STORAGE
Store below 30°C in a dry place, protect from light.
To be dispensed on the prescription of a registered medical practitioner only.
Keep out of the reach of children

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
دوا کو ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر خشک جگہ پر رکھیں،
روشنی سے بچائیں۔ صرف رجسٹرڈ ڈاکٹر کے نسخے پر فروخت کریں۔
بچوں کی پہنچ سے دُور رکھیں۔

Note: Product contains lactose. **نوٹ:** پروڈکٹ میں لیکٹوز شامل ہے۔

Manufactured by:
Platinum
Pharmaceuticals (Pvt) Ltd.
A-20, North Western Industrial Zone,
Bin Qasim, Karachi-75020, Pakistan.

QAR No.AW21-0746

Losar-K
(Losartan Potassium)

لوسار-کے
(لوسارٹن پوٹاشیم)

COMPOSITION:
Each film-coated tablet contains
Losartan Potassium (U.S.P.) ... 50 mg
Product Complies U.S.P. Specs.

DESCRIPTION:
Losartan Potassium, the first of a new class of antihypertensives, is an angiotensin II receptor (type AT_1) antagonist. Losartan Potassium, a non-peptide molecule, is chemically described as 2-butyl-4-chloro-1-[p-(o-1H-tetrazol-5-ylphenyl)-benzyl]imidazole-5-methanol monopotassium 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 AT_1 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 AT_1 receptor and have much greater affinity (about 1000 fold) for the AT_1 receptor than for the AT_2 receptor. In vitro binding studies indicate that Losartan Potassium is a reversible, competitive inhibitor of the AT_1 receptor. The active metabolite is 10 to 40 times more potent by weight than Losartan Potassium and appears to be a reversible, non-competitive inhibitor of the AT_1 receptor. Neither Losartan Potassium nor its active metabolite inhibits ACE (kininase II, the enzyme that convert 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 P_{450} 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 treatment. The terminal half-life of Losartan Potassium is about 2 hours and of the metabolite is about 6-9 hours. The pharmacokinetics of Losartan Potassium and its 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 accumulates 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 high 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 excreted unchanged in the urine and about 6% is excreted in urine as active metabolite. Biliary excretion contributes to the elimination of Losartan Potassium and its metabolites. Following oral ^{14}C-labeled Losartan Potassium, about 35% of radioactivity is recovered in the urine and about 60% in the feces. Following an intravenous dose of ^{14}C-labeled Losartan Potassium, about 45% of radioactivity is recovered in the urine and 50% in the feces.

INDICATIONS: Losar-K is indicated for the treatment of hypertension. It may be used alone or in combination with other antihypertensive agents.

DOSAGE & ADMINISTRATION: The usual starting and maintenance dose of Losar-K is 50 mg once daily for most patients. The maximal antihypertensive effects attained within 3-6 weeks after initiation of therapy. Some patients may received an additional benefit by increasing the dose to 100 mg once daily. For patients with intravascular volume-depletion (e.g. Those treated with high dose diuretics), a starting dose of 25 mg once daily should be considered. (see PRECAUTIONS). 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 patient with a history of hepatic impairment (see PRECAUTION) Losar-K may be administered with other antihypertensive agents. Losar-K may 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 intravascular 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 has 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 AND 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 weather 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 infant, a decision should be made weather 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 ELDERLY: In clinical studies there was no age-related difference in the efficacy or safety profile of Losartan Potassium.

DRUG INTERACTIONS: No significant drug pharmacokinetic interactions have been found in interaction studies with hydrochlorothiazide, digoxin, warfarin, cimetidine, phenobarbital and ketoconazole. As with other drugs that block angiotensin II or its effects, concomitant use of potassium-sparing diuretics (e.g. spironolactone, triamterene, and amiloride), potassium supplements, or salt substitutes 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 hypertension; 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 drug related that occurred with an incidence greater than placebo in 1% or more of patients treated with Losartan Potassium. In addition, dose-related orthostatic effects were seen in less than 1% of the patients. Rarely, rash was reported, although the incidence in controlled clinical trial was less than placebo.
The following additional adverse reactions were reported:
Hypersensitivity: angioedema including swelling of the larynx and glottis causing airway obstruction and/or (swelling of the face, lips, pharynx and/or tongue) have been reported rarely with Losartan; some of these patients previously 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.

OVER DOSAGE: 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 (vagal) stimulation. If symptomatic hypotension should occur, supportive treatment should be instituted.
Neither Losartan Potassium nor its active metabolite can be removed by hemodialysis.

PRESENTATION: Box of 20 film-coated tablets packed in blister.