction catalyzed by angiotensin converting enzyme (ACE, kininase II), is a potent vasoconstrictor, the primary vasoactive hormone of the renin-angiotensin system and an important component in the pathophysiology of hypertension. It also stimulates aldosterone secretion by the adrenal cortex. Losartan potassium 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 AT1 receptor found in many tissues, (e.g., vascular smooth muscle, adrenal gland). There is also an AT_2 receptor found in many tissues but it is not known to be associated with cardiovascular homeostasis. Both Losartan potassium and its principal active metabolite do not exhibit any partial agonist activity at the AT1 receptor and have much greater affinity (about 1000-fold) for the AT1 receptor than for the AT2 receptor. In vitro binding studies indicate that Losartan potassium is a reversible is 10 to 40 times inhibitor of the AT1 receptor. The active metabolite is 10 to 40 times more potent by weight than Losartan potassium and appears to be a reversible, non-competitve inhibitor of the AT1 receptor. Neither Losartan potassium nor tis active metabolite in hibits ACE (Kininase II, the enzyme that converts angiotensin I to angiotensin II and degrades bradykinin); nor do they bind to or block other hormone receptors or ion channels known to be important in cardiovascular regulation.

Pharmacokinetics

Losartan potassium 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 Losartan potassium treatments. The terminal half-life of Losartan potassium is about 2 hours and of the metabolite is about 6-9 hours. The pharmacokinetic of Losartan potassium and ots active metabolite are linear with oral Losartan potassium doses up to 200 mg and do not change over time. Neither Losartan potassium nor its metabolite accumlates in plasma upon repeated once-daily dosing.

Following oral administration, Losartan potassium is well absorbed (based on absorption of radio-labeled losartan) and undergoes substantial first-pass metabolism; the systemic bioavailability of Losartan potassium is approximately 33%. Mean peak concentrations of Losartan potassium and its active metabolite are reached in 1 hour and in 3-4 hours, respectively. Both Losartan potassium and its active metabolite are highly bound to plasma proteins, primarily albumin, with plasma free fractions of 1.3% and 0.2% respectively. The volume of distribution of Losartan potassium is about 34 liters and of the active metabolite is about 12 liters. Total plasma clearance of Losartan potassium and the active metabolite is about 600 ml/min and 50 ml/min, respectively with renal clearance of about 75 ml/min and 25 ml/min, respectively. When Losartan potassium is administered orally, about 4% of the dose is exceted unchanged in the urine and about 6% is exceted in urine as active metabolite. Biliary excretion contributes to the elimination of Losartan potassium and its metabolites. Following oral 14C-labeled Losartan potassium, about 35% of radioactivity is recovered in the urine and about 60% in the feces. Following an intravenous dose of 14C-labeled Losartan potassium, about 45% of radioactivity is recovered in the urine and 50% in the feces.

INDICATIONS:

TANSIN® & TANSIN-DS® is indicated for the treatment of hypertension. It may be used alone or in combination with other antihypertensive agensts.

DOSAGE & ADMINISTRATION:

The usual starting and maintenance dose is 50 mg once daily for most patients. The maximal antihypertensive effect is attained within 3-6 weeks after initiation of therapy. For patients with intravascular volume - depletion (e.g., those treated with high - dose diuretics), a starting dose of 25mg once daily should be considered (see PRE-CAUTIONS). Losartan can be administered once or twice daily with total daily doses ranging from 25mg to 100mg.No initial dosage adjustment is necessary for elderly patients or for patients with renal impairment including patients on dialysis. A lower dose should be considered for patients with a history of hepatic impairment (see PRE CAUTIONS). TANSIN® & TANSIN-DS® my be administered with other antihypertensive agents.TANSIN® & TANSIN-DS® can be administered with or without food.

CONTRAINDICATIONS:

Losartan potassium is contraindicated in patients who are hypersensitive to any component of this product.

PRECAUTIONS:

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 Losartan potassium. These conditions should be corrected prior to administration of Losartan Potassium or a lower starting dose should be used (see DOSAGE & ADMINISTRATION).

Impaired Renal Function:

As a consequence of inhibiting the renin-angiotensin system, changes in renal function including renal failure have been reported in susceptible individuals; these changes in renal function may be reversible upon discontinuation of therapy.

Other drugs that affect the renin-angiotensin system may increase

blood urea and serum creatinine in patients with bilateral renal artery stenosis or stenosis of the artery to a solitary kidney. Similar effects have been reported with Losartan potassium; these changes in renal function may be reversible upon discontinuation of therapy.

Impaired Hepatic Function:
Based on pharmacokinetic data, which demonstrates significantly increased plasma concentrations of Losartan potassium in cirrhotic patients, a lower dose should be considered for patients with impaired liver function (see DOSAGE & ADMINISTRATION).

PREGNANCY:
Drugs that act directly on the renin-angiotensin system can cause fetal and neonatal morbidity and death when administered to pregnant women. When pregnancy is detected Losartan potassium should be discontinued as soon as possible.

NURSING MOTHERS:
It is not known whether Losartan potassium is excreted in human milk. Because many drugs are excreted in human milk and because of the potential of adverse effects on the nursing infact, 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.

USE IN THE ELDERLY:
In clinical studies there was no age-related difference in the efficacy or safety profile of Losartan potassium.

DRUG INTERACTIONS:
No significant drug-drug pharmacokinetic interactions have been found in interaction studies with hydrochlorothiazide, digoxin, warfarin, cimetidine and phenobarbital and ketoconazole. 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 substituts containing potassium may lead to increases in serum potassium.

ADVERSE REACTIONS:
Losartan potassium has been found to be generally well tolerated in controlled clinical trials for hypertnesion; side effects have usually been mild and transient in nature and have not required discontinuation of therapy. The overall incidence of side effects reported with Losartan potassium was comparable to placebo. In controlled clinical trials for essential hypertension, dizziness was the only side effect reported as drugs related that occurred with an incidence greater than placebo in one percnet ot more of patients treated with Losartan potassium. In addition, dose-related orthostatic effects were seen in less than one percent of the patients. Rarely, rash was reported, although the incidence in controlled clinical trials was less than placebo.
The following additional adverse reactions were reported:
Hypersenitivity : Angioedema including swelling of the larynx and glottis causing airway obstruction and/or (sweling of the face, lips, pharynx and/or tongue) has been reported rarely with losartan; some fo these patients previosly experienced angioedema with other drugs including ACE inhibitors.
Gastrointestinal: Hepatitis (reported rarely), liver function abnormalities;
Hematologic: Anemia
Musculoskeletal: Myalgia
Nervous System/Psychiatric:Migraine
Skin: Urticaria, pruritus.

LABORATORY TEST FINDINGS:
In controlled clinical trials, clinically important changes in standard laboratory parameters were rarely associated with administration of Losartan potassium. Hyperkalemia (serum potassium > 5.5mEq/L) occurred in 1.5% of patients. Elevations of ALT occurred rarely and usually resolved upon discontinuation of therapy.

OVERDOSAGE:
Limited data are available in regard to overdosage in humans. The most likely manifestation of overdosage would be hypotension and tachycardia; bradycardia could occur from parasympathetic (vagai) stimulation. If symptomatic hypotension should occur, supportive treatment should be instituted.
Neither Losartan potassium nor its active metabolite can be removed by hemodialysis.

STORAGE:
Store below 30 C, protect from light and moisture.

PRESENTATION:
TANSIN® Box of 10 film-coated tablets packed in blister.
TANSIN-DS® Box of 10 film-coated tablets packed in blister.

ہدایت:۔

ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
تمام دوائیں بچوں کی پہنچ سے دُور رکھیں۔
صِرف رجسٹرڈ ڈاکٹر کے نسخہ پر ہی فروخت کی جائے۔
روشنی اور نمی سے محفوظ ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔

PharmEvo®

Our dream, a healthier society

Manufactureed by:

PharmEvo (Pvt.) Ltd.

Plot # A-29, North Western Industrial Zone,
Port Qasim Karachi-75020, Pakistan.
www.pharmevo.biz