were rarely associated with administration of **Losar Plus**. Hyperkalemia (serum potassium >5.5 mEq/L) occurred in 0.7% of patients, but in these trials, discontinuation of **Losar Plus** due to hyperkalemia was not necessary. Elevations of ALT occurred rarely and usually resolved upon discontinuation of therapy.

Overdosage
No specific information is available on the treatment of overdosage with **Losar Plus**. Treatment is symptomatic and supportive. Therapy with **Losar Plus** should be discontinued and the patient observed closely. Suggested measures include induction of emesis if ingestion is recent, and correction of dehydration, electrolyte imbalance, hepatic coma and hypotension by established procedures.

Losartan
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 nor the 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.

How supplied
Losar Plus tablets are supplied in blister pack of 20 tablets (10's X 2 strips).

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 دور رکھیں۔

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

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

QAR No. AW21-0762

Losar - Plus

(Losartan Potassium & Hydrochlorothiazide)

Tablets

لوسار- پلس

(لوسارٹن پوٹاشیم / ہائیڈروکلوروتھیازائڈ)

گولیاں

COMPOSITION:
Each film coated tablet contains:
Losartan Potassium (U.S.P.) ... 50 mg
Hydrochlorothiazide (U.S.P.).... 12.5 mg
Product Complies U.S.P. Specs.

Therapeutic class
Losar Plus (losartan potassium and hydrochlorothiazide) is the combination of an angiotensin II receptor (type AT_1) antagonist and a diuretic.

Indications
Losar Plus is indicated for the treatment of hypertension, for patients in whom combination therapy is appropriate.

Dosage and administration
The usual starting and maintenance dose of **Losar Plus** is one tablet of **Losar Plus** (losartan 50 mg/ hydrochlorothiazide 12.5 mg) once daily. For patients who do not respond adequately to **Losar Plus**, the dosage may be increased to two tablets of **Losar Plus** once daily. The maximum dose is two tablets of **Losar Plus** once daily. In general, the antihypertensive effect is attained within three weeks after initiation of therapy.

Warnings
Losar Plus should not be initiated in patients who are intravascularly volume-depleted (e.g,. those treated with high-dose diuretics).
Losar Plus is not recommended for patients with severe renal impairment (creatinine clearance ≤30mL/min.) or for patients with hepatic impairment.

No initial dosage adjustment is necessary for elderly patients.
Losar Plus may be administered with other antihypertensive agents.
Losar Plus may be administered with or without food.

Contraindications
Losar Plus is contraindicated in:
- Patients who are hypersensitive to any component of this product.
- Patients with anuria.
- Patients who are hypersensitive to other sulfonamide-derivatives.

Hepatic and Renal Impairment
Losar Plus is not recommended for patients with hepatic impairment or severe renal impairment (creatinine clearance ≤30 mL/min).

Losartan
Renal Function Impairment
As a consequence of inhibiting the renin-angiotensin aldoesteron 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 aldoesteron 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; these changes in renal function may be reversible upon discontinuation of therapy.

Hydrochlorothiazide

Hypotension and electrolyte/fluid imbalance

As with all antihypertensive therapy, symptomatic hypotension may occur in some patients. Patients should be observed for clinical signs of fluid or electrolyte imbalance, e.g. volume depletion, hyponatremia, hypochloremic alkalosis, hypomagnesemia or hypokalemia which may occur during inter current diarrhea or vomiting. Periodic determination of serum electrolytes should be performed at appropriate intervals in such patients.

Metabolic and Endocrine Effects

Thiazide therapy may impair glucose tolerance. Dosage adjustment of anti-diabetic agents, including insulin, may be required.

Thiazides may decrease urinary calcium excretion and may cause intermittent and slight elevation of serum calcium. Marked hypercalcemia may be evidence of hidden hyperparathyroidism. Thiazides should be discontinued before carrying out tests for parathyroid function.

Increases in cholesterol and triglyceride levels may be associated with thiazide diuretic therapy.

Thiazide therapy may precipitate hyperuricemia and / or gout in certain patients. Because losartan decreases uric acid, losartan in combination with hydrochlorothiazide attenuates the diuretic-induced hyperuricemia.

Other

In patients receiving thiazides, hypersensitivity reactions may occur with or without a history of allergy or bronchial asthma. Exacerbation or activation of systemic lupus erythematosus has been reported with the use of thiazides.

Pregnancy

When used in pregnancy during the second and third trimesters, drugs that act directly on the renin-angiotensin system can cause injury and even death to the developing fetus. When pregnancy is detected, **Losar Plus** should be discontinued as soon as possible. Although there is no experience with the use of **Losar Plus** in pregnant women, animal studies with losartan potassium have demonstrated fetal and neonatal injury and death, the mechanism of which is believed to be pharmacologically mediated through effects on the renin-angiotensin system. In humans, total renal perfusion, which is dependent upon the development of the renin-angiotensin system, begins in the second trimester; thus, risk to the fetus increases if **Losar Plus** is administered during the second or third trimesters of pregnancy.

Thiazides cross the placental barrier and appear in cord blood. The routine use of diuretics in otherwise healthy pregnant women is not recommended and exposes mother and fetus to unnecessary hazard including fetal or neonatal jaundice, thrombocytopenia and possibly other adverse reactions which have occurred in the adult. Diuretics do not prevent development of toxemia of pregnancy and there is no satisfactory evidence that they are useful in the treatment of toxemia.

Nursing Mothers

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 children have not been established.

Use In The Elderly

In clinical studies, there were no clinically significant differences in the efficacy and safety profiles of Losar Plus in older (≥ 65 years) and younger patients (< 65 years).

Drug Interactions

Losartan

In clinical pharmacokinetic trials, no drug interactions of clinical significance have been identified with hydrochlorothiazide, digoxin, warfarin, cimetidine, Phenobarbital (see Hydrochlorothiazide, Alcohol, barbiturates or narcotics below), ketoconazole and erythromycin. Rifampin and fluconazole have been reported to reduce levels of active metabolite. The clinical consequences of these interactions have not been evaluated.

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.

As with other antihypertensive agents, the antihypertensive effects of losartan may be attenuated by the non-steroidal anti-inflamatory drug indomethacin.

Hydrochlorothiazide

When give concurrently, the following drugs may interact with thiazide diuretics:

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.

Other antihypertensive drugs – additive effect.

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.

Pressor amines (e.g., adrenaline) – possible decreased response to pressor amines but not sufficient to preclude their use.

Skeletal muscle relaxants, nondepolarizing (e.g., tubocurarine) – possible increased responsiveness to the muscle relaxant.

Lithium – Diuretic agents reduce the renal clearance of lithium and add a high risk of lithium toxicity; concomitant use is not recommended. Refer to the package inserts for lithium preparations before use of such preparations.

Non – Steroidal Anti-inflammatory drugs – In some patients, the administration of a non-steroidal anti-inflammatory agent can reduce the diuretic, natriuretic and antihypertensive effects of diuretics.

Drug/Laboratory Test Interactions

Because of their effects on calcium metabolism. Thiazides may interfere with tests for parathyroid function.

Side Effect

In clinical trials with losartan potassium-hydrochlorothiazide, no adverse experiences peculiar to this combination drug have been observed. Adverse experiences have been limited to those that were reported previously with losartan potassium and / or hydrochlorothiazide. The overall incidence of adverse experiences reported with the combination was compareable to placebo. The percentage of discontinuations of therapy was also comparable to placebo.

In general, treatment with losartan potassium-hydrochlorothiazide was well tolerated. For the most part, adverse experiences have been mild and transient in nature and have not required discontinuation of therapy.

In controlled clinical trials for essential hypertension, dizziness was the only adverse experience reported as drug related that occurred with an incidence greater than placebo in one percent or more of patients treated with losartan potassium – hydrochlorothiazide.

The following additional adverse reactions have been reported in post-marketing experience:

Hypersensitivity: Anaphylactic reactions, angioedema including swelling of the larynx and glottis causing airway obstruction and / or swelling of the face, lips, pharynx and / or tongue has been reported rarely in patients treated with losartan; some of these patients previously experienced angioedema with other drugs including ACE inhibitors.

Gastrointestinal: Hepatitis has been reported rarely in patients treated with losartan, diarrhea.

Respiratory: Cough has been reported with losartan.

Laboratory Test Findings

In controlled clinical trials, clinically important changes in standard laboratory parameters